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Trends in the incidence of colorectal cancer in Greater Cuiabá, Mato Grosso (Brazil), from 2000 to 2016

Tendência da incidência de câncer colorretal na Grande Cuiabá, Mato Grosso (Brasil), de 2000 a 2016

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ABSTRACT: ***Objective***: To analyze the temporal incidence trend of colorectal cancer (CRC), according to sex and age, in the Greater Cuiabá, Mato Grosso, Brazil, from 2000 to 2016. ***Methods***: Ecological time series study, with cases of CRC (C18 to C21) diagnosed from 2000 to 2016, of residents of the Greater Cuiabá (Cuiabá and Várzea Grande), in Mato Grosso. The information on the cases was obtained from the Population-Based Cancer Registry and population data from the Brazilian Institute of Geography and Statistics (IBGE). The rates were adjusted by world population. The age groups considered ranged from 30 to 39 years, 40 to 49 years, 50 to 59 years, 60 to 69 years, 70 to 79 years and 80 years and older. Joinpoint regression was used to analyze the trend of incidence. ***Results***: A total of 1,715 cases of CRC were registered with information on sex and age, with an adjusted rate of 16.4 new cases/100,000 men and 16.1 new cases/100,000 women. Men presented trend of increasing incidence rates in the age group of 70 to 79 years, with increase of 4.0% per year, while women presented trend of increase in the age group 50 to 59 years, with increase of 2.7% per year. ***Conclusion***: Older men showed a more significant trend towards an increase in the incidence of CRC, but in women this occurred in a younger age group, highlighting the importance of considering age related information in the analyzes of occurrence of the disease in this population.

Keywords: Time series studies. Colorectal neoplasms. Demographic data. Regression analysis.

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RESUMO: ***Objetivo:*** Analisar a tendência temporal da incidência do câncer colorretal (CCR) segundo sexo e faixa etária, na Grande Cuiabá, Mato Grosso (Brasil), de 2000 a 2016. ***Métodos***: Estudo ecológico de séries temporais, com casos de CCR (C18 a C21) diagnosticados de 2000 a 2016 em residentes da Grande Cuiabá (Cuiabá e Várzea Grande), em Mato Grosso. As informações dos casos foram provenientes do Registro de Câncer de Base Populacional e os dados populacionais do Instituto Brasileiro de Geografia e Estatística. As taxas foram ajustadas pela população mundial. Consideraram-se as faixas etárias de 30 a 39 anos, 40 a 49 anos, 50 a 59 anos, 60 a 69 anos, 70 a 79 anos e 80 anos ou mais. Para análise da tendência temporal da incidência, empregou-se a regressão por *joinpoint*. ***Resultados***: Foram registrados 1.715 casos de CCR com informação de sexo e idade, com taxa ajustada de 16,4 casos novos/100 mil homens e 16,1 casos novos/100 mil mulheres. Os homens apresentaram tendência temporal de aumento das taxas de incidência na faixa etária de 70 a 79 anos, com acréscimo de 4,0% ao ano, e as mulheres apresentaram tendência temporal de aumento na faixa etária de 50 a 59 anos, com acréscimo de 2,7% ao ano. ***Conclusão***: Os homens mais velhos apresentaram tendência temporal de aumento da incidência de CCR de forma mais expressiva, porém nas mulheres isso ocorreu em faixa etária mais jovem, ressaltando a importância de considerar a informação sobre a idade nas análises sobre a ocorrência da doença nessa população.

Palavras-chave: Estudos de séries temporais. Neoplasias colorretais. Dados demográficos. Análise de regressão.

INTRODUCTION

Chronic non-communicable diseases have constituted a public health issue of great magnitude due to its high economic burden on health services and society as a whole, to deaths and early disability. Among these diseases, cancer stands out, which has a direct impact on the population's quality of life[1].

The International Agency for Research on Cancer (IARC) estimates that, globally, one in five people will develop cancer in their lifetime and that one in eight men and one in 11 women will die from the disease. As for survival, these estimates suggest that within a period of up to five years after a cancer diagnosis, 50 million people will be alive[2].

