







Colorectal cancer mortality trend in Mato Grosso, Brazil, 2000 to 2019

Tendência da mortalidade por câncer colorretal em Mato Grosso, Brasil, de 2000 a 2019

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ABSTRACT: *Objective:* To analyze the time series of colorectal cancer (CRC) mortality, according to sex and age group, in Mato Grosso, Brazil, from 2000 to 2019. *Methods:* Ecological time series study, with standardized mortality rates from CRC (C18 to C21) among residents of Mato Grosso. Information on deaths was provided by the Mato Grosso State Health Department, comprising the Mortality Information System and demographic information obtained from the Brazilian Institute of Geography and Statistics. The joinpoint regression analysis was used in the analysis of temporal trend. *Results:* A total of 2,406 deaths from CRC were identified in Mato Grosso between 2000 and 2019. The highest rates were found among the age group from 60 to 79 years. There was an increasing trend in mortality rates among men due to CRC for almost all age groups, with the exception of those aged 40 to 49 years and 80 years and older. For women, there was a significant increase in the age groups from 50 to 59 years and 80 years and older. *Conclusion:* The results showed an increase in mortality rates from CRC in the state of Mato Grosso, from 2000 to 2019, in certain age groups for both sexes, but especially for men. Knowledge about the evolution of mortality can provide data on the epidemiological situation of cancer at the local level and, thus, contribute to the development of actions to control and prevent this disease.

Keywords: Mortality. Colorectal neoplasms. Epidemiology. Time series studies.

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RESUMO: *Objetivo:* Analisar a tendência temporal da mortalidade por câncer colorretal (CCR) segundo sexo e faixa etária, em Mato Grosso, Brasil, de 2000 a 2019. *Métodos:* Estudo ecológico de série temporal das taxas ajustadas de mortalidade pelo CCR (C18 a C21) de residentes de Mato Grosso. As informações sobre os óbitos foram fornecidas pela Secretaria de Estado de Saúde de Mato Grosso e compõem o Sistema de Informações sobre Mortalidade, e as informações demográficas foram obtidas do Instituto Brasileiro de Geografia e Estatística. Para a tendência temporal, foi empregada a análise de regressão por *joinpoint*. *Resultados:* Foram identificados 2.406 óbitos por CCR em Mato Grosso no período de 2000 a 2019. As maiores taxas foram encontradas entre as faixas etárias de 60 e 79 anos. Para os homens, evidenciou-se tendência crescente das taxas de mortalidade por CCR para quase todas as faixas etárias, com exceção das de 40 a 49 anos e de 80 anos ou mais. Para as mulheres, houve aumento significativo nas faixas etárias de 50 a 59 anos e de 80 anos ou mais. *Conclusão:* Os resultados do estudo mostraram aumento das taxas de mortalidade por CCR no estado do Mato Grosso, no período de 2000 a 2019, em determinadas faixas etárias de ambos os sexos, mas sobretudo para os homens. O conhecimento sobre a evolução da mortalidade pode oferecer dados da situação epidemiológica do câncer em nível local e, assim, contribuir para a elaboração de ações de controle e prevenção desse agravo.

Palavras-chave: Mortalidade. Neoplasias colorretais. Epidemiologia. Estudos de séries temporais.

INTRODUCTION

Colorectal cancer (CRC) comprises malignant tumors that affect the colon, rectosigmoid junction, rectum, anus, and anal canal. Its development is complex and involves several factors¹⁻³, but, regardless of its complexity, it is among the types of cancer that most respond to prevention measures, due to the carcinogenesis, which goes through a long process, and can be extended for up to ten years and enable early identification and treatment⁴.

Worldwide, CRC ranks third among all types of cancer incidence and second in mortality, accounting for one-third of the entire burden of cancer incidence and mortality in the world, along with lung and female breast cancer. Estimates show that more than 1.8 million new cases of CRC and 881,000 deaths occurred in 2018 worldwide and, by 2030, according to projections by the International Agency for Research on Cancer (IARC), more than 1.1 million deaths are expected⁵.

Incidence and mortality rates are increasing rapidly in many low- and middle-income countries, while in developed countries, despite the highest rates in the world, the trends have been stabilizing or decreasing, which reinforces the epidemiological significance of CRC^{6,7}.

