ABSTRACT: Objective: To analyze the trend of colorectal cancer mortality adjusted for selected indicators, according to sex, by Brazilian federative units and regions, and countrywide from 1996 to 2012. Methods: This is a temporal time series on colorectal cancer mortality rates, using linear regression analysis, in which the independent variable was the centered year. Models were adjusted for selected indicators. Results: There was an increase in standardized colorectal cancer mortality rates for males in all states and for females in 21 states. In the model adjusted for mortality rate from ill-defined causes, for gross domestic product, and for Gini coefficient, the upward trend remained statistically significant (p < 0.05) countrywide only for men, with 0.17 deaths per 100 thousand inhabitants per year (py). In the States of Piauí (0.09 and 0.20 py), Ceará (0.17 and 0.19 py) and Rio Grande do Sul (0.61 and 0.42 py), there was an increase for both men and women, respectively; only among men in the States of Paraíba (0.16 py), Espírito Santo (0.28 py), São Paulo (0.24 py) and Goiás (0.31 py); and among women in Roraima (0.41 py), Amapá (0.97 P/Y), Maranhão (0.10 py), Sergipe (0.46 P/Y), Mato Grosso do Sul (0.47 py), and the Federal District (0.69 py). Conclusion: The increase in colorectal cancer mortality remained significant when assessing Brazil as a whole only among men; in seven States among men, and in nine States among women, regardless of the studied indicators. These differences could be related to the possible increase in incidence and to late access to diagnosis and treatment. Keywords: Colorectal neoplasms. Mortality. Mortality registries. Temporal distribution. Social inequity. Trends.
INTRODUCTION

In 2012, the standardized incidence rate of colorectal cancer was 17.2 per 100,000 inhabitants worldwide with an increasing trend, especially in high-income countries and urban areas of low and middle-income countries. The standardized mortality rate was 8.3 per 100,000 inhabitants. When locations were considered, it was ranked fifth and fourth in incidence and mortality relevance, respectively, the highest rates being found among males.

In addition to differences between countries, there were variations between rates within each country. In the United States, disparities between population groups were described, with colorectal cancer incidence 23% higher among black men and 22% higher among black women compared to white men and women, respectively. Jemal et al. reported disparities in mortality when rates in southern States of the United States. Such differences were attributed to racial-ethnic, socioeconomic and geographical inequalities which reflected in access to health services for timely diagnosis and treatment. In China, trends for cancer mortality identified in urban and rural areas were distinct.

Geographical differences in rates may be related to socioeconomic features. As for incidence, there is an association with unhealthy dietary habits, obesity, smoking, among others. Concerning to mortality, it seems to stem from inequality in access to health services, making early diagnosis and timely treatment difficult. Given that in Brazil there is evidence of such disparities between States, our purpose was to analyze colorectal cancer...
mortality trends adjusted for selected indicators, according to gender, as well as for Brazilian federative units and regions, and countrywide from 1996 to 2012.

**METHODS**

This is an ecological study, whose units of analysis were federation units and regions of Brazil and the country as a whole, from 1996 to 2012, having the rates of mortality by colorectal cancer analyzed (malignant neoplasm of the colon – C18, rectosigmoid junction – C19, and rectum – C20, as per the tenth revision of the International Classification of Diseases – ICD-10)

Data were obtained from the Mortality Information System (SIM), which is publicly available on the website of the Department of Informatics of the National Health System (DATASUS), Ministry of Health, in aggregated form, without personal identification or any prejudice to individuals, in line with the National Health Council’s Resolution 466, as of December 12, 2012.

The proportional colorectal cancer mortality was calculated by dividing deaths by colorectal cancer by the total number of other cancer deaths (Chapter II of ICD-10), so as to verify ranking changes of this type compared to all cancers.

Crude and age-standardized colorectal cancer mortality rates were calculated per 100,000 inhabitants, according to region of residence, sex, for Brazil’s federation units and regions, and the country as a whole. The populations available in DATASUS were used as denominator. For standardization means, the world population proposed by Segi, and revised by Doll and Smith, was used. The standardized mortality rates were compared considering the percentage difference between 2012 and 1996.

In trend analysis, the standardized colorectal cancer mortality rate was considered a dependent variable, and the centered year (year-2004) was the independent variable. The choice of polynomial function stemmed from the scatter plots between mortality rates and the years of study. In order to check for perfect colinearity (correlation coefficient > 0.95), a correlation matrix was built. After regression analysis, the residue analysis was performed to verify the homoscedasticity assumption.

