https://doi.org/10.1590/1980-549720220006.supl.1

ORIGINAL ARTICLE / *ARTIGO ORIGINAL*

Socioeconomic development and colorectal cancer mortality in a state of the Brazilian Legal Amazon from 2005 to 2016

Desenvolvimento socioeconômico e mortalidade por câncer colorretal em uma unidade federativa da Amazônia Legal, de 2005 a 2016

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ABSTRACT: ***Objective:*** To analyze the correlation between colorectal cancer (CRC) mortality rates and socioeconomic factors in the five mesoregions (North, Northeast, Southeast, Southwest and Center-South) of the state of Mato Grosso, from 2005 to 2016. ***Methods:*** Ecological study that considered deaths from CRC (C18 to C21) of residents of the state. Mortality rates were standardized by the direct method, using the world standard population. For the analysis of socioeconomic factors, the Firjan Municipal Development Index (IFDM) and its components (education, income and employment and health) were used. Means of mortality rates and socioeconomic factors between the mesoregions were tested using ANOVA, and Pearson's correlation coefficient was used to analyze the correlation between mortality rates due to CRC and these factors. ***Results:*** In the period from 2005 to 2016, 1,492 deaths from CRC were registered in the state of Mato Grosso. The Southwest mesoregion had the highest average for both the crude rate and standardized CRC mortality rates (3.47 and 3.86 deaths/100,000 inhabitants, respectively). There was a significant correlation between mortality rates from the disease with the following indicators: Overall IFDM for the North, Southeast and Center-South mesoregions; education for the North and Southeast mesoregions; income and employment for the North and Center-South mesoregions; and health for the North, Southeast and Center-South mesoregions. ***Conclusion:*** There was a correlation between CRC mortality rates and better socioeconomic development in the state.

Keywords: Mortality; Colorectal neoplasms; Socioeconomic factors; Correlation of data

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Conflict of interests: none to declare – **Financial support:** Mato Grosso State Health Department, funding of the extension project "Surveillance of cancer and its associated factors: update of population- and hospital-based registry" (contract 088/2016); and Ministry of Labor, 23rd Region, funding of the research project "Cancer and its associated factors: analysis of population- and hospital-based registry" (technical cooperation agreement 08/2019).
Associated editors: Elisete Duarte, Gulnar Azevedo e Silva
Scientific editor: Cassia Maria Buchalla
This document has an erratum: https://doi.org/10.1590/1980-549720220006.supl.1erratum

RESUMO: ***Objetivo:*** Analisar a correlação entre as taxas de mortalidade por câncer colorretal (CCR) e os fatores socioeconômicos nas cinco mesorregiões (norte, nordeste, sudeste, sudoeste e centro-sul) do estado de Mato Grosso, de 2005 a 2016. ***Métodos:*** Estudo ecológico que considerou os óbitos por CCR (C18 a C21) de residentes do estado. As taxas de mortalidade foram padronizadas pelo método direto, utilizando-se a população padrão mundial. Para a análise dos fatores socioeconômicos, foram usados o Índice Firjan de Desenvolvimento Municipal Geral (IFDM) e seus componentes (educação; renda e emprego; saúde). Foram testadas as médias das taxas de mortalidade e dos fatores socioeconômicos entre as mesorregiões por meio da análise de variância (ANOVA), e empregou-se o coeficiente de correlação de Pearson para análise da correlação entre as taxas de mortalidade por CCR e esses fatores. ***Resultados:*** No período de 2005 a 2016, foram registrados 1.492 óbitos por CCR no estado de Mato Grosso. A mesorregião com a maior média tanto da taxa bruta quanto da taxa padronizada de mortalidade por CCR foi a sudoeste (3,47 e 3,86 óbitos/100 mil habitantes). Houve correlação significante entre as taxas de mortalidade por CCR com os seguintes indicadores: IFDM geral para as mesorregiões norte, sudeste e centro-sul; educação para as mesorregiões norte e sudeste; renda e emprego para as mesorregiões norte e centro-sul; e saúde para as mesorregiões norte, sudeste e centro-sul. ***Conclusão:*** Houve correlação da taxa de mortalidade de CCR com melhor desenvolvimento socioeconômico no estado.