Projections for 2025 In Brazil point to an increase in the number of deaths of 75.8% among men and 67.5% among women mainly as a result of the population aging process⁸.

Aging has been an important non-modifiable risk factor for CRC mortality; however, in recent decades, there has been a progressive downward trend in diagnoses and deaths in the younger population, although this is still not fully understood^{9,10}. Regarding sex, some

studies in Brazil have shown higher mortality for females^{11,12}, while others have not found significant differences between men and women^{6,13,14}.

Although Brazil's rates have progressively increased in recent decades^{9,15,16}, in Mato Grosso, the trend in mortality rates from CRC is still poorly understood. Considering the dynamics related to the health-disease process in specific territories contributes to the creation of a set of instruments and mechanisms for planning, managing and financing health actions and services, aimed at providing and organizing a regionalized system, especially for the identification of health demands and needs of the population¹⁷. Thus, the present study aimed to analyze the temporal trend of CRC mortality in the State of Mato Grosso, according to sex and age groups, from 2000 to 2019.

METHODS

This is an ecological time series study on CRC mortality rates. Data about deaths of individuals aged 20 years or older, residing in the State of Mato Grosso, from 2000 to 2019, were used. Information on deaths was provided by the Mato Grosso State Health Department (SES-MT), which composes the Mortality Information System (SIM) of the Information Technology Department of the Brazilian Unified Health System (DATASUS).

Located in the midwest Region of the country, the State of Mato Grosso has 903,202,446 km² and an estimated population, in 2016, of 3,305,531 inhabitants. It comprises 141 municipalities and its human development index (HDI) is 0.725, ranking 11th among Brazilian states^{18,19}.

To identify deaths from CRC, the following codes were considered as the underlying cause, according to the 10th edition of the International Classification of Diseases and Related Health Problems (ICD-10): C18 (malignant neoplasm of the colon), C19 (malignant neoplasm of the rectosigmoid junction), C20 (malignant neoplasm of the rectum), and C21 (malignant neoplasm of the anus and anal canal).

The CRC mortality rate was calculated as the ratio between the number of deaths from CRC and the total number of inhabitants of the locale of interest, presented per 100,000 inhabitants and estimated by sex (male and female) and age group (30 to 39 years old, 40 to 49 years old, 50 to 59 years old, 60 to 69 years old, 70 to 79 years old and 80 years old and older). As the state as whole had a proportion of less than 10% for ill-defined causes in all years of the period considered, data correction for these causes was not required²⁰.

Population data, according to sex and age group, were obtained with the Brazilian Institute of Geography and Statistics (IBGE), from the Demographic Census of 2000 and 2010 and from population estimates for the other years (intercensus). Rates were adjusted for all years of the period studied by direct method, using the standard world population provided by the World Health Organization (WHO)²¹ and modified by Doll²².

To analyze the temporal trend of CRC mortality, the joinpoint regression analysis was used, assessing whether at some points in the time series (joinpoints) there were

significant changes in the trend pattern. The logarithmic transformation of mortality rates was considered as dependent variable and the years of the study period, as independent variable²³.

To adjust the different models, a different number of modification points in the temporal trend was assumed from zero (in which case the trend is represented by a single line segment) to a maximum number desired, taking into account the amount of observations. Joinpoint regression analysis uses Monte Carlo permutation tests to compare different models²³, and the model chosen was the one with the highest number of points and which maintained statistical significance ($p < 0.05$).

After defining the model, the annual percent change (APC) was calculated for each segment (with respective confidence intervals) and used to describe and quantify the temporal trend, as well as to assess whether the changes were statistically significant ($p < 0.05$). In this case, the null hypothesis is $APC = 0$, that is, mortality rates are not changing either upwards or downwards, being characterized as stable^{23,24}. The APC informs about the direction and magnitude of results of the temporal trends for each line fragment²⁴.

The results are presented in absolute numbers (number of deaths), rates and variations over the timeframe analyzed. Statistical analyzes were made in Joinpoint Regression Program software, version 8.3.6.112²⁵.

SIM data are in the public domain and were forwarded by SES-MT for the analyses, without identifying the study population. The study was approved by the Ethics Committee of Hospital Universitário Júlio Muller (opinion 3,048,183, of November 20, 2018) and by the Ethics Committee of Mato Grosso State Health Department (opinion 3,263,744, of April 12, 2019).