The simple linear regression model was defined as model 1 \( (Y = \beta_0 + \beta_1X_1) \).

The models were adjusted for ill-defined mortality rate (model 2), socioeconomic indicators, gross domestic product (GDP) per capita and Gini coefficient (model 3), and all three indicators (model 4).

Ill-defined mortality rates (codes R00-R99, according to ICD-10) were calculated per 100,000 inhabitants, the denominator being the population of July 1 of each year. GDP per capita indicates the average aggregate value per individual, at market currencies and value, relating to final goods and services produced. The Gini coefficient expresses the inequalities in per capita income distribution among individuals. The index varies from 0, when there is no inequality, to 1, maximum value of inequality. These data were all extracted from DATASUS.
A trend was considered significant when the model had p value < 0.050. Thematic maps were plotted for a full view of results and, to represent the description of the indicators, quintiles of average mortality rates and means of the period (2004) for socioeconomic indicators were used. The trends were adjusted for models. The analyses were performed using Microsoft Excel (version 10), Tabwin and Stata11 software.

RESULTS

In Brazil, in 1996 and 2012, there were 2,801 and 6,878 deaths by colorectal cancer among men, respectively (Table 1). This cancer accounted for 5.1% (1996) and 6.9% (2012) of all deaths by cancer in the country, ranking fifth and fourth in respective years. The standardized rates were 4.9 (1996) and 7.3 (2012) per 100,000 men all over Brazil, with the highest standardized rates observed in the States of Southeast, South and Midwest regions. However, the highest percentage increases were observed in the States of the North and Northeast regions over the 16-year period of study. Among men, standardized rates increased between 1996 and 2012 in all States, except Roraima.

Among women (Table 1), there were 3,272 (1996) and 7,386 (2012) deaths by colorectal cancer, representing 6.9% (1996) and 8.2% (2012) of all cancer deaths in 1996 and 2012, respectively. This cause ranked fifth and third in respective years, gaining two positions in the period. Southeast, South and Midwest regions also had the highest standardized rates. All States had increase in rates, except Roraima and Amapá, with the highest variations observed in North and Northeast States.

Figure 1 shows the geographic distribution of standardized mortality rates for colorectal cancer, ill-defined mortality rates, and socioeconomic indicators in 2004. For both sexes, the highest standardized mortality rates (fifth quintile) were found in States of the South and Southeast regions; and the highest (fourth and fifth quartile) average ill-defined mortality rates (per 100,000 inhabitants) were identified in northern and northeastern States. These regions also had the lowest quintiles of GDP per capita, as well as Gini coefficient highest quintiles (greater inequality).

Figure 2 displays the trend analysis results. In model 1, for males, a significant increase (p<0.05) in the standardized mortality rate was observed in all States, as well as regions and countrywide, with 0.14 deaths per 100,000 inhabitants per year (py). The most relevant increases in mortality rate occurred in Mato Grosso do Sul (0.28 py), Espírito Santo (0.21 py), Ceará (0.21 py), Tocantins (0.20 py) and Piauí (0.20 py). As for the regions, the greatest increase was found in the Midwest region (0.19 py). Among females, the increase was statistically significant (p<0.05) in 21 States. The highest were found in Espírito Santo (0.20 py), Tocantins (0.18 py), the Federal District (0.18 py) and Goiás (0.17 py). In Brazil as a whole, the increase was 0.07 py.

In model 2, when adjusted for ill-defined mortality rate among males, the upward trend was maintained (p<0.05) countrywide (0.11 py) and in 20 States. For women, the trend was
Table 1. Number, proportional mortality and station, crude and standardized colorectal cancer mortality ratios, and comparison per 100,000 inhabitants according to gender. Brazilian federative units and regions, and countrywide, 1996 to 2012.

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<tr>
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<td>2.2</td>
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<td>8.2 (3)</td>
<td>7.5</td>
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N: number; PM: proportional mortality; P: ranking position; CMR: crude mortality rate; SMR: standardized mortality ratio; C: comparison.
Mean standardized colorectal cancer mortality rate (per 100,000 inhabitants) according to gender

A. Ill-defined mortality rate (per 100,000 inhabitants)

B. Gross domestic product per capita and Gini coefficient, 2004

AMR: average mortality rate; IDMR: ill-defined mortality rate; GDP: gross domestic product per capita.