Considering colorectal cancer (CRC), it is known that the incidence and mortality of the disease are decreasing in some developed countries (Iceland, Australia, New Zealand, Japan). In developing countries, these rates have been increasing, and Brazil is one of the countries that have shown an increase in both incidence and mortality from CRC, especially among men[3].

In the country, in 2014, 15,070 new cases of colon and rectal cancer were estimated in men and 17,530 in women, corresponding to a crude rate of 15.44 new cases/100,000 men and 17.24/100,000 women[4]. For the year of 2020, 20,520 cases of these cancers are estimated in men and 20,470 in women, corresponding to a crude rate of 19.63 new cases/100,000 men and 19.03/100,000 women[5].

According to data from the National Cancer Institute, for the state of Mato Grosso there was an increase in estimates of the crude incidence rate of this neoplasm. In 2014, the rate was

7.86 cases/100,000 men and 9.07 cases/100,000 women, and in 2002, 8.64 cases/100,000 men and 10.58 cases/100,000 women. For Cuiabá (MT), the opposite behavior was registered for this period, going from 11.32 to 7.51 cases/100,000 men and from 13.59 to 13.09 cases/100,000 women[4,5], with women from the capital presenting values higher than those of the state as a whole.

According to Santos et al.[6], "the finding of an increase in CRC incidence and mortality in Brazil highlights the importance of controlling this cancer, especially in a context of demographic transition (population aging), epidemiological transition (changes in risk patterns) and weaknesses in the health systems".

Knowledge of the distribution and magnitude of the population cancer is an important factor for planning, research and disease control programs. Thus, the objective of this study is to analyze the temporal trend of CRC incidence according to sex and age group in the Greater Cuiabá, in the state of Mato Grosso, from 2000 to 2016.

METHODS

This is an ecological time series study of CRC incidence, considering cases diagnosed from 2000 to 2016 in residents of the Greater Cuiabá, Mato Grosso.

The Greater Cuiabá is made up of the cities of Cuiabá and Várzea Grande. Cuiabá has a territorial area of 3,291,696 km^2, and Várzea Grande of 724,279 km^2. In 2000, the estimated population of Greater Cuiabá was 698,644 inhabitants, concentrating 27.9% of the entire population of the state, and in 2010 it was 803,694 inhabitants (26.5%). These two cities are the ones with the largest populations in Mato Grosso[7]. Data from the 2010 census revealed that Cuiabá had, in that year, an illiteracy rate of 4.5%, a proportion of people with low income (less than 0.5 minimum wage) of 20.0% and an average household income per capita of 1,124.88 reais[8]. For Várzea Grande, these values were, respectively, 5.5%, 27.3% and 635.21 reais[7].

The database with information on the number of true cases (incidents) and other variables of interest was exported from the Population-Based Cancer Registry (PBCR) of Cuiabá (which includes data from Cuiabá and Várzea Grande) by an authorized technician, to subsequent calculation of the incidences. The PBCR are systematized centers for the collection, storage and analysis of the occurrence and characteristics of new cancer cases, with the objective of knowing the distribution and temporal trend of the disease in the population belonging to the geographical coverage area[9].

One of the purposes of the registry is to provide data for the production of reliable statistics. Among the indicators that can be used to verify the validity of its data, there is the proportion of cases with histological verification of the diagnosis and the proportion of cases registered only with information from the death certificate (DCO)[10].

The analysis of these two indicators in the PBCR-Cuiabá showed that the proportion of histological verification in the analyzed period for CRC ranged from 76.6% (2016) to 95.0%

(2005) for males and from 77.8% (2013) to 95.0% (2001) for females, while the proportion of DCO for these values ranged from 3.3% (2005) to 15.6% (2015) and from 0% (2005 and 2010) to 19.8% (2013), respectively. Although the null percentage for the DCO indicates the need to review the death certificate cases, these values meet IARC standards[11]. Even so, one of the limiting factors regarding the use of PBCR is the lack of current data on the occurrence of new cases of the disease in the population that the registry serves.