Palavras-chave: Mortalidade. Neoplasias colorretais. Fatores socioeconômicos. Correlação de dados.

INTRODUCTION

In 2012, worldwide estimates showed colorectal cancer (CRC) as the third most common type of cancer among men, with 746,000 new cases (10% of all cancers), and the second most common among women, with 614,000 new cases (9.2% of all cancers). For mortality, 694,000 cases were estimated in both sexes (8.5% of total deaths), most of them in countries with a low human development index, where the prognosis of the disease is poor[1].

In Brazil, CRC was the third most frequent cancer in men and the second in women[1], and the fourth in mortality in men and third in women, in 2016[2]. In that same year, of the federative units belonging to Brazilian Legal Amazon (Acre, Amapá, Amazonas, Maranhão, Mato Grosso, Pará, Rondônia, Roraima and Tocantins)[3], Mato Grosso stood out as the first in CRC[1] incidence and also in mortality[2].

CRC has its origin, in large part, in benign lesions, more precisely in polyps, which are small raised clumps of cells on the colon and/or rectum wall that grow slowly growth, taking many years to become malignant[4]. Therefore, some developed countries have adopted early polyp screening, resulting in stabilization or decrease in CRC incidence and mortality. However, in developing countries, such as those in Latin America, these rates have increased, since socioeconomic status influences the rate of participation in screening programs[5,6].

Brazil does not yet have organized tracking for CRC. Screening should be directed at patients with a family history of the disease or suspected hereditary syndromes, performed

in a specialized genetics and gastroenterology service, where there is a low offer of colonoscopy; patients with suspected cancer are then prioritized[7].

CRC is associated with several risk factors, including those related to the socioeconomic characteristics of the areas[8]. Mato Grosso is among the 11 states that have a municipal human development index classified as high (0.725)[9] and has a gross domestic product (GDP) of R$ 123.8 billion, occupying the 13th position in the ranking of states with the highest values in 2016[10]. It is also ranked 11th in CRC[1] incidence estimates and 13th in national mortality estimates[2].

Knowing that cancer estimates vary between and across countries[8] and to understand the behavior of CRC in the state, it is necessary to consider that Mato Grosso has an area of 906,806.9 km^2. This state is one of the largest states in the country and is divided into five mesoregions, distinct from each other, especially economically[11], where the Center-South mesoregion stands out, as it encompasses Cuiabá and Várzea Grande, the two most populous municipalities in the state.

Thus, the objective of this study was to analyze the correlation between CRC mortality rates (CRCMRs) and socioeconomic factors in the five mesoregions (North, Northeast, Southeast, Southwest and Center-South) of the state of Mato Grosso, from 2005 to 2016.

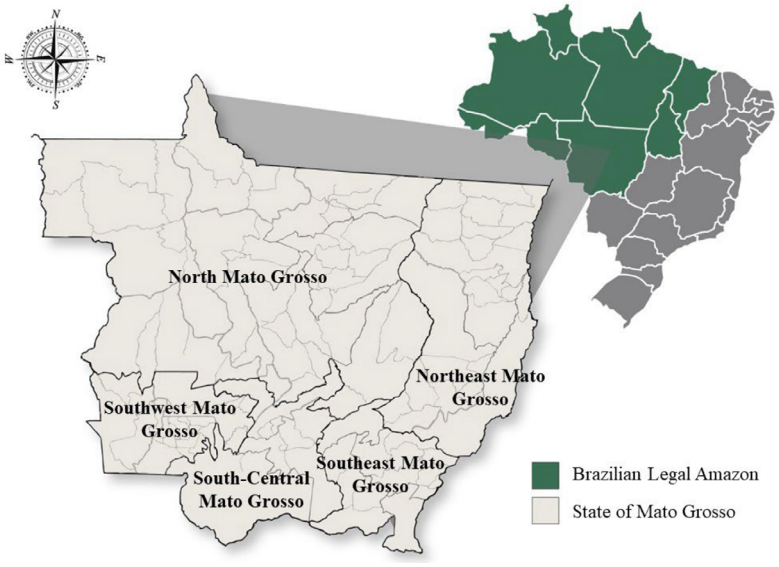
METHODS

We conducted an ecological study of CRCMRs of residents in the mesoregions of Mato Grosso, from 2005 to 2016. The state is the only one in the Central-West region that makes up the Legal Amazon. With an area of 5,015,067.75 km^2, the region occupies almost 60% of the Brazilian territory and was created with the objective of defining the geographic delimitation of the political region that gets tax incentives, with a view to promoting its regional development (Figure 1)[3].