RESULTS

A total of 2,406 deaths from CRC were identified in Mato Grosso from 2000 to 2019: 1,229 among men (51.1%) and 1,177 among women (48.9%). The adjusted rates ranged from 2.02 (2001) to 6.51 deaths/100,000 inhab. (2019) for males, and from 2.75 (2003) to 6.18 deaths/100,000 inhab. (2017) for females (data not shown).

Table 1 shows the adjusted CRC mortality rates for men, by year and age group. With the exception of the age group from 40 to 49 years, the highest rates were identified from the second half of the analyzed period. The age group from 30 to 39 years old had the lowest adjusted rates and the group from 60 to 69 years old, had the highest. Comparing the mean rates of the first five years with the mean rates of the last five years of the historical series, there was an increase of 100% in the age group from 30 to 39 years (from 0.09 to 0.18), of 50% in the age group from 40 to 49 years (from 0.34 to 0.51), of 105.9% in the age group from 50 to 59 years (from 0.51 to 1.05), of 302.1% in the age group from 60 to 69 years old (from 0.47 to 1.89), of 67.1% in the age group from 70 to 79 years old (from 0.79 to 1.32) and of 46.9% in the age group of 80 years and older (from 0.49 to 0.72).

Table 1. Adjusted colorectal cancer mortality rates for men (per 100,000 inhabitants), by year and age group, Mato Grosso, Brazil, 2000 to 2019.

Year	n	30–39 years	40–49 years	50–59 years	60–69 years	70–79 years	80 years and older
2000	27	0.12	0.67	0.32	0.28	0.66	0.79
2001	19	0.17	0.16	0.30	0.54	0.63	0.15
2002	29	0.06	0.31	0.58	0.78	0.96	0.55
2003	26	0.05	0.22	0.55	0.50	1.03	0.38
2004	30	0.05	0.35	0.78	0.24	0.65	0.59
2005	47	0.05	0.68	0.66	1.38	1.04	0.44
2006	46	0.10	0.52	0.71	1.32	0.99	0.41
2007	29	0.10	0.25	0.60	0.63	0.66	0.19
2008	60	0.20	0.49	0.72	1.52	1.16	0.73
2009	52	0.05	0.65	0.75	0.68	1.02	0.76
2010	54	0.14	0.52	0.33	1.11	1.06	0.78
2011	72	0.14	0.34	0.81	1.68	1.64	0.74
2012	81	0.13	0.39	1.08	1.78	1.51	0.70
2013	77	0.18	0.44	0.92	1.70	1.16	0.67
2014	74	0.17	0.27	0.72	1.55	1.53	0.51
2015	90	0.21	0.85	0.97	1.55	1.34	0.42
2016	95	0.13	0.31	1.20	1.83	1.35	0.69
2017	93	0.17	0.46	0.71	1.55	1.24	1.08
2018	107	0.16	0.30	0.98	2.18	1.43	0.97
2019	121	0.24	0.64	1.38	2.33	1.26	0.44
Total/mean	1,229	0.13	0.44	0.75	1.26	1.12	0.60

The highest adjusted CRC mortality rates for women also occurred from the second half of the period onwards. The age groups from 60 to 69 years old and from 70 to 79 years old had the highest adjusted rates, while the age group from 30 to 39 years old had the lowest. Comparing the means rates of the first five years with the mean rates of the last five years of the historical series, there was an increase of 30.8% in the age group from 30 to 39 years (from 0.13 to 0.17), 57.6% in the age group from 40 to 49 years (from 0.33 to 0.52), 124.4% in the age group from 50 to 59 years (from 0.45 to 1.01), 8.9% in the age group from 60 to

69 years (from 1.35 to 1.47), 127.9% in the age group from 70 to 79 years (from 0.61 to 1.39) and 97.8% in the age group of 80 years and older (from 0.45 to 0.89). Thus, the increase among men was more marked in the age groups from 50 to 59 years old and from 60 to 69 years old, while among women, in the age groups from 50 to 59 years old and from 70 to 79 years old (Table 2).

In the analysis of the time series for men, there was an upward trend in CRC mortality rates for almost all age groups, with the exception of those aged 40 to 49 years and those

Table 2. Adjusted colorectal cancer mortality rates for women (per 100,000 inhabitants), by year and age group, Mato Grosso, Brazil, 2000 to 2019.

