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Reported mortality for colorectal cancer in Brazil in the first 16 years of the 21st century

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ABSTRACT

Introduction: Colorectal cancer (CRC) is a malignant neoplasm with major impact on health today. There is, however, an efficient method for prevention and screening, which varies in different protocols according to each institution or country. The objective is to evaluate the mortality rate and the economic cost of CRC in Brazil during the first 16 years of the 21st century.

Method: A retrospective, temporal aggregation study was conducted with an exploratory, documentary quantitative approach on CRC mortality from 2000 to 2016, based on the Mortality Information System database provided by the Brazilian Ministry of Health.

Results: In the study period, 218,000 deaths due to CRC were recorded. The CRC mortality rate was 6.2 (95% confidence interval, 5.59-6.81) per 100,000 population, with no significant difference between men and women. Of the 17 age subgroups analyzed, eight had a significant increase from 2000 to 2016, including all subgroups aged over 50 years.

Conclusion: There was an increase in mortality due to CRC in the study period.

Keywords: *Mortality; colorectal cancer; Brazil*

The epidemiology of colorectal cancer (CRC) varies considerably according to each region, but worldwide it is the second leading cause of death in women and the third in men[1-3]. In Brazil, according to the National Cancer Institute (Inca), CRC mortality follows the same global trend when compared to other neoplasms, and 2018 estimates indicate that women are more frequently affected than men (18,980 × 17,380 cases, respectively)[4].

CRC screening methods are widely consolidated as preventive measures that have a significant impact on mortality, reducing it by up to 30%[5]. The gold standard for CRC screening is colonoscopy, which allows visualizing the entire large bowel, inspecting it with biopsy and performing polypectomy of adenomatous polyps[6-8]. However, there are other methods available such as high sensitivity fecal occult blood test that, if positive, require colonoscopy[9].

Screening methods are aimed at detecting and removing precursor lesions of CRC at an early stage, before clinical presentation[3,10]. Significant impacts on CRC mortality have been observed with screening tests, especially serial colonoscopy every 10 years starting at age 55 years[9].

Currently, in Brazil, there is a recommendation to begin population screening at age 50 years. There are different methods available, and colonoscopy is preferred because of its greater sensitivity and specificity[11-13].

An epidemiological analysis of CRC in the United States has shown gradual declines in incidence and mortality for decades, but with significant reduction in the mid-2000s, especially for the adult population aged over 65 years. Changes in lifestyle were related to a 50% drop in incidence and to an over 30% drop in mortality, but the use of more effective screening and

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treatment practices also contributed to significant reductions after the 2000s[14-17].

However, according to the American Cancer Society (ACS), there was a 11% increase in mortality between 2005 and 2015 for adults aged under 55 years. Based on these data, ACS updated its guideline in 2018, modifying the age to begin screening from 50 to 45 years for CRC intermediate risk groups[9].

Due to changes in CRC occurrence and mortality patterns in several countries, analyzing variations in CRC mortality over the years in Brazil is fundamental, as well as investigating geographical differences in mortality given the vastness of the Brazilian territory and important cultural, behavioral and economic differences across Brazilian regions. Another objective of the study is to evaluate the economic cost of CRC in the public health system.

METHOD

A retrospective, temporal aggregation study was conducted with an exploratory, quantitative documentary approach. CRC-related mortality data were collected from the Mortality Information System (SIM) available at the Information Technology Department of the Brazilian Unified Health System (DATASUS)[18], referring to a period of 17 years (2000 to 2016). Demographic data for each year, age group and sex were obtained from the Brazilian Institute of Geography and Statistics (IBGE)[19].

The variables observed were the total number of deaths due to CRC, subdivided into malignant neoplasms of colon (ICD-10, C18), rectosigmoid junction (ICD-10, C19) and rectum (ICD-10, C20), with analysis of registries divided into the 27 Brazilian states and the Federal District (according to the IBGE). For a better analysis, the five administrative regions of Brazil – South, Southeast, Midwest, North and Northeast – were also analyzed. The data were divided according to year of death, sex and age (0-4, 5-9, 10-14, 15-19, 20-24, 25-29, 30-34, 35-39, 40-44, 45-49, 50-54, 55-59, 60-64, 65-69, 70-74, 75-79, 80+ years). To calculate mortality, rates were standardized for specific age groups. The data were described in calculations per 100,000 population and for each sex.

