

Incidence, mortality and survival of prostate cancer in two municipalities with a high human development index in Mato Grosso, Brazil

Incidência, mortalidade e sobrevida do câncer de próstata em dois municípios com alto índice de desenvolvimento humano de Mato Grosso, Brasil

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ABSTRACT: *Objective:* To analyze the incidence, mortality and survival of prostate cancer in Cuiabá and Várzea Grande, Brazil from 2000 to 2016. *Methods:* Data from the Population-based Cancer Registry and the Mortality Information System were used. Mortality and incidence trends were analyzed using joinpoint regression models by age group. Survival analyses were performed using the Kaplan-Meier method, and hazard ratio was estimated by age group. *Results:* From 2000 to 2016, 3,671 new cases and 892 deaths for prostate cancer were recorded. The average incidence and mortality rates were 87.96 and 20.22 per 100,000, respectively. Decreasing incidence trend was noted for all age groups from 2006 to 2016 (APC=-3.2%) and for men with 80+ years of age from 2000 to 2016 (APC=-3.0%), and increasing mortality trend for men 60-69 years of age from 2000 to 2009 (APC=3.2%). The specific five-year survival rate for prostate cancer was 79.6% (95%CI 77.2-81.9), and the rate decreased with advanced age (HR=2.43, 95%CI 1.5-3.9, for those 70 to 79 years old and HR=7.20, 95%CI 4.5-11.5, for those 80 or older). *Conclusion:* The incidence rate of prostate cancer showed a decreasing trend from 2006 for all age groups; the mortality rate was stable in that period, and worse prognosis was observed in men 70 years or older.

Keywords: Prostate cancer. Incidence. Mortality. Survival.

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RESUMO: *Objetivo:* Analisar a incidência, a mortalidade e a sobrevida por câncer de próstata em Cuiabá e Várzea Grande, no período de 2000 a 2016. *Métodos:* Foram utilizados os dados do Registro de Câncer de Base Populacional e do Sistema de Informações sobre Mortalidade. Para a análise de tendência da incidência e mortalidade, foi utilizada a regressão por *Joinpoint* segundo faixa etária. Para estimar a probabilidade de sobrevivência foi utilizado o método de Kaplan-Meier e, para avaliar a associação com a faixa etária, foi estimado o *hazard ratio* (HR). *Resultados:* De 2000 a 2016, registraram-se 3.671 casos novos e 892 óbitos por câncer de próstata. A média das taxas no período (100.000 habitantes) foi de 87,96 para incidência e 20,22 para mortalidade. Verificou-se tendência decrescente da taxa de incidência para todas as idades de 2006 a 2016 (variação percentual anual — APC=−3,2%) e para homens com 80 anos ou mais de 2000 a 2016 (APC=−3,0%), bem como tendência crescente da taxa de mortalidade nos homens de 60–69 anos de 2000 a 2009 (APC=3,2%). A probabilidade de sobrevida específica em cinco anos foi de 79,6% (intervalo de confiança — IC95%: 77,2; 81,9) e diminuiu com o aumento da faixa etária (HR=2,43; IC95%: 1,5; 3,9 para aqueles de 70 a 79 anos e HR= 7,20; IC95%: 4,5;11,5 para aqueles de 80 anos ou mais). *Conclusão:* A taxa de incidência de câncer de próstata apresentou tendência de decréscimo a partir de 2006 para todas as idades, a taxa de mortalidade foi estável no período e o pior prognóstico foi observado em homens com 70 anos ou mais. *Palavras-chave:* Câncer de próstata. Incidência. Mortalidade. Sobrevida.

INTRODUCTION

According to the Global Cancer Statistics (GLOBOCAN), excluding non-melanoma skin cancer, it was estimated in the world for the year 2020, that there were 19.3 million new cases of cancer and 9.9 million related deaths, where 10.1 million (52.3%) and 5.5 million (55.5%), respectively, were in men. Prostate cancer has an estimated risk ranging from 6.3 to 83.4/100,000, with higher levels in China and Eastern European countries such as Belarus, Bulgaria and Slovakia¹.

In Brazil, in 2020, there were 98,000 new cases of prostate cancer¹. In 2019, in Brazil, it was the second leading cancer-causing death in men, with 15,983 deaths². A study that analyzed survival in 71 countries found that in Brazil, this type of cancer had a five-year survival rate of 92.8% during the 2000–2004 quadrennium, 94.8% in 2005–2009 and 94.1% in 2010–2014³.