For the identification of CRC cases, the following codes registered according to the 10th edition of the International Statistical Classification of Diseases and Related Health Problems were considered: C18 (malignant neoplasm of the colon), C19 (malignant neoplasm of the rectosigmoid junction), C20 (malignant neoplasm of rectum) and C21 (malignant neoplasm of anus and anal canal) [5].

Incidence rates were calculated with the numerator as the number of cases of the disease and the denominator as the total number of inhabitants of the population of interest (estimates from IBGE) for each year of the study, presented per 100,000 inhabitants and estimated by sex (male and female) and age group (30 to 39 years, 40 to 49 years, 50 to 59 years, 60 to 69 years, 70 to 79 years and 80 years and older). The rates were adjusted by age group using the direct method, using the standard world population[12,13]. Eleven cases of unknown age, three cases of unknown gender and 39 cases aged less than 30 years old were excluded because they did not occur for both sexes for all years of the study.

To analyze the temporal trend of CRC incidence, regression models were estimated using the Joinpoint Trend Analysis program, version 4.7.0.0[14], allowing it to verify if in some points (joinpoints) there were significant alterations of the observed trend pattern. It has the advantage of being able to test whether several fragments of the line better explain a trend in time than a single line, but it is not applicable when there are no observations at some point in the historical series. For the analysis, the logarithmic transformation of the incidences was considered as the dependent variable and the years of study as the independent variable[15].

To fit the models, the joinpoint regression analysis uses Monte Carlo permutation tests, assuming a different number of temporal trend modification points, from zero (in which case the trend is represented by a single line segment) to a maximum number that was desired, taking into account the number of observations. The model chosen was the one with the highest number of points that maintained statistical significance ($p<0.05$) [15].

When the model was defined, the annual percentage change (APC) and the average annual percentage change (AAPC) for each segment were calculated (with their respective confidence intervals) and used to describe and quantify the temporal trend and assess whether it was statistically significant ($p<0.05$). In this situation, the null hypothesis is APC or AAPC=0, that is, the incidences are not varying significantly, either up or down[15,16]. It is noteworthy that the APC informs about the direction and magnitude of the results of the temporal trends for each fragment of the straight line, while the AAPC is estimated by calculating the weighted geometric mean of the different APCs, that is, considering the entire period, with equal weight to the segment size for each interval of time. When the phenomenon can be described by only one straight line, the APC and AAPC values will be the same[16].

The results are presented in absolute numbers (number of cases), proportions, rates and variations over the time analyzed.

RESULTS

In the period from 2000 to 2016, 1,715 CRC cases with information on gender and age were recorded, 53.1% of which were female. In both sexes, there was also a higher proportion of cases in the age groups 50 to 59 years and 60 to 69 years, which together accounted for at least 50% of all the cases (Table 1).

Females had a crude CRC incidence rate slightly higher than males (29.3 cases / 100,000 inhabitants females and 27.8 cases / 100,000 men, respectively). Crude rates increased with increased age, especially in the 70-79 age groups and 80 years or older, for both sexes, with the latter age group having a 25.9 times higher CRC incidence rate than the first category for males. For females, this value was 23.7 times higher (Table 1).

Table 1. New cases (absolute number and proportion), crude and adjusted rates of colorectal cancer (per 100,000 inhabitants) by sex and age group, Greater Cuiabá (MT), Brazil, 2000 to 2016.

Age Distribution by Sex	n (%)	Crude rates	Adjusted rates*
Males (years)	805 (46.9)	27.8	16.4
30–39	55 (6.8)	5.0	0.6
40–49	131 (16.3)	15.8	1.9
50–59	201 (25.0)	37.0	3.3
60–69	218 (27.1)	79.1	5.5
70–79	147 (18.2)	125.8	3.8
80 or older	53 (6.6)	129.7	1.3
Females (years)	910 (53.1)	29.3	16.1
30–39	64 (7.1)	5.7	0.7
40–49	136 (14.9)	15.6	1.9
50–59	235 (25.8)	40.5	3.7
60–69	223 (24.5)	71.9	5.0
70–79	169 (18.6)	115.9	3.5
80 or older	83 (9.1)	135.0	1.4
Total	1,715	28.6	16.2