The SIM system consists of a free access database of unidentified patient information provided by the Brazilian Ministry of Health, with the purpose of allowing epidemiological analysis of reported data. The economic cost of CRC treatment and the average cost of CRC hospital admission were obtained from the Hospital Information System (SIH), also available at the DATASUS website.

Municipal distribution maps were developed using data from the SIM system and IBGE geographical distribution reports. Their correlation was analyzed in Tableau, version 2018.1, an interactive data visualization software.

The data were treated statistically and analyzed quantitatively in Microsoft Excel 2010 (Microsoft Corp., United States) and GraphPad Prism 6. For statistical comparisons across the years, Student's t-test was used for parametric variables and Mann-Whitney U test for nonparametric variables. Data were also treated descriptively. The results were reported as graphs and tables for better interpretation. Values were considered significant if $p \leq 0.05$.

RESULTS

In the study period, 218,000 deaths were due to CRC in Brazil, with 21.8% (62,000) described as rectal cancer, 64.5% (140,000) as colon cancer and 6.7% (14,000) as rectosigmoid junction cancer (Table 1). CRC mortality rate was 6.2 (95% confidence interval – CI, 5.59-6.81) per 100,000 population, and there was no significant difference in mortality rates between men and women ($p = 0.4410$).

As shown in Graph 1, the most affected age groups were older populations. According to the death registry, mean age was 67 (95% CI, 66.8-67.5) years for men and 67.9 (95% CI, 67.7-68.2) years for women ($p < 0.0001$) (Graph 2).

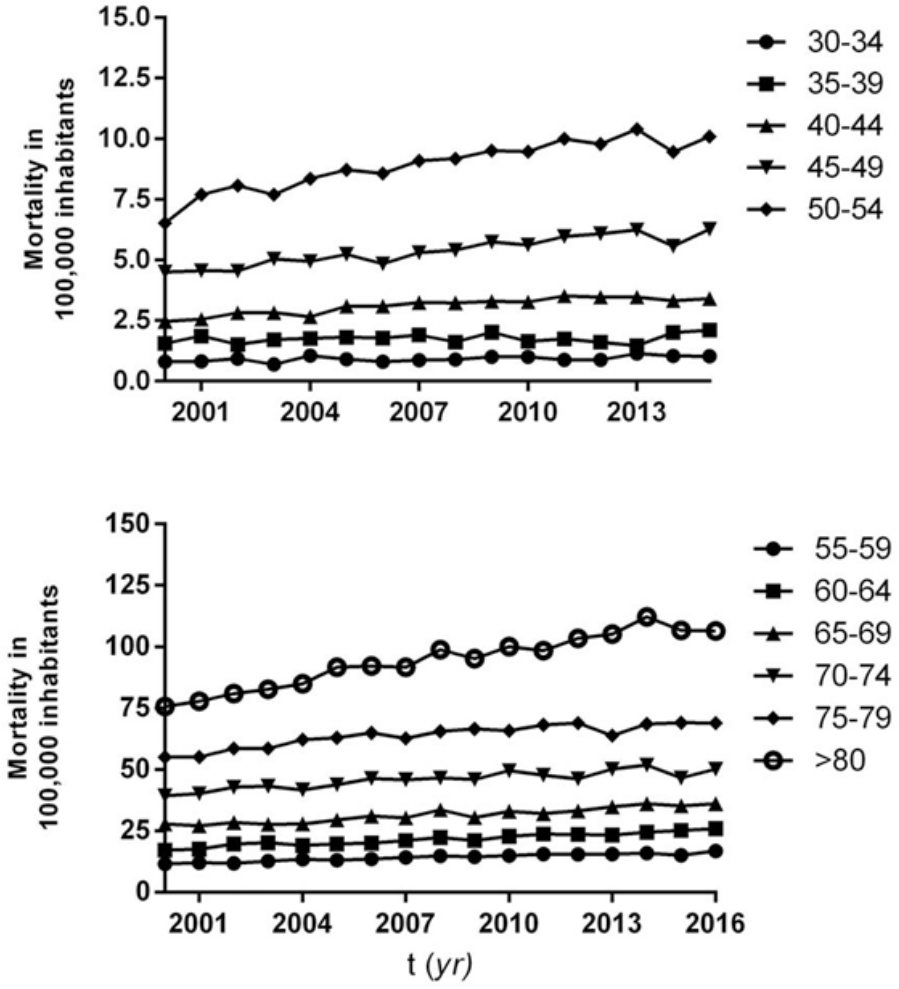
In Brazil, there was an 84.8% increase in the number of CRC death reports from 2000 to 2016 ($p < 0.0001$), as shown in Table 2, that this increase was observed in four of the five Brazilian regions. A municipal distribution analysis (Figure 1) comparing the period from 2000 to 2016 visually represents the significant increase in CRC mortality, especially in the Northeast and North regions.