There are some well-known risk factors for the development of prostate cancer that may explain its incidence, including advanced age (due to their slow growth, small prostate cancers may remain unknown), ethnicity (some studies show that black men have a higher incidence than white men) and hereditary origin (having a family history of prostate cancer increases the risk of developing it)^{4,5}.

It should be noted that cancer mortality trends result from previous trends in incidence and survival, and these three indicators are summary measures that provide instantaneous information on a long-term, that is, time-dependent, process. Thus, the joint analysis of the three indicators has the potential to provide a clearer picture of the progress of a particular type of cancer than any isolated measure⁶.

The objective of the study was to analyze the incidence, mortality and survival for prostate cancer in the cities of Cuiabá and Várzea Grande, Brazil from 2000 to 2016.

METHODS

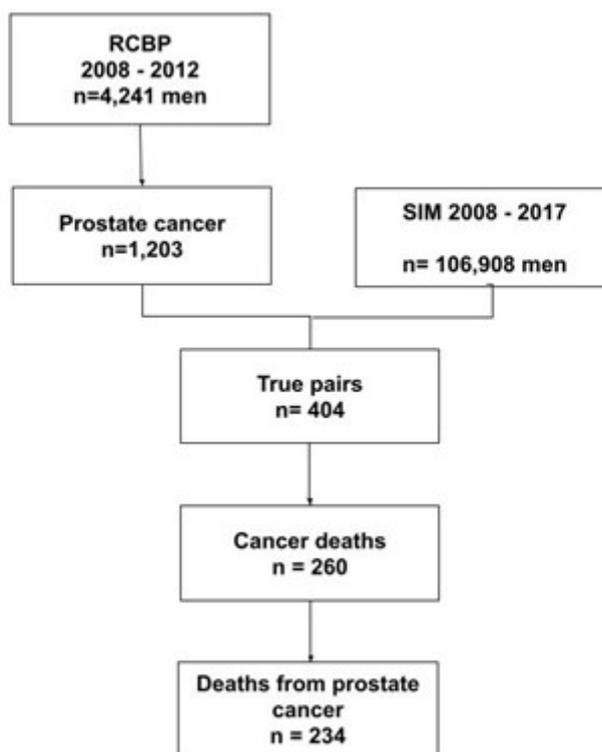
This was a study on the incidence, mortality and survival of prostate cancer in the two most populous cities of Mato Grosso State, Cuiabá and Várzea Grande. In 2010, Cuiabá had a population of 551,098 inhabitants (48.8% males), a population density of 157.66 inhab./km² and a human development index (HDI) of 0.785. Várzea Grande, in turn, had a population of 252,596 inhabitants (52.5% males), a population density of 240.98 inhab./km² and an HDI of 0.734⁷.

The municipalities of Cuiabá and Várzea Grande were selected because of the availability of incidence data that were obtained from the Population-Based Cancer Registry (RCBP) of Cuiabá, considering the period from 2000 to 2016, available on the RCBP system website (BasepopWeb), developed by the José Alencar Gomes da Silva National Cancer Institute (INCA). The data from the Cuiabá RCBP cover Cuiabá and Várzea Grande and those corresponding to the period from 2008 to 2016 were updated through the extension project “Surveillance of Cancer and its associated factors: updating of population-based and hospital records”, in partnership with the Mato Grosso State Health Department (SES-MT).

The source of data on deaths that occurred between 2000 and 2017 was the Mortality Information System (SIM), data provided by SES-MT, while the population data were obtained from the Census Demographics of 2000 and 2010, and for the intercensal periods, population estimates obtained from the Information Technology Department of the Unified Health System were used⁷.

Incidence and mortality rates (per 100,000 inhabitants) for prostate cancer (C61 in chapter II of the 10th edition of the International Statistical Classification of Diseases and Related Health Problems) were calculated for each year between 2000 and 2016. Specific crude rates were obtained for each age group using ten-year intervals and standardized by age, using the direct method, considering the world standard population proposed by Segi⁸ and modified by Doll et al.⁹.

For the analysis of specific five-year survival, new cases of prostate cancer from 2008 to 2012 and related deaths from 2008 to 2017 were considered. The period for men to enter the cohort was from January 1, 2008 to December 31, 2012, with follow-up until December 31, 2017, the date established as the end of the study. These periods were selected on the basis of availability of data from the RCBP and SIM and the possibility of a relationship between them, considering a maximum time of five years between diagnosis and death. The probabilistic relationship of the bases (Figure 1) was carried out with the LinkPlus software, using the variables name of the individual and mother's name, taking into account the first name and date of birth. Deaths from prostate cancer were considered as failure, and loss of



RCBP: Population-based Cancer Registry; SIM: Mortality Information System.