Year	n	30–39 years	40–49 years	50–59 years	60–69 years	70–79 years	80 years and older
2000	23	0.12	0.37	0.61	1.16	0.00	0.47
2001	30	0.12	0.09	0.81	2.20	0.59	0.14
2002	27	0.12	0.33	0.44	1.04	0.99	0.38
2003	25	0.11	0.48	0.10	0.71	0.81	0.47
2004	35	0.17	0.38	0.29	1.62	0.64	0.77
2005	41	0.11	0.66	0.83	1.41	0.96	0.21
2006	37	0.00	0.56	0.79	0.86	1.02	0.39
2007	36	0.10	0.14	0.91	0.12	1.27	0.75
2008	45	0.10	0.72	0.39	1.67	0.89	0.26
2009	47	0.39	0.32	0.67	0.95	1.03	0.33
2010	50	0.24	0.55	0.85	0.80	0.97	0.38
2011	71	0.14	0.60	0.81	1.52	1.59	0.64
2012	65	0.27	0.41	0.77	1.08	1.19	0.81
2013	84	0.22	0.62	0.80	1.71	1.82	0.70
2014	82	0.04	0.55	0.94	1.79	1.73	0.48
2015	79	0.26	0.43	1.02	1.69	0.69	0.85
2016	78	0.26	0.53	0.81	1.02	1.18	0.75
2017	106	0.13	0.41	1.15	1.94	1.49	1.05
2018	110	0.08	0.66	1.01	1.05	2.42	0.80
2019	106	0.13	0.54	1.08	1.63	1.18	0.97
Total/mean	1,177	0.16	0.47	0.75	1.30	1.12	0.58

aged 80 years and over. The group with the highest annual increase was 60 to 69 years old (APC=9.5%, 95% confidence interval, 95%CI 5.9%–13.1%). Among the younger than 50 years, there was an increase in the age group from 30 to 39 years (APC=3.5%, 95%CI 1.2%–5.8%) (Figure 1 and Table 3).

Due to the lack of records of deaths from CRC, it was not possible to estimate the temporal trend for the age groups from 30 to 39 years old and from 70 to 79 years old for women. In this group, the age groups that showed an increasing temporal trend were 50 to 59 years old and 80 years old and older, the latter showing the highest annual increase (APC=6.2%, 95%CI 2.7%–9.9%) (Figure 2 and Table 3).

DISCUSSION

The results showed an increase in CRC mortality rates in the State of Mato Grosso from 2000 to 2019 in certain age groups for both sexes, but especially for men. In addition, the results of the joinpoint analysis did not show inflection points for the analyzed trends.

The increase in CRC mortality rates has been shown by other studies with data from Brazil and also from the midwest region^{11,26,27}. A study by Dutra et al.¹⁴, for example, which aimed to describe the distribution pattern of CRC mortality in Brazil and regions according to sex, between 1996 and 2015 using SIM data, showed an increasing trend in CRC mortality for both sexes in Brazil and all Brazilian regions.

The increase in CRC mortality in Mato Grosso and in developing countries reflects the growing trends of chronic noncommunicable diseases in recent decades, and can be explained, in part, by changes in the prevalence of modifiable risk factors such as high alcohol intake^{28,29}, low consumption of fruits and vegetables, high consumption of red and processed meats, obesity³⁰ and smoking³¹.

Environmental factors related to exposure to pesticides are also to be mentioned. Chronic poisoning can be caused by multiple exposure to these factors by means of residues in fresh and processed foods, as well as particles dispersed in the air³². Although this study did not analyze lifestyle and environmental factors, it is possible that both contribute to the increase in CRC mortality rates in the population of Mato Grosso, mainly because the state is the largest consumer of pesticides in the country³³.

Considering this exposure scenario, according to the WHO³⁴, cancer is expected to be the main cause of death and the most important barrier to increasing life expectancy in the 21st century.