To calculate the CRCMR per year, the ratio between the number of deaths from the disease and the size of the population of interest was considered. Deaths from CRC were considered to be those whose underlying cause belonged to Chapter II of the 10th revision of the International Statistical Classification of Diseases and Related Health Problems (ICD-10)[12], identified by the following codes: C18 (colon cancer), C19 (colon cancer), rectosigmoid junction), C20 (rectal cancer) and C21 (anus and anal canal cancer), according to the José Alencar Gomes da Silva National Cancer Institute (INCA) [1,13].

Data on CRC death were provided by the Mato Grosso State Health Department and are part of the Mortality Information System. Information about the number of inhabitants of the study population was obtained from the Brazilian Institute of Geography and Statistics, from the demographic census for the year 2010, and from population estimates for the other years[14].

Rates were calculated per 100,000 inhabitants and standardized by the direct method, using the world standard population provided by the World Health Organization[15] and



*Comprising the states of Acre, Amapá, Amazonas, Maranhão, Mato Grosso, Pará, Rondônia, Roraima and Tocantins[3].
Figure 1. State of Mato Grosso in the Brazilian Legal Amazon* and its mesoregions.

modified by Doll et al.[16], which is used by the International Agency for Research on Cancer and the INCA.

There are five mesoregions in the state: North (55 municipalities), Northeast (25 municipalities), Southwest (22 municipalities), Center-South (17 municipalities) and Southeast (22 municipalities) [11].

As a socioeconomic variable, the Firjan Municipal Development Index (IFDM) and its components were used. The IFDM is a composite indicator that assesses the level of regional socioeconomic development, using a simple average of the results obtained in each of the three main areas of human development: income and employment, education and health. It is based on official public statistics, made available by the Ministries of Labor, Education and Health. Its values range from 0 to 1, and the closer to 1, the higher the level of development of the municipality[17].

Based on the IFDM result, municipalities can be classified into:

- low stage of development: IFDM between 0 and 0.4;
- regular stage of development: IFDM between >0.4 and 0.6;
- moderate stage of development: IFDM between >0.6 and 0.8;
- high stage of development: IFDM between >0.8 and 1[17].

The overall IFDM and its components were considered separately: education IFDM, income and employment IFDM and health IFDM.

For each municipality, the CRCMR and the values of IFDM and its components were obtained for each year of study. These values were then averaged to obtain the total value

for each municipality. Subsequently, the municipalities were grouped into their corresponding mesoregions, obtaining the average of the indicators for each mesoregion. To describe these indicators by mesoregion, means, standard deviation and minimum and maximum values were calculated.

The means of the overall IFDM and its components, as well as the CRCMR of the mesoregions, were compared using analysis of variance (ANOVA). The assumptions of normality and homogeneity of variances were satisfied using the Shapiro-Wilk test and Levene test, respectively. Subsequently, the post-hoc Bonferroni test was used for multiple comparisons.

To calculate the percent variation of the standardized CRCMR and IFDM and its components by mesoregion, the averages were obtained for two periods: from 2005 to 2010 and from 2011 to 2016.

The correlation between IFDM and its components and the standardized CRCMR was determined using Pearson's correlation coefficient (r), and assumption of normality of the variables was satisfied by the Shapiro-Wilk test. Correlations were considered statistically significant when $p<0.05$. Statistical analyses were performed using the Statistical Package for the Social Sciences (SPSS), version 22.

RESULTS

In the period of 2005 to 2016, 1,492 CRC deaths were recorded in the state of Mato Grosso, 49.1% in the Center-South mesoregion, 20.2% in the North, 17.2% in the Southeast, 8.4% in the Southwest and 5.1% in the Northeast.