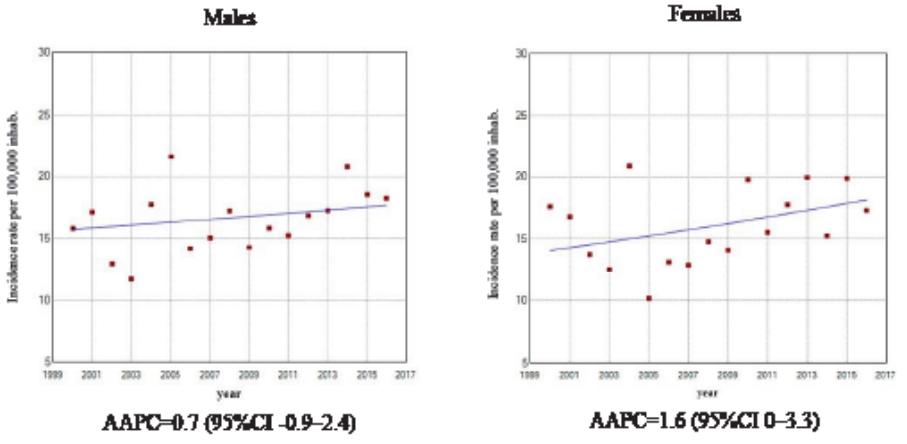
*By age, according to the standard world population[12,13].
Source: Population-Based Cancer Registry of Cuiabá (MT).

The adjusted rates were similar between the sexes (16.4 new cases/100,000 inhabitants for males and 16.1 new cases/100,000 inhabitants for females) and, unlike the gross rates, they increased up to the age group from 60 to 69 years old for both sexes, with a decrease thereafter. The age group from 60 to 69 years old stands out, presenting the highest adjusted rates in both males (5.5 cases/100,000 men) and females (5.0 cases/100,000 women) (Table 1).

In the analysis of the time trend of the adjusted CRC incidence rates considering only sex, males had an AAPC of 0.7 (95% confidence interval [95%CI]-0.9-2.4) and females of 1.6 (95%CI 0-3.3), that is, the percentage change in the adjusted rates for women was 2.3 times higher than for men. However, the variations for both sexes were not statistically significant (Figure 1).

In the analysis of the time trend by age group, stratified by sex, for males, a downward trend in the adjusted CRC rates was observed for the age groups from 30 to 59 years and also for those aged 80 years or older, but these decreases were not statistically significant. For the age groups from 60 to 69 years and 70 to 79 years, there was a tendency to increase the adjusted rates in the period, but only with statistical significance for the age group from 70 to 79 years, with an AAPC of 4.0 (95%CI 0.4-7.6) (Figure 2 and Table 2).

For females, four temporal trends were identified for the age group from 40 to 49 years, with decrease in the periods from 2004 to 2007 and from 2011 to 2016 and increase in the periods from 2000 to 2004 and from 2007 to 2011. The age groups from 60 to 69 years and from 70 to 79 years also showed a decreasing trend, but none of them with statistical significance. On the other hand, the age groups from 30 to 39 years, 50 to 59 years and 80 years and older showed a temporal tendency to increase in the adjusted rates, but only the age group from 50 to 59 years showed a significant increase in the period, with an AAPC of 2.7 (95%CI 0.4-5.1) (Figure 3 and Table 2).



AAPC: average annual percent change; 95%CI: 95% confidence interval.
Source: Population-Based Cancer Registry of Cuiabá (MT).

Figure 1. Time trend of adjusted rates of colorectal cancer incidence by sex, Greater Cuiabá, Mato Grosso (Brazil), 2000 to 2016.