In eight of the 17 age subgroups analyzed, there was an increase in reported mortality, including 30-34, 40-44, and all subgroups aged over 50 years. Increases ranged from 25% to 51% between 2000 and 2016.

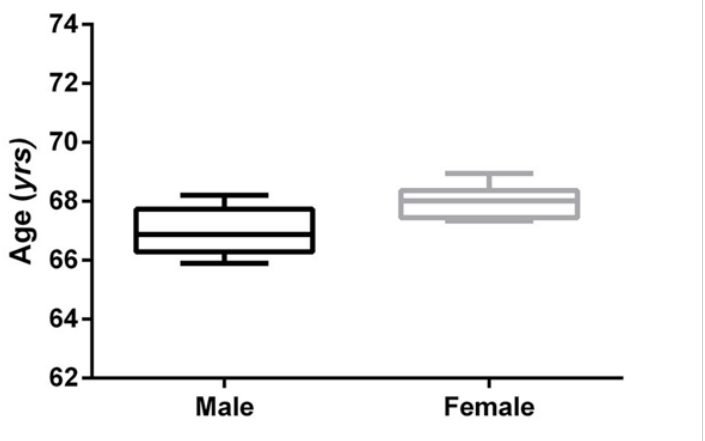
The present study also analyzed CRC treatment cost data provided by the Brazilian Unified Health System. Between 2000 and 2016, there was a 1,100% increase in treatment cost per year, from R$ 15 million to R$ 180 million, with an average hospital cost of R$ 1,700 (Graph 3).

Table 1: Distribution of death notification and mortality according to anatomical location of colorectal cancer per federal unit in Brazil.

Topography of colorectal cancer/ Federal Unit	Rectum		Colon		Rectosigmoid junction	
	Deaths	Mortality per 100,000 population	Deaths	Mortality per 100,000 population	Deaths	Mortality per 100,000 population
Brasil	62,888	1.61-1.97	140,666	3.63-4.37	14,708	0.35-0.48
South	11,145	2.17-2.59	29,129	5.73-6.72	2,594	0.49-0.62
Rio Grande do Sul	4,826	2.35-2.88	15,115	7.58-8.79	1,462	0.7-0.89
Santa Catarina	1,862	1.6-1.95	4,686	4.02-4.92	479	0.36-0.55
Paraná	4,457	2.24-2.75	9,328	4.76-5.68	653	0.31-0.42
Southeast	36,544	2.03-2.42	86,588	4.83-5.7	887	0.46-0.64
São Paulo	18,281	2.41-2.77	45,345	6-6.85	4,377	0.51-0.73
Rio de Janeiro	7,905	2.71-3.18	18,477	6.32-7.43	1,451	0.45-0.63
Minas Gerais	5,179	1.34-1.75	11,383	2.98-3.81	1,586	0.4-0.55
Espírito Santo	1,070	1.55-1.95	2,484	3.47-4.66	202	0.27-0.39
Midwest	3,696	1.4-1.75	7,641	2.83-3.69	775	0.29-0.37
Mato Grosso do Sul	707	0.9-2.54	1,743	2.23-6.27	120	0.15-0.43
Mato Grosso	538	0.87-1.28	1,029	1.63-2.48	148	0.22-0.37
Goiás	1,690	1.48-1.87	3,006	2.56-3.41	379	0.3-0.45
Distrito Federal	761	1.59-1.98	1,863	3.88-4.86	128	0.24-0.36
North	2,035	0.63-0.91	2,441	0.79-1.06	401	0.12-0.19
Acre	62	0.39-0.65	83	0.45-0.94	20	0.05-0.28
Rondônia	221	0.61-1.01	139	0.38-0.64	70	0.18-0.33
Amazonas	575	0.81-1.15	606	0.89-1.17	96	0.1-0.23
Roraima	44	0.38-0.81	57	0.52-1.02	11	0.06-0.24
Pará	975	0.63-0.93	1,201	0.81-1.11	135	0.08-0.13
Amapá	52	0.32-0.63	61	0.34-0.76	14	0.02-0.23
Tocantins	106	0.34-0.57	294	0.96-1.57	55	0.16-0.32
Northeast	9,468	0.86-1.2	14,867	1.37-1.91	1,938	0.17-0.26
Maranhão	632	0.46-0.7	895	0.63-1.01	120	0.08-0.14
Piauí	998	1.5-2.31	759	1.08-1.82	66	0.09-0.16
Ceará	1,665	0.97-1.37	2,617	1.55-2.14	505	0.26-0.45
Rio Grande do Norte	634	0.99-1.35	1,027	1.57-2.23	178	0.25-0.41
Paraíba	630	0.79-1.19	862	1.04-1.67	153	0.17-0.31
Pernambuco	1,662	0.95-1.27	3,390	1.94-2.59	248	0.14-0.19
Alagoas	371	0.55-0.83	449	0.64-1.04	83	0.11-0.19
Sergipe	347	0.84-1.14	603	1.41-2.04	61	0.11-0.24
Bahia	2,529	0.86-1.19	4,265	1.47-1.99	524	0.14-0.28