Men and women had a similar percentage of deaths from CRC in this study. Similarity between sexes was also identified for the midwest region from 2005 to 2015¹¹. In the analysis of rates by sex and age group, for both sexes, they were higher among the aged 50 to 79 years. Although CRC mortality rates have been reported higher in people aged 60 years or older³⁵, in this study, the trend of increased mortality from the disease was significant from 50 of age onwards, with emphasis on the group from 30 to 39 years for men. A study by Oliveira

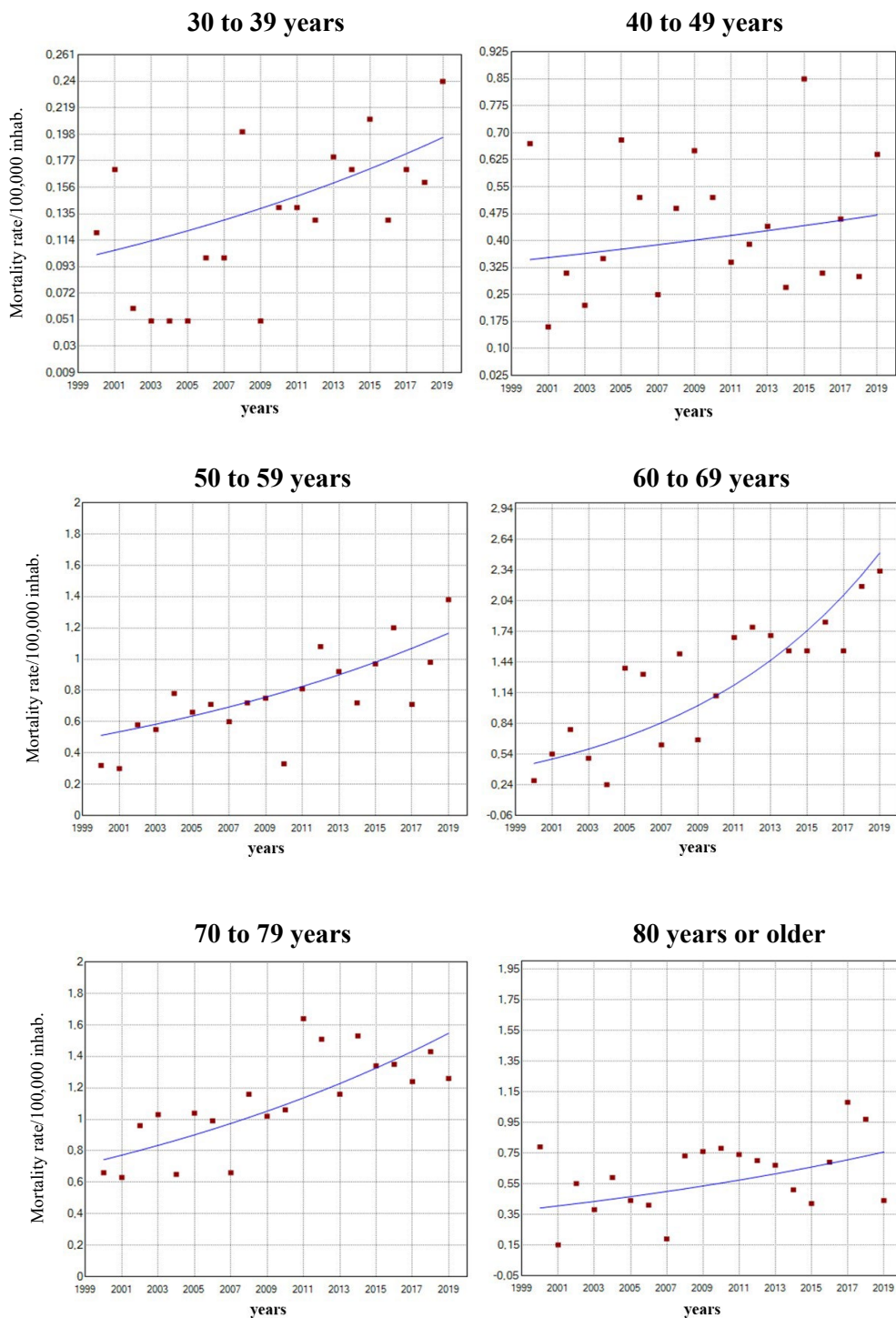


Figure 1. Temporal trend of adjusted colorectal cancer mortality rates for men, by age group, Mato Grosso, Brazil, 2000 to 2019.

Table 3. Temporal trend of adjusted colorectal cancer mortality rates, by sex and age group, Mato Grosso, Brazil, 2000 to 2019.