The mesoregion with the highest mean for both the crude rate and the standardized CRCMR was the Southwest (3.47 and 3.86 deaths/100,000 inhabitants, respectively), while the Northeast mesoregion was the one with the lowest values for these rates (1.27 and 1.53 deaths/100,000 inhabitants, respectively). There was a significant difference between the crude rates of the Northeast mesoregion and those of the Southeast and Southwest mesoregions and between the standardized rates of the Northeast mesoregion and those of the North and Southwest mesoregions (Table 1).

Regarding socioeconomic indicators, mean overall IFDM ranged from 0.59 (Northeast) to 0.68 (North). The Northeast mesoregion showed a significant difference in overall IFDM compared to the North and Southeast. For education, the values showed the smallest variation between the mesoregions (0.62 for the Northeast and 0.69 for the Southeast), but there was a significant difference for the Northeast mesoregion compared to the North, Southwest and Southeast mesoregions. For the health-related indicator, the variation observed was the highest between the mesoregions (0.59 for the northeast and 0.76 for the north), with a significant difference between the Northeast mesoregion and the other mesoregions. For the income and employment indicator, the values ranged from 0.52 (Center-South) to 0.60 (North), and there was no significant difference between the mesoregions (Table 1).

Table 1. Description of colorectal cancer mortality rates (per 100,000 inhabitants) and the Firjan Municipal Development Index (IFDM) and its components according to mesoregions of Mato Grosso, Brazil, from 2005 to 2016.

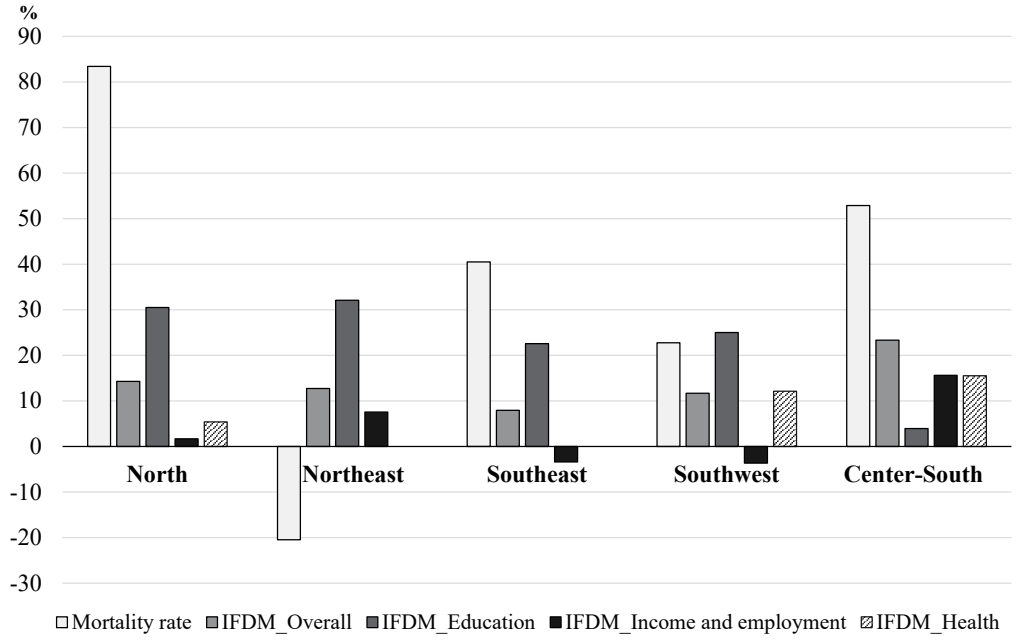
Mesoregion	North		Northeast		Southwest		Center-South		Southeast	
Indicator	Mean (SD)	Min Max	Mean (SD)	Min Max	Mean (SD)	Min Max	Mean (SD)	Min Max	Mean (SD)	Min Max
Crude rate	2.3 (1.58)	0 6.26	1.27[a,b] (1.48)	0 4.60	3.47[a] (2.15)	0.76 11.31	2.81 (1.83)	0 7.15	2.95[b] (2.06)	0 7.14
Standardized rate	3.24[a] (2.36)	0 8.52	1.53[a,b] (1.63)	0 4.91	3.86[b] (1.89)	0.74 8.90	2.84 (2.21)	0 8.28	2.91 (2.21)	0 7.44
IFDM overall	0.68[a] (0.07)	0.47 0.86	0.59[a,b] (0.08)	0.42 0.73	0.64 (0.05)	0.52 0.73	0.63 (0.07)	0.52 0.78	0.66[b] (0.09)	0.49 0.80
IFDM education	0.68[a] (0.06)	0.50 0.83	0.62[a,b,c] (0.08)	0.46 0.79	0.67[b] (0.05)	0.54 0.75	0.67 (0.05)	0.58 0.78	0.69[c] (0.06)	0.55 0.79
IFDM income and employment	0.60 (0.11)	0.43 0.85	0.55 (0.08)	0.43 0.70	0.54 (0.10)	0.39 0.77	0.52 (0.11)	0.40 0.80	0.58 (0.11)	0.41 0.81
IFDM health	0.76[a] (0.08)	0.50 0.92	0.59[a,b,c,d] (0.11)	0.36 0.79	0.70[b] (0.07)	0.55 0.85	0.69[c] (0.09)	0.48 0.84	0.70[d] (0.13)	0.34 0.89