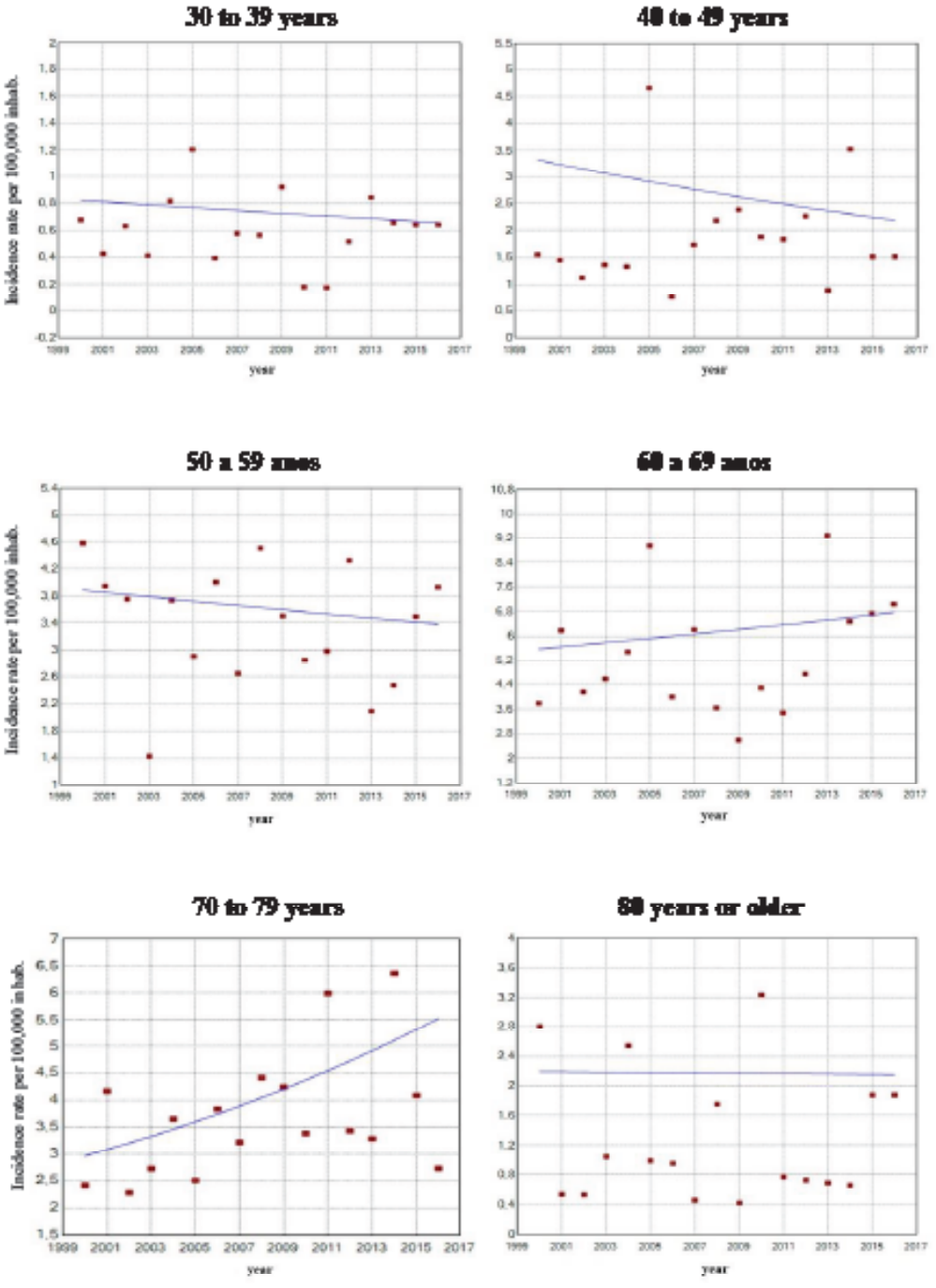


Figure 2. Temporal trend of adjusted rates of colorectal cancer incidence for males, by age group, Greater Cuiabá (MT), 2000 to 2016.

Table 2. Temporal trend of adjusted rates of colorectal cancer incidence according to sex and age group, Greater Cuiabá (MT), Brazil, 2000 to 2016.