Graph 1: Distribution of reported mortality by age group.



Graph 2: Graphical analysis of notification of colorectal cancer in the first 16 years of the 21st century according to age and sex in Brazil.

Table 2: Analysis of differences in reported mortality across administrative regions from 2000 to 2016 in Brazil.

Locality	2000	2016	Analysis	
	Mortality (per 100,000 population)	Mortality (per 100,000 population)	Difference in %	Significance
Brazil	4.24	8.32	+ 96.29	p < 0.0001
South	6.63	11.79	+ 77.89	p = 0.0286
Southeast	5.67	10.49	+ 84.87	p = 0.159
Midwest	3.09	6.92	+ 123.89	p = 0.0079
North	1.08	1.84	+ 18.67	p = 0.002
Northeast	1.52	4.58	+ 201.57	p < 0.0001

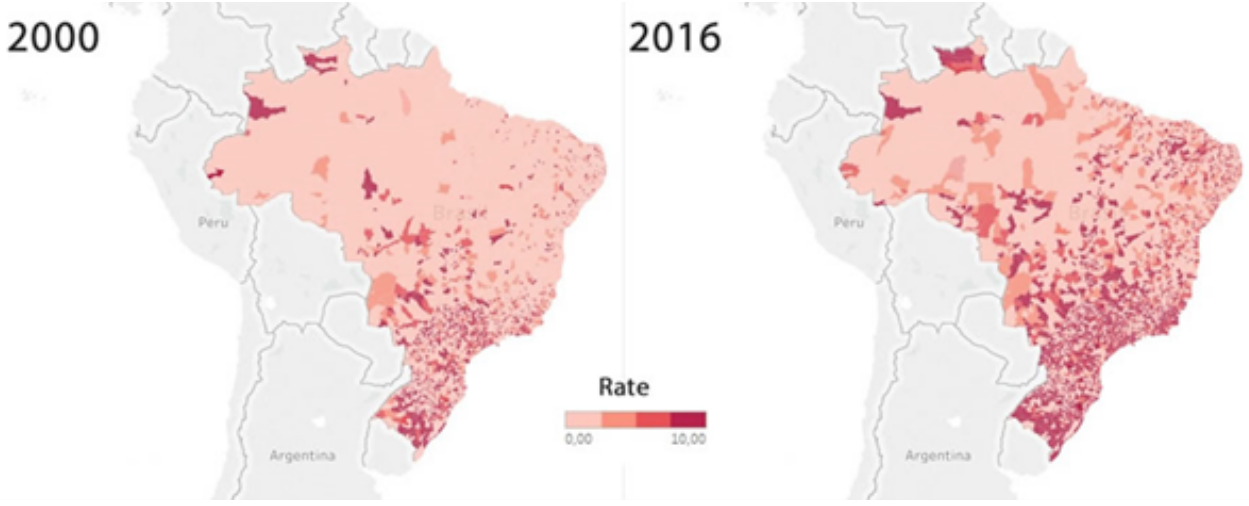
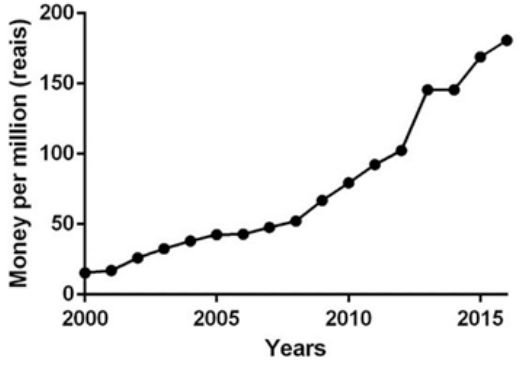


Figure 1: Difference in municipal distribution of death notification due to colorectal cancer from 2000 to 2016 in Brazil.