SD: standard deviation; Min: minimum value; Max: maximum value; [a,b,c,d]same letters indicate the mesoregions that showed a difference between their values with $p<0.05$ (*post hoc* Bonferroni test).

Figure 2 shows the percent change in the standardized CRCMR and the overall Firjan index and its components by mesoregion. For mortality rates, the Northeast mesoregion showed a decrease of 20.5%. However, all the others showed an increase from one period to the other, and the mesoregion with the greatest change was the North, with an increase of 83.4 %.

All mesoregions showed an increase in overall IFDM, ranging from 7.9 (Southeast) to 23.3% (Center-South). The education indicator was the one that showed the highest percent increase, especially for the Northeast (32.1%) and North (30.5%) mesoregions. With regard to income and employment IFDM, two mesoregions showed a decrease in this indicator: the Southwest (3.6%) and Southeast (3.4%), and this was the only indicator to show a negative change. On the other hand, the Center-South mesoregion was the one with the highest percent increase, 15.6%. Considering the health indicator, two mesoregions showed stable values (0% change), Northeast and Southeast, while the Center-South region had the highest percent increase (15.5%) (Figure 2).

For overall IFDM, the northeast mesoregion was the only one to have some of its municipalities with a low level of development (4% of its municipalities), while the North mesoregion was the only one to have municipalities with a high level of development (1.8%).



IFDM: Firjan Municipal Development Index.

Figure 2. Percentage variation in colorectal cancer mortality rate and socioeconomic indicators in the mesoregions of the state of Mato Grosso, Brazil, comparing the periods of 2005 to 2010 and 2011 to 2016.

The most frequent level for this indicator was regular. For education, the municipalities of all the mesoregions exhibited a regular or moderate level of development, and the most frequent was moderate, with the exception of the Northeast mesoregion, where most of its municipalities had a regular level (64%) (Figure 3).

Considering income and employment, this was the component with the highest percentage of low development level — all mesoregions had at least 7.3% of their municipalities showing this. Only the northern region had a high level (1.8% of its municipalities), but for all the mesoregions the most frequent level was regular. Finally, the health indicator had the highest percentages for the high level: 18.2% for the Southeast mesoregion and 16.4% for the North. On the other hand, the Northeast mesoregion showed 8% of its municipalities at the low level, and the Southeast with 4.5%. For this indicator, besides the Northeast mesoregion, all others had most of their municipalities classified as having a moderate level of development (Figure 3).

Table 2 shows the results of correlations between standardized CRCMR and socioeconomic indicators. The North mesoregion showed a positive and statistically significant correlation for all these indicators, while the Southeast showed a correlation for overall IFDM and education and health IFDM and the Center-South for overall IFDM and health and