Males					
Age group (years)	Period	APC	95%CI	AAPC	95%CI
30 to 39	2000–2016	-	-	-1.4	-5.4– 2.8
40 to 49	2000–2016	-	-	-2.6	-9.0–4.3
50 to 59	2000–2016	-	-	-0.9	-3.6–2.0
60 to 69	2000–2016	-	-	1.2	-3.0–5.6
70 to 79	2000–2016	-	-	4.0*	0.4–7.6
80 or older	2000–2016	-	-	-0.1	-6.5–6.7
Females					
Age group (years)	Period	APC	95%CI	AAPC	95%CI
30 to 39	2000–2016	-	-	0.8	-1.9–3.5
40 to 49 (trend 1)	2000–2004	8.6	-10.2–31.2	2.3	-10.3–16.8
40 to 49 (trend 2)	2004–2007	-23.6	-63.3–59.0		
40 to 49 (trend 3)	2007–2011	25.8	-4.6–65.9		
40 to 49 (trend 4)	2011–2016	-1.5	-12.2–10.5		
50 to 59	2000–2016	-	-	2.7*	0.4–5.1
60 to 69	2000–2016	-	-	-1.4	-3.7–1.1
70 to 79	2000–2016	-	-	-1.4	-3.6 –0.8
80 or older	2000–2016	-	-	1.0	-2.4–4.7

APC: annual percent change; 95%CI: 95% confidence interval; AAPC: average annual percent change. *statistically significant ($p<0.05$).
Source: Population-Based Cancer Registry of Cuiabá (MT).

DISCUSSION

The results of this study showed that, in the period of 2000 to 2016, men from the Greater Cuiabá showed a temporal tendency to increase the incidence rate of CRC in the age group from 70 to 79 years, while women showed a tendency to increase in the age group of 50 to 59 years.

Women had a slightly higher proportion of cases of the disease when compared to men (53.1%), a percentage similar to that found in other locations, inside and outside of Brazil, such as 56.0% in Cali between 1983 and 2021, 51.0% in Costa Rica between 1983 and 2007,