Figure 1. Distribution of indicators by quintiles. Brazilian federative units.
Colorectal cancer mortality trend

**Model 1**
- Male
- Female

**Model 2**
- Male
- Female

**Model 3**
- Male
- Female

**Model 4**
- Male
- Female

**Trend**
- Upward
- Stable

**p < 0.05**

Model 1: centered year; model 2: centered year adjusted for ill-defined cause (rate per 100,000 inhabitants); model 3: centered year adjusted for gross domestic product per capita and Gini coefficient; model 4: centered year adjusted for all three indicators.

**Figure 2.** Colorectal cancer mortality trend according to gender. Brazilian federative units, 1996 a 2012.
stable across all Brazil and ascendant in 10 States, with highest values in Tocantins (0.20 py), Mato Grosso (0.17 py) and the Federal District (0.18 py).

When adjusted for two socioeconomic indicators (model 3) among males, the upward trend remained significant in 10 States and not significant countrywide; among females, 14 States maintained a significant increase (p<0.05), the highest value being found in Amapá (0.78 py), the Federal District (0.63 py), Sergipe (0.51 py) and Mato Grosso (0.48 py), with a significant increase (p<0.05) in Midwest (0.41 py), South (0.32 py) and Northeast (0.11 py) regions, as well as in Brazil as a whole (0.14 py).

In model 4, adjusted for three indicators, the upward trend remained significant in the States of Piauí (0.09 and 0.20 py), Ceará (0.17 and 0.19 py) and Rio Grande do Sul (0.61 and 0.04 py) for males and females, respectively; among males, the increase was identified countrywide and in the States of Paraíba (0.16 py), Espírito Santo (0.28 py), São Paulo (0.24 aa) and Goiás (0.31 py); as for women, significant States were Roraima (0.41 py), Amapá (0.97 aa), Maranhão (0.10 py), Sergipe (0.46 py), Mato Grosso do Sul (0.47 py) and the Federal District (0.69 py); in Brazil as a whole, there was no significant increase.

**DISCUSSION**

Colorectal cancer has lifestyle-related risk factors, including inadequate diet, sedentarism, smoking, and alcohol consumption; and these are habits that vary according to socioeconomic conditions. Brazil has noticeable differences in the prevalence of risk factors and socioeconomic conditions according to regions. The highest incidence of risk factors was found in southern and southeastern States, and the lowest in Northern and Northeastern States. On the other hand, States of the South, Southeast and Midwest regions have better socioeconomic conditions, including schooling rate, *per capita* household income, and best offer of health services compared to States in the North and Northeast regions.

According to estimates by the Globocan 2012, standardized mortality rates in South America are at intermediate levels (9.4 per 100,000 men and 7.7 per 100,000 women), that is, higher than those found in Brazil (7.3 per 100,000 men and 6.2 per 100,000 women). Only the States of Rio de Janeiro, São Paulo, Rio Grande do Sul and the Federal District for both men and women, and Santa Catarina only as related to men, presented rates that were higher than that of South America.

Although this type of cancer has one of the highest mortality rates among all cancer types, there are different trends in colorectal cancer mortality rates across the world. While countries in South America show an upward trend, some European-Union countries have shown a downward trend. Possible explanations for the decrease in rates are the greater offer of exams for early diagnosis, the endoscopic resection of adenomatous polyps, and the improvement in cancer treatment techniques.
In this study, the standardized colorectal cancer mortality rates were found to have increased in all States among males and, for the most part, among females, as seen in model 1 (first stage). However, when the model was adjusted for ill-defined mortality rate, the upward trend was maintained in 20 States among males and in 10 States among females, which shows the influence of quality of information in trend analysis. Using the indicator ill-defined mortality rate as a proxy for quality of the SIM was important, as correction techniques help acquiring knowledge about an event’s actual trend, because increase can be identified simply by improving data collection.

When using correction techniques for the distribution of ill-defined and underreported death causes in the group of the main noncommunicable diseases (NCD) — cardiovascular diseases, neoplasms, chronic respiratory diseases, and diabetes — for the period comprising 1991 through 2009, a study reported an inversion in upward trends of mortality by NCD in North and Northeast regions. In a study that applied the same correction techniques in 2011, aiming to correct proportional mortality between NCD, a 6.3% increase in proportion of mortality attributed to neoplasms was estimated, with corrected-data proportion being 30.4% and crude, 28.6%.