Age group (years)	Males		
	Time frame	APC	95%CI
30 to 39	2000–2019	3.5*	(1.2–5.8)
40 to 49	2000–2019	1.6	(-1.9–5.3)
50 to 59	2000–2019	4.4*	(2.7–6.2)
60 to 69	2000–2019	9.5*	(5.9–13.1)
70 to 79	2000–2019	3.9*	(2.3–5.6)
80 or older	2000–2019	3.5	(-0.3–7.5)
Age group (years)	Females		
	Time frame	APC	95%CI
30 to 39	2000–2019	-	-
40 to 49	2000–2019	3.9	(-0.0–8.1)
50 to 59	2000–2019	2.8*	(1.2–4.5)
60 to 69	2000–2019	2.0	(-3.1–7.3)
70 to 79	2000–2019	-	-
80 or older	2000–2019	6.2*	(2.7–9.9)

APC: annual percent change; 95%CI: 95% confidence interval; *Statistically significant ($p < 0.05$).

et al.¹² evaluated CRC mortality in the city of São Paulo and reported higher adjusted rates of the disease in individuals aged 50 years and over.

It is known that the demographic transition underway in Brazil also contributes to the increase in CRC mortality due to population aging. Changes in population structure generate a series of changes in society, mainly for health systems and services, but also in the epidemiological profile of diseases^{36,37}.

Aging naturally brings progressive bodily limitations, that result in greater vulnerability to diseases due to longer exposure to carcinogens, and weakness of the immune system, which leads to more expressive mortality rates in older age groups^{9,38}.

The involvement of these groups shows that younger people are also getting sick and dying of this cancer in the state. In the United States, for example, estimates have showed that while the overall death rate from this cancer is decreasing, deaths among people under 55 have increased by 1% per year since 2007¹⁰.