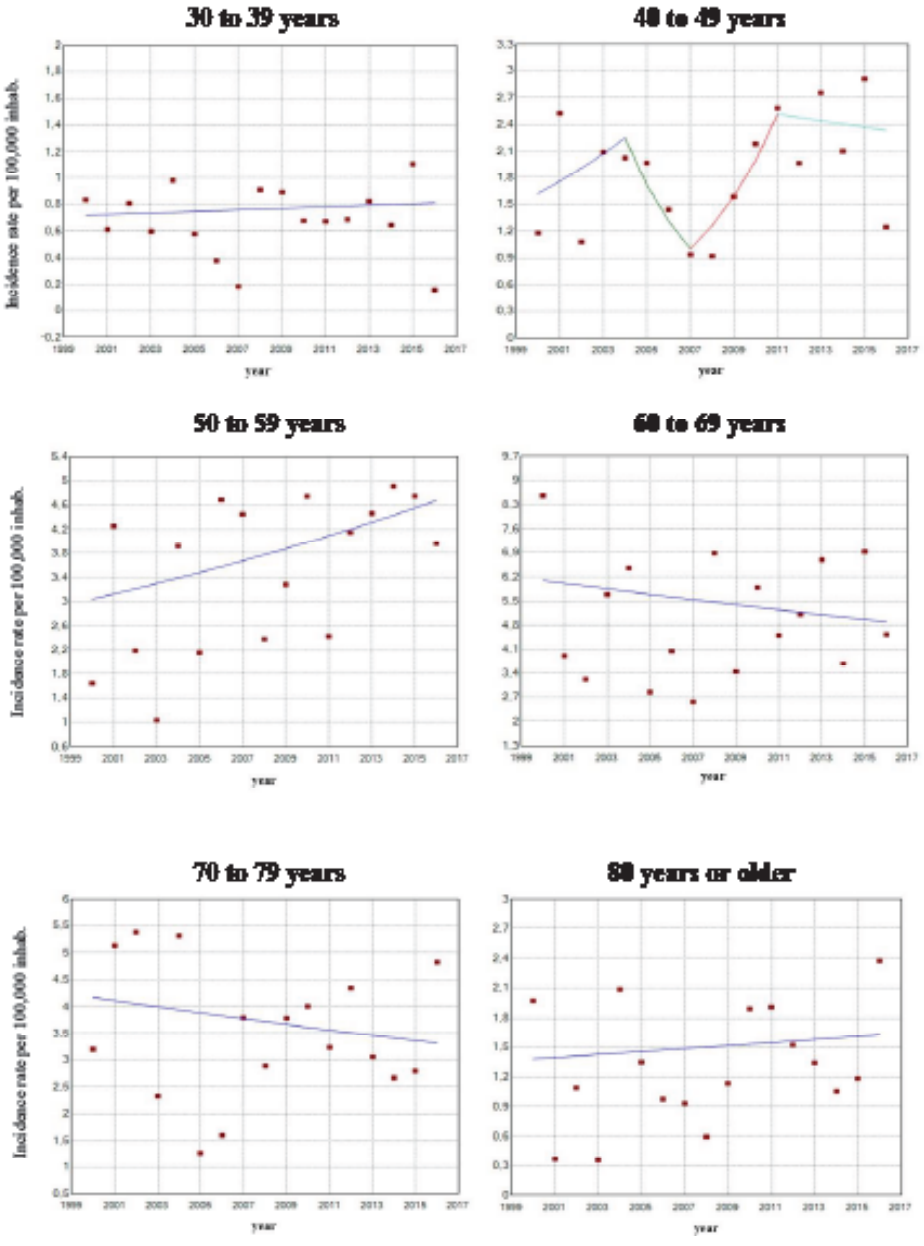


Figure 3. Temporal trend of adjusted rates of colorectal cancer incidence for females, by age group, Greater Cuiabá (MT), 2000 to 2016.

56.0% in Quito between 1988 and 2012, 54.0% in Goiânia (GO) in the same period[17] and 52.5% in São Paulo (SP) between 1997 and 2009[18].

The adjusted CRC incidence rates were similar between the sexes. For this disease, the rates have generally been equal between men and women[19]. The adjusted rate found in this

study was lower than that found in São Paulo, where, from 1999 to 2013, men had an adjusted rate of 29.7 cases/100,000 men and women 23.4 cases/100,000 women, but without including the malignant neoplasm of the anus and anal canal[20]. It was also lower than that found in Goiânia, where men had an adjusted rate of 32.3 cases/100,000 men and women of 28.6 cases/100,000 women in the period from 1988 to 2012[17]. Estimates for Cuiabá for the year 2020 indicate, however, higher incidence rates (gross and adjusted) of CRC for women[5].

The adjusted rates were highest in the 50-79 age groups, with subsequent decline. The peak of the incidence rate at a certain age, in the case of this study in the age group 60 to 69 years, with a drop at more advanced ages, may mean the existence of a risk subgroup[17]. It is known that age has been considered an important source of variation between rates, due to the increased risk of death with the biological process of aging[21], when the number of cell division increases, and deoxyribonucleic acid replication errors that lead to mutations may occur[22].

The occurrence of the disease at an older age can also be explained by the fact that, over the years, individuals are more exposed to other CRC risk factors, such as inadequate eating habits, physical inactivity, sedentary lifestyle, obesity and even diabetes[23].

Results from the Surveillance System of Risk Factors for Chronic Non-Communicable Diseases (Vigitel) showed that, in 2019, men from Cuiabá had the five highest prevalences for: passive smoking in the workplace, consumption of soft drinks on five or more days of the week, insufficient practice of physical activity and consumption, in the last 30 days, of five or more doses of alcoholic beverage on the same occasion. The city was among the five capitals with the lowest prevalences for: consumption of fruits and vegetables on five or more days of the week, consumption of five or more daily servings of fruits and vegetables, and practice of physical activities during free time equivalent to at least 150 minutes of moderate-intensity activity per week. The women were among the five highest prevalences of second-hand smoke in the workplace[24]. Although the Vigitel data refer only to Cuiabá, it is possible that they may apply to the Greater Cuiabá, showing that this population has risk factors that have been associated with an increase in CRC incidence[25].

A meta-analysis study that analyzed the strength of the associations between selected risk factors and the occurrence of CRC showed that the risk of the disease was significantly associated with inflammatory bowel disease, history of CRC in a family member, body mass index, smoking and red meat consumption and that physical activity and consumption of fruit and vegetables proved protective[25].