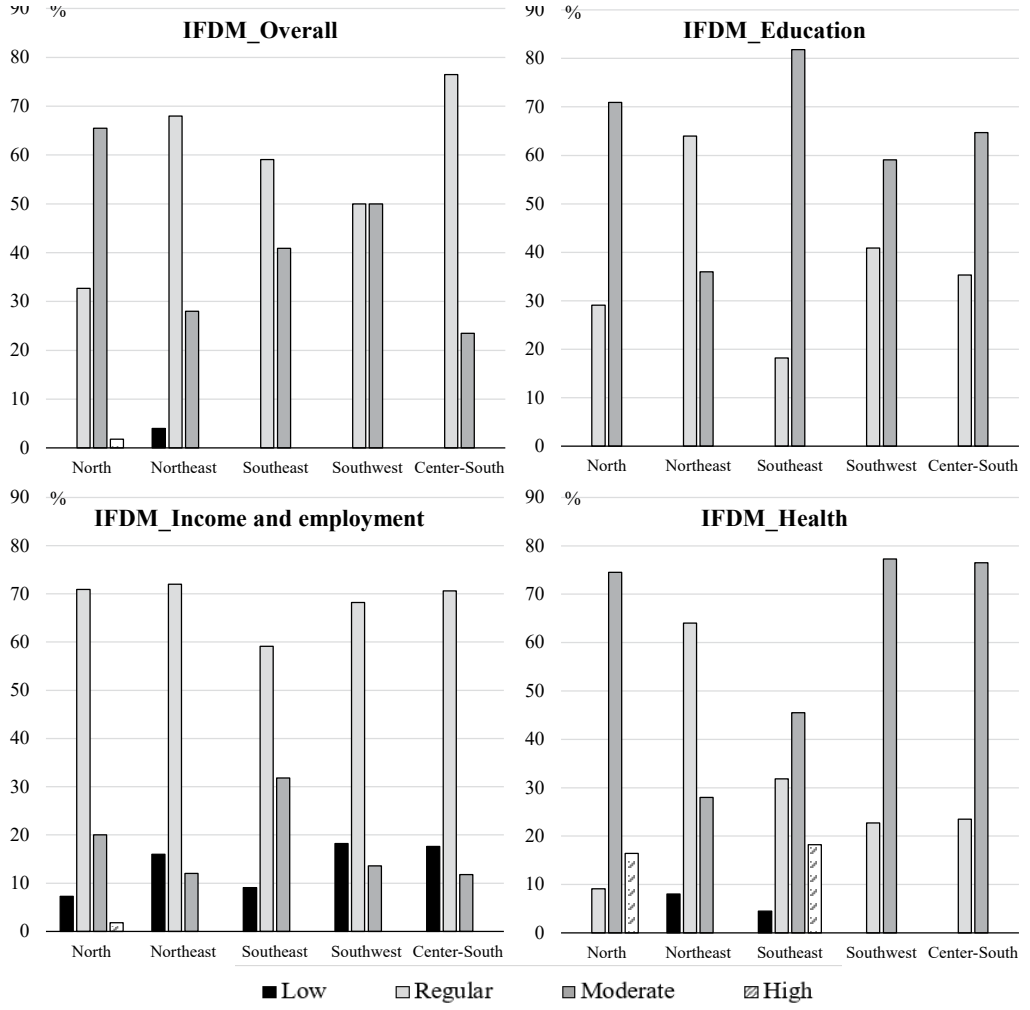


Figure 3. Firjan Municipal Development Index (IFDM) and its components, according to the mesoregions of Mato Grosso, Brazil, from 2005 to 2016.

Table 2. Correlation between adjusted mortality rates and socioeconomic indicators according to mesoregions of Mato Grosso, Brazil, from 2005 to 2016.

Mesoregion	Indicator			
	IFDM overall	IFDM education	IFDM income and employment	IFDM health
North	0.14*	0.13*	0.08*	0.12*
Northeast	0.07	0.08	0.00	0.08
Southeast	0.20*	0.14*	0.11	0.19*
Southwest	0.01	0.01	0.10	0.02
Center-South	0.25*	0.04	0.19*	0.32*

IFDM: Firjan Municipal Development Index; *p<0.05.

income and employment IFDMs. There was no significant correlation for the Northeast and Southwest mesoregions (Table 2).