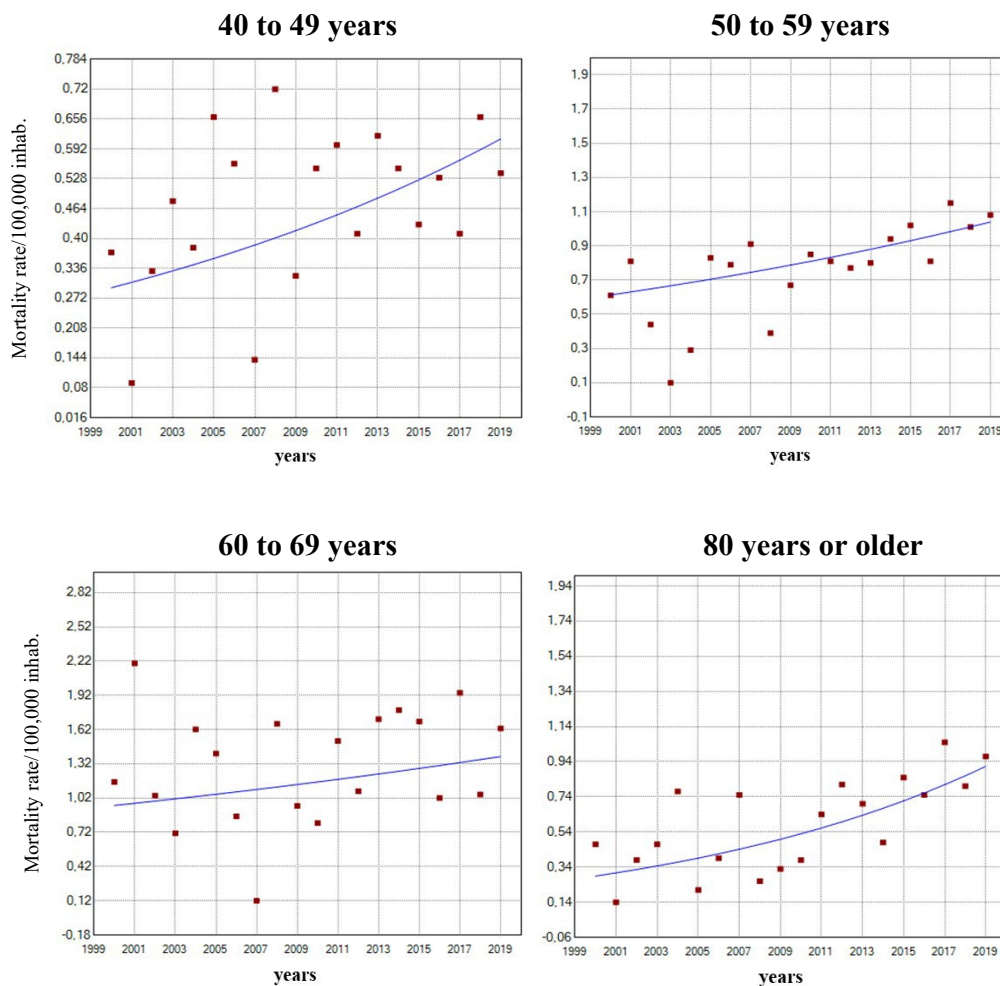


Figure 2. Temporal trend of adjusted colorectal cancer mortality rates for women, by age group, Mato Grosso, Brazil, 2000 to 2019.

Changes in risk factors over time among younger adults, including higher-fat diets and increased body mass index, have been positively associated with CRC risk and may be related to the upward trend of deaths in this population^{39,40}.

In addition, genetic factors have also contributed to the increase in CRC mortality trends in the younger population, with emphasis on hereditary CRC syndromes such as Lynch syndromes I and II and familial adenomatous polyposis, characterized by the early development of multiple colorectal adenomas^{41,42}.

Different diagnostic methods can be used for CRC for both early-stage polyp and cancer. Both are recommended for individuals over 50 years of age, so younger people (such

as men aged 30 to 39 years in this study) may be less diagnosed with the disease^{43,44}, and those aged 50 years or older may be less aware of preventive measures and early diagnosis.

Mortality rates increased significantly in almost all age groups for men, especially from 50 to 79 years old, ages with the highest annual increases when compared to women. Other studies also reported a more pronounced increase in men^{26,45}.

Men are known to seek health services less than women and, often they are already in more advanced stages and with greater severity of illness when they do. As a consequence, they become more vulnerable to mortality due to late diagnoses^{46,47}.

Women also had an increase in CRC adjusted mortality rates, for which estimation was possible, but only significant for the age groups of 50 to 59 years of age and 80 years of age or older.

Guidelines for CCR screening in countries that adopt them generally do not make gender-specific recommendations. However, right-sided (proximal) colon cancer is more aggressive than left-sided (distal) colon cancer⁴⁸, and a larger number of patients with the first type are women^{49,50}.

In addition, the hypothesis of lower CRC mortality in women at younger ages has been considered due to the favorable effect of endogenous female sex hormones at reproductive age, which would then favor higher CRC mortality in postmenopausal women⁵¹. The trend of higher growth rates in both age groups for women may be related to the fact that it is necessary to go beyond the diagnosis, which is noticeably more present in this group⁵².

According to the Ministry of Health, implementing population-based screening programs for CRC is not considered viable and cost-effective in Brazil. CRC screening is done opportunistically in the country, and the recommendations are based on guidelines combined with early diagnosis, dissemination of warning signs to the population and health professionals, immediate access to diagnostic procedures in suspected cases, and early treatment⁵³. However, this characteristic of CRC care in Brazil generates inequalities in access to diagnosis and, consequently, in the survival and mortality from the disease¹².

The deficit in supply of specialized services and late treatment do not favor the control of the disease, with a greater chance of worse prognosis and, consequently, higher mortality^{9,15,16}. The coverage of oncology services for diagnosis and treatment is fundamental in this context and, in Mato Grosso, it is overall restricted to large centers, which causes inequality in the offer of services, diagnosis and treatment of the disease. Thus, the network must be expanded to meet the entire demand of the state for cancer care⁵⁴.

The increase in rates may also reflect weaknesses in public policies for coping with the disease, since factors such as improvements in treatment and increased early detection actions can contribute to reducing CCR mortality^{55,56}.

This study had limitations such as the possibility of incorrect coding of information, underreporting and incomplete data⁵⁷. Despite this, vital statistics are low cost, easy to interpret, available in a large number of countries and allow analysis over long periods of time⁵⁸. In 2013, SIM had 97.1% coverage in Brazil. In Mato Grosso, considering general mortality

data, SIM coverage is between 91 and 95%⁵⁹, and the general quality index has shown gradual improvement over the years, rising from 70.5% in 2000 to 75.9% in 2015^{59,60}.

In view of this scenario, the need to implement local measures aimed at reducing the burden of CRC in the State is unquestionable, as well as actions aimed at screening programs and proposals for effective early detection and timely treatment.

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