Graph 3: Distribution of costs in million reais (R$) per year of diagnosis and treatment of colorectal cancer in Brazil.

DISCUSSION

CRC is a malignant tumor with high incidence and high mortality, requiring a large volume of resources for its treatment. Contrasting to what has been observed in other countries, such as the United States, where there was a reduction in CRC incidence and mortality[9,20], in Brazil there was an increase in the notification of deaths caused by CRC. Besides, elevated mortality also occurred in younger age groups which are not included in the routine population screening of the disease.

Behavioral and dietary changes associated with Western lifestyle have led to increased risk of CRC, such as smoking, excess body weight, dietary habits, including high alcohol and processed meat consumption, low fruit/vegetable, fiber and calcium intake, in addition to a sedentary lifestyle[21-23].

Moreover, aging is the most significant risk factor for the development of sporadic CRC[3]. For decades in Brazil, there has been an increase in the longevity of the population[22], which also contributes to this growth in CRC cases. In a historical CRC cohort conducted in Rio de Janeiro, men began to show significant increases in mortality at age 55 years and women at age 40 years[24].

Delayed diagnosis and deficiencies in population screening may also have contributed to an increase in mortality observed in Brazil. In a study conducted in

New Orleans, United States, the average time between onset of symptoms and diagnosis of neoplasia was 4.9 months, while in a Brazilian sample the average time was 9.1 ± 3.6 months. This delay between first clinical presentation and diagnosis is mainly due to administrative and structural difficulties in performing the exams, lack of interest or personal denial of health condition[24].

A study conducted in the United States has shown that behavioral and dietary factors such as fruit and fiber intake and physical activity can reduce the incidence of CRC by up to 35%[25]. Also, reduced mortality in the United States can be partially attributed to measures of population screening through colonoscopy, rectosigmoidoscopy and fecal occult blood examination[5,9].

The increase in CRC mortality in younger age groups found in the present study and in American epidemiological studies are worrisome. In addition, this clinical condition is symptomatic in 86% of the individuals diagnosed at age below 50 years, and this presentation is associated with more advanced disease and poorer prognosis[3,10,25].

Elevated CRC mortality in octogenarian groups can be attributed to an increase in life expectancy of the Brazilian population. However, the increase observed in the age groups 45-49 years and 50-54 years are more concerning. This trend coincides with that observed in other countries and has been the reason for reviewing the protocols of population screening with a reduction in the indicated age to begin population screening and guidance[10,26].

The impact of cancer mortality is significantly higher in regions with a high human development index (HDI), accounting for 40% of global disease burden but only 15% of the world population. While in low HDI regions, the impact is only 2% for 6% of the population[24].

The costs of treatment and rehabilitation of patients with CRC are high, as they involve diagnosis, hospital stay, downtime, rehabilitation and clinical follow-up. United States estimates suggest that the individual cost of surgically treated patients with CRC amounts to nearly US$ 30,000 for treatment with 1-year follow-up. The present study used data provided by the Brazilian Ministry of Health, which only accounts for intrahospital cost, excluding rehabilitation or clinical follow-up costs[27].

The limitations of the present study are related to underreporting and qualitative issues (incorrect information and errors in the processing of primary cause codes), which may overestimate or underestimate mortality coefficients, reducing the accuracy of the study. However, in death notifications in which the underlying cause is a neoplasm, qualitative limitations are assumed to be minimized because of the evolutionary nature of the disease, which requires prolonged hospital stay and complementary confirmatory tests. In the DATASUS system, rectosigmoid cancer cases are not specified in intraperitoneal and extraperitoneal diseases, which is crucial for the therapeutic approach.

CONCLUSION

Mortality due to CRC in Brazil has remained high and has been increasing in some regions and in some age groups. The most commonly affected ages are those that should benefit the most from CRC screening measures. In addition, there has been massive investment in intrahospital treatment and diagnostic programs; however, such efforts are not accompanied by decreases in mortality, as observed in the United States.

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