DISCUSSION

The results of this study showed that there was an increase in mortality rates in the period from 2005 to 2016 for four of the five mesoregions and an improvement in socioeconomic indicators, with the exception of the values for the income and employment indicator for the Southeast and Southwest mesoregions. In general, the mesoregions displayed more discrepant values between themselves for the health indicator and more similar values for the education indicator. For overall IFDM and education and health indicator, most municipalities had a moderate level of development, and for the income and employment indicator, a regular level. This was also the indicator for which the mesoregions showed the worst levels of development, while education demonstrated the best ratings. The North, Southeast and Center-South mesoregions showed a positive and statistically significant correlation with socioeconomic indicators.

The Northeast mesoregion had the lowest mortality rates, as well as a reduction in the standardized rate, and despite exhibiting an increase in values for overall, education and income and employment IFDMs, its values were the lowest for overall and education and health IFDMs. It was also the one that had the worst ratings for these indicators; however, its rates did not show a correlation with the socioeconomic indicators.

This result is in opposition to what has been found in the literature, in which low socioeconomic development and low levels of schooling and literacy have been associated with an increased risk of developing CRC[18].

The Northeast mesoregion does not have a high-complexity care unit (UNACOM)[19], and lower established medical capacity, together with lower human development, is associated with worse treatment results, having an impact on deaths[20]. The low rates shown by this mesoregion compared to other wealthier ones, may be a consequence of the underreporting of cases.

The North mesoregion, even with the highest means for overall and health IFDMs, showed an increase in socioeconomic indicators and better ratings for overall, health and income and employment IFDMs. It also had the second highest standardized rate of the disease, the highest increase between the periods analyzed, in addition to being the only one to show a positive and significant correlation between standardized rates and all socioeconomic indicators.

This mesoregion is the wealthiest compared to the others and had five municipalities (Campos de Júlio, Santa Rita do Trivelato, Nova Ubiratã, Sapezal and Diamantino) that were among the 50 with the highest GDP per capita in the country in 2016[21]. In addition, six of the top ten municipalities that make up the state's overall IFDM ranking are from this region[22].

In 2013, the National Policy for Cancer Prevention and Control was instituted in the Health Care Network for People with Chronic Diseases within the scope of the Unified Health System (SUS), in which cancer care should be given in a regionalized and decentralized way, expanding the spectrum of access[23]. The North mesoregion, even containing a single UNACOM and also suffering from the effects of the established policy, does not explain an 83.4% increase in mortality rates, suggesting that there may be other factors contributing to this increase in addition to those evaluated here, such as the use of and exposure to pesticides, since most of its municipalities have an economy based on agribusiness[19,21].

The Center-South mesoregion had the highest crude rate and also increased the standardized rate and all socioeconomic indicators, especially health-related. In addition, the correlation was positive and significant between its standardized rate and the overall, income and employment and health IFDMs. It should be added that the Center-South mesoregion, in addition to being the most populous, also has a high GDP[24]. Considering that this mesoregion has three UNACOM[19], which allows for more options for accessing the oncology service, lower CRC mortality would be expected.

The Southeast mesoregion also showed an increase in mortality rates and in overall and education IFDM indicators, but a reduction in income and employment IFDM. It also showed a significant correlation between their rates and overall, education and health IFDMs.

Finally, the southwest mesoregion had the highest standardized CRCMR, and despite having shown a reduction in values for income and employment, it showed an increase for the standardized rates and for overall, education and health IFDM indicators. It also had the second-best ranking of the level of development of its municipalities, but there was no correlation between its mortality rates and socioeconomic indicators. Most municipalities in this mesoregion do not have a Support Center for the Family Health Team or UNACOM, although the mesoregion provides some cancer care services, such as imaging, cytopathological, blood and biopsy examinations[19].

It appears from the results of the mesoregions that better socioeconomic development would be associated with higher CRC mortality rates in these mesoregions. In the case of the North, Center-South and Southeast regions, this may suggest a deficit in the distribution of their wealth, resulting in social inequality, since the socioeconomic group to which the individual belongs influences the early detection of CRC, the rate of lesions found and, consequently, their mortality[5,20]. In addition, the mesoregion has an extensive area, which can make access to health services difficult, delaying early diagnosis and treatment.