Underreporting, especially in the North and Northeast regions, may have interfered in rate calculation, since the higher the ill-defined mortality rate, the lower the specific-causes mortality rates. Despite the improvement in data collection and data quality over the decades, especially with the use of active search in the regions in question, so as to correct estimates of vital statistics, there is still a limitation regarding the use of data corrected by under-registration, since DATASUS only provides data gathered per chapter of ICD-10. The improvement in vital statistics — in this case, colorectal cancer mortality — is essential because it allows generating information that supports the formulation of public policies in areas demanding greater investments.

In the second step, models were adjusted by two socioeconomic indicators (GDP per capita and Gini coefficient) so as to control the effects of improvement in social conditions over the years. Comparing model 1 (centered year) and the model adjusted by social indicators, in some States the upward trend remained statistically significant, occurring in both states with higher GDP per capita and states that still show income inequality, especially Northeastern ones. These results show that there may be factors interfering with mortality other than those studied here.

The increase in incidence would be likely explained the rise in mortality; however, this cannot be ascertained, as there are no data on incidence of cancer across all Brazil. Currently, cancer incidence is estimated based on data from SIM and Population-Based Cancer Registries across the country. These records cover data from different periods, though.

Brazil, in the last decades, experienced major socioeconomic changes, but they did not occur evenly throughout the territory. States are at different stages in demographic, epidemiological and nutritional transition, and this is one of the possible explanations for the increase in incidence and, consequently, the growth in colorectal cancer mortality, especially
in the States showing the greatest reduction in socioeconomic inequality such as those in the North and Northeast regions.

The increased incidence of colorectal cancer is related to eating habits such as increased intake of meat, fat and total calories. This change in population’s diet is especially seen in more developed regions, due to the higher consumption of ultraprocessed foods that comes with the increase in income of the underprivileged populations. Other behaviors such as smoking and sedentarism also increase the risk of developing this cancer. Studies indicate that these habits are directly associated with economic development, which ends up leading people to a western-like lifestyle.

Finally, when adjusting the model for all indicators studied (last step), the upward trend remained significant in Brazil as a whole and in seven States among men; in nine States, but not all over Brazil, among women. The differences in mortality rates and upward mortality trends found in this study could also be related to the unequal distribution of specialized cancer services. In a study dealing with colorectal cancer mortality in European countries, unequal access to health services was pointed out as one of the main explanations for an upward mortality trend. In Brazil, as in Latin America, service offering is still unequal, because the infrastructure for cancer prevention, diagnosis and treatment tends to concentrate in more developed areas.

In addition to the matter of service offering organization, when it comes to prevention and early diagnosis, unlike in the United States, Brazil lacks a consensus as to the implementation of screening programs aimed at these types of cancer. However, there is evidence that this practice reduces both incidence and mortality. The Brazilian Society of Coloproctology and the National Cancer Institute recommend that screening be started at age 50 in low-risk individuals, through fecal occult blood screening (yearly) and sigmoidoscopy every five years. From the age of 60 on, colonoscopy or barium enema is indicated every ten years. There is no data for Brazil regarding the prevalence of exams in the target population. The few local studies available indicate a low prevalence (<20%) Data about the proportion of cases diagnosed according to staging are also unknown.

Brazilian initiatives such as the CNCD Coping Plan, the Plan to Strengthen the Network for Cancer Prevention, Diagnosis and Treatment and the Radiotherapy Expansion Plan, which provides for the creation of a radiotherapy service and the expansion of existing services, are efforts that seek to organize the network aimed at prevention, detection, timely treatment and consequent increase in survival rates for cancer patients across the country. This subject is currently in vogue and poses a challenge, as the law that guarantees initiation of cancer treatment in up to 60 days after diagnosis must be obeyed.

**CONCLUSION**

In this study, the increase in rate of mortality from colorectal cancer remained significant in Brazil as a whole only among men; in seven States, among men; and in nine
States, among women, regardless of the indicators studied. Differences according to gender may stem from both changes in risk factors and late access to health services for diagnosis and treatment.

The differences in colorectal cancer mortality rates and the temporal evolution according to States and regions may reflect socioeconomic inequalities, which are directly related to risk factors for this type of cancer and to access to health services.

Colorectal cancer usually has favorable prognosis when diagnosed timely\(^8,9\). The implantation of the CNCD Coping Plan\(^4\), the Plan to Strengthen the Network for Cancer Prevention, Diagnosis and Treatment\(^5\) and the Radiotherapy Expansion Plan\(^6\), in addition to the law that guarantees the initiation of cancer treatment up to 60 days after diagnosis\(^7\), the consequent reorganization and better distribution of health services may contribute to a decrease in colorectal cancer mortality rates.

REFERENCES


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