Although the risk of CRC in individuals younger than 50 years is lower, tracking the time trend of the disease in this group has been a key indicator of recent changes in risk factor exposures, and often foreshadows the future burden of cancer[26]. In the United States and Canada, for example, the increase in CRC cases in younger patients led to the modification of the recommended age for starting colonoscopy to 45 years[27].

The results of the temporal trends of disease incidence over the analyzed period did not show significant changes when only sex information was considered. However, when age was considered, it was noticed that women showed a significant temporal trend of increasing

CRC incidence rates in younger age groups when compared to men. On the other hand, men showed a more expressive increase trend. Thus, it is recommended that information on age be incorporated into this type of analysis and the identification of symptoms of the disease in the younger population, as well as studies aimed at identifying risk factors in this group.

It is known that women have a higher prevalence of use of health services, especially for routine and preventive exams[28], and this more frequent contact with health services can allow the diagnosis of the disease at younger ages, as well as in earlier stages when compared to men. In addition, a possible protective effect of female hormones on the oncogenic process of CRC has been described, evidenced by the use of oral contraceptives and hormone replacement therapy[29].

As for men, they recognize less the signs and symptoms of the disease, such as alterations in the functioning of the intestine, reflecting on late diagnosis[30]. The more pronounced increase in incidence rates in this group, also identified in other studies[31,32], may be related, in part, to a less healthy lifestyle, a fact that may give them a higher risk for the disease[33].

Global patterns of CRC incidence have varied widely between locations. In Brazil, adjusted incidence rates ranged from 5.6/100,000 (Acre) to 33.1/100,000 (São Paulo) for men, and from 5.5/100,000 (Amapá) to 25.1/100,000 (Santa Catarina) for women in 2020[5], however, in general, the incidence of CRC has increased in low and middle-income countries, but is stabilizing, or even decreasing, in high-income countries, especially in those who have implemented some screening for the disease[3].

It is known that the implementation of screening strategies can reduce the incidence of CRC through the identification and removal of precancerous polyps[34], since they evolve to a benign lesion in approximately 10 to 15 years, with a long preclinical interval with possibilities of detection and removal[35]. On the other hand, screening itself can also increase observed rates of disease due to early detection of CRC[25].

In Brazil, there are no specific guidelines for CRC screening, which already happens for the cervix. In other countries, such as Denmark, every two years all of its citizens aged 50 to 74 years are called for CRC screening[36].

The recommendation in the Brazilian Unified Health System is that early diagnosis and personalized approach actions be prioritized only for the high-risk group due to the different epidemiological realities and health networks. There is also a need for studies on the feasibility of introducing screening in different national contexts[37]. In this sense, the Barretos Cancer Hospital developed a CRC screening program based on a fecal immunochemical test. To analyze the quality and performance measures in the first two years of the program, a study was developed with 6,737 individuals from 2015 to 2017. The results showed that the program achieved desirable quality metrics, in line with the European Union guidelines[38].

This study provided information on the temporal trend of CRC incidence in the Greater Cuiabá, using the most current data on the disease, a period not identified, to date, in any other study. Thus, it is expected that the resulting data can help strengthen the Oncology Care Action Plan in the state of Mato Grosso, so that the adjustments of the care line and

service network and the levels of cancer management can be established for the early diagnosis and treatment of the disease in the state.

As a limitation, the fact that it is based on secondary data must be highlighted, which may present problems of underreporting, filling and coding errors[39]. For the analysis of the temporal trend, it should also be considered that the data can be influenced by the improvement of the quality of the information over time[5].

Health surveillance comprises groups of actions to know, detect and prevent factors that act in the health-disease process. Cancer surveillance requires information for estimates on incidence, cases assisted in the oncology care network, deaths from cancer, among others, allowing managers and the population to have access to data on the disease in Brazil. The effective and efficient planning of cancer prevention and control programs in the country depends on the construction of indicators, which can be provided by the information from the PBCR.

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ETHICS COMMITTEE IDENTIFICATION/APPROVAL NUMBER

Ethics Committee of Hospital Universitário Júlio Muller: opinion number 3,48,183 of 11/20/2018; Ethics Committee of the Mato Grosso Health Department; opinion number 3,263,744 from 04/12/2019.

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