A study by Ribeiro and Nardocci[25] that investigated associations between socioeconomic status and incidence and mortality from cancer and its types, through a review of 32 ecological studies, found a positive and consistent association of the socioeconomic level of the living area with CRC mortality for both men and women. The authors argue that factors such as high consumption of red meat and fats, low consumption of fruits and vegetables, physical inactivity, obesity and alcohol consumption have been identified as the main risk

factors for this cancer and that the differential and dynamic prevalence of these factors by classes could explain, in part, these gradients.

Data from the National Health Survey showed that the prevalence of overweight in the population of Mato Grosso, for example, was 59.8% and that of obesity was 24.4%, being the fifth state to have the highest prevalence of some degree of overweight[26].

A similar result was found in the study by Guimarães et al.[27], who estimated the correlation between the average per capita income and the CRCMR in Brazil between 2001 and 2009. There was a reduction in the trend of poverty and inequality in income and growth of GDP per capita, family income and standardized CRCMR in Brazil. According to the authors, the increase in income and the reduction in inequality may explain, in part, the increase in the occurrence of CRC, possibly due to the differentiated access to foods recognized as risk factors for the occurrence of the disease, such as red meat with high fat content, and therefore, it is important to assess the priorities of public health programs focused on nutrition in countries with intermediate economies, such as Brazil.

Brazil has experienced, in recent decades, remarkable and complex socioeconomic transformations, but they have not occurred uniformly in the country, not even in the states themselves and in their mesoregions. One of the possible explanations for the increase in the incidence of CRC, and the consequent increase in mortality from the disease, especially in places that showed greater reductions in socioeconomic inequality, are the different demographic, epidemiological and nutritional stages in which these regions are found[28].

The indicator used here, IFDM, is a reference for monitoring Brazilian socioeconomic development, with a methodology that makes it possible to determine whether the relative improvement that occurred in a given municipality was due to the adoption of public policies, or if the result obtained was just a reflection of the decline of the other municipalities. Its results, over the years, have shown that the last decade was marked by the development of the Central-West region, which more than doubled its participation among the 500 most developed municipalities in the country[17].

The findings of this study must be analyzed with caution, considering that they were generated on the basis of secondary data, which present problems related to the coverage and quality of the recorded data. However, it should be noted that mortality data in Brazil are those that show the greatest increase in coverage in recent years, having one of the highest coverages of the information systems today[29].

Ecological studies can, in particular, assess how the social and environmental contexts affect the health of population groups, whose measurements collected at the individual level are unable to adequately reflect the processes that occur at the collective level[30].

The present study contributed to our understanding of the distribution of CRC mortality in the mesoregions of the state of Mato Grosso, as well as to identifying the positive correlation of the disease with indicators related to socioeconomic development. In etiological investigations, approaches with an individual focus or with aggregated data should be complementary, to make it possible to highlight the different aspects of the health-disease process, contributing to a better understanding of the multiple factors that modify the

cancer distribution profile among the different socioeconomic strata, supporting public policies aimed at fighting the disease.

ACKNOWLEDGMENTS

To Coordination for the Improvement of Higher Education Personnel (CAPES) for the post-graduation scholarships (master's and doctoral); to the José Alencar Gomes da Silva National Cancer Institute (INCA) for its contribution to the training of cancer registrars; and to the Institute of Collective Health of the Federal University of Mato Grosso for the facilities.

CEP APPROVAL

Research Ethics Committee of Júlio Müller University Hospital (CEP-HUJM) (Approval No. 3.048.183, 11/20/2018); Research Ethics Committee of the Mato Grosso State Health Department (CEP-SES-MT) (Approval No. 3.263.744, 12/04/2019).

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Received on: 08/20/2021
Revised on: 10/24/2021
Accepted on: 12/03/2021
Preprint: 04/25/2022
https://preprints.scielo.org/index.php/scielo/preprint/view/3981
Corrected on: 09/13/2024

Authors' contributions: Caló, R.S.: formal analysis, conceptualization, data curation, writing - first draft and revision and editing, research, methods, software, validation and visualization. Souza, R.A.G.: formal analysis, conceptualization, data curation, writing - first draft and revision and editing, investigation, methods, software, supervision, validation and visualization. Alves, M.R.: writing - revision and editing. Carvalho, A.E.: writing - revision and edition. Galvão, N.D.: project management, writing - revision and editing and obtaining funding and resources.