Figure 1. Flowchart of the probabilistic relationship between population-based prostate cancer records from 2008 to 2012 and mortality from 2008 to 2017, in Cuiabá and Várzea Grande, 2000 to 2016.

follow-up and death from other causes were considered as censor. The five-year survival time in months was obtained by the difference between the date of death and the date of diagnosis of prostate cancer.

Analysis of incidence and mortality trends was with joinpoint regression, using the calendar year as the regression variable. Serial autocorrelation was determined using the Durbin-Watson test, and the model of correlated errors was used for the analysis of incidence, The annual percent change (APC) and average annual percent change (AAPC), i.e., weighted geometric mean of the different APCs with weight equal to the size of the follow-up for each time interval, were calculated^{10,11}. The analysis by age group was performed from 50 years old or more, because in joinpoint regression, the series cannot have null values. The Kaplan-Meier method was used to determine the probability of specific survival at five years in general and by age group (<50 years; 50 to 59 years; 60 to 69 years; 70 to 79 years; 80 years or more). The hazard ratio (HR) and 95% confidence intervals were estimated using

the Cox regression model. The assumption of the Cox model was confirmed by Schoenfeld residuals. Analyses were performed using the Joinpoint Regression Program, version 8.3.6.1 (Statistical Research and Applications Branch, National Cancer Institute, Bethesda, MD, USA) and STATA, version 16.0. A significance level of 5% was adopted.

This study was part of the research project titled “Cancer and its associated factors: analysis of population-based and hospital records”, approved by the Ethics Committee of the Hospital Universitário Júlio Muller (CEP-HUJM) under approval No. 3.048.183, of November 20, 2018, and by the Research Ethics Committee of the Mato Grosso State Health Department (SES-MT) under approval No. 3.263.744, of April 12, 2019. The project had the advantage of partnering with the Ministry of Public Work 23rd Region and receiving funding, from July 2019 to July 2023.

RESULTS

In the period from 2000 to 2016, 3,671 new cases of prostate cancer were recorded in the municipalities studied, 74% of which were in Cuiabá. As for the distribution by age group, 2.6% were men under 50 years old, 15.2% for 50 to 59, 37% for 60 to 69, 32% for 70 to 79 and 13.3% for 80 or older. Regarding mortality, there were 892 deaths (68% in Cuiabá), with 0.6% in the 40 to 49 age group, 5.5% in the 50 to 59 group, 21.6% in the 60 to 69 group, 38.2% in the 70 to 79 group and 33.9% for those aged 80 years or over.

The average age-standardized incidence rates of prostate cancer in the period was 87.96 (per 100,000 inhabitants). The highest rates were recorded in 2004 (105.87), 2006 (110.56) and 2007 (107.52), and from 2006 onwards, there has been a steady decline, reaching 59.79 per 100,000 inhabitants in 2016. In the analysis by age group, the highest incidence rates in the period were observed between 60 and 69 years and between 70 and 79 years (Figure 2).

As for mortality, a mean age-standardized rate of 20.22 (per 100,000 inhabitants) was observed, with less variation over the period, from 27.71 in 2000 to 22.93 in 2016. The differences observed between age groups were smaller than those observed for incidence, with much higher values from 60 years onwards (Figure 2).

The age-standardized incidence rate for prostate cancer showed a stable trend until 2006 and a decrease between 2006 and 2016 (APC=-3.2%; 95%CI -6.1--0.3). In the analysis by age group, there was a downward trend only among those aged 80 years or older and in the period from 2000 to 2016 (APC=-3.0%; 95%CI -5.7--0.3). The trend of the age-standardized mortality rate, considering all of them, was stable during the period studied. Regarding age groups, only men 60 to 69 years showed an increasing trend between 2000 and 2009 (APC=3.2%; 95%CI 0.2--6.2), followed by stability between 2009 and 2016 (Table 1).

Between 2008 and 2012, 1,203 men were diagnosed with prostate cancer. When followed-up for five years, 234 died from the disease (Figure 1). The specific five-year survival of men diagnosed with prostate cancer in the study period was 79.6% (95%CI 77.2--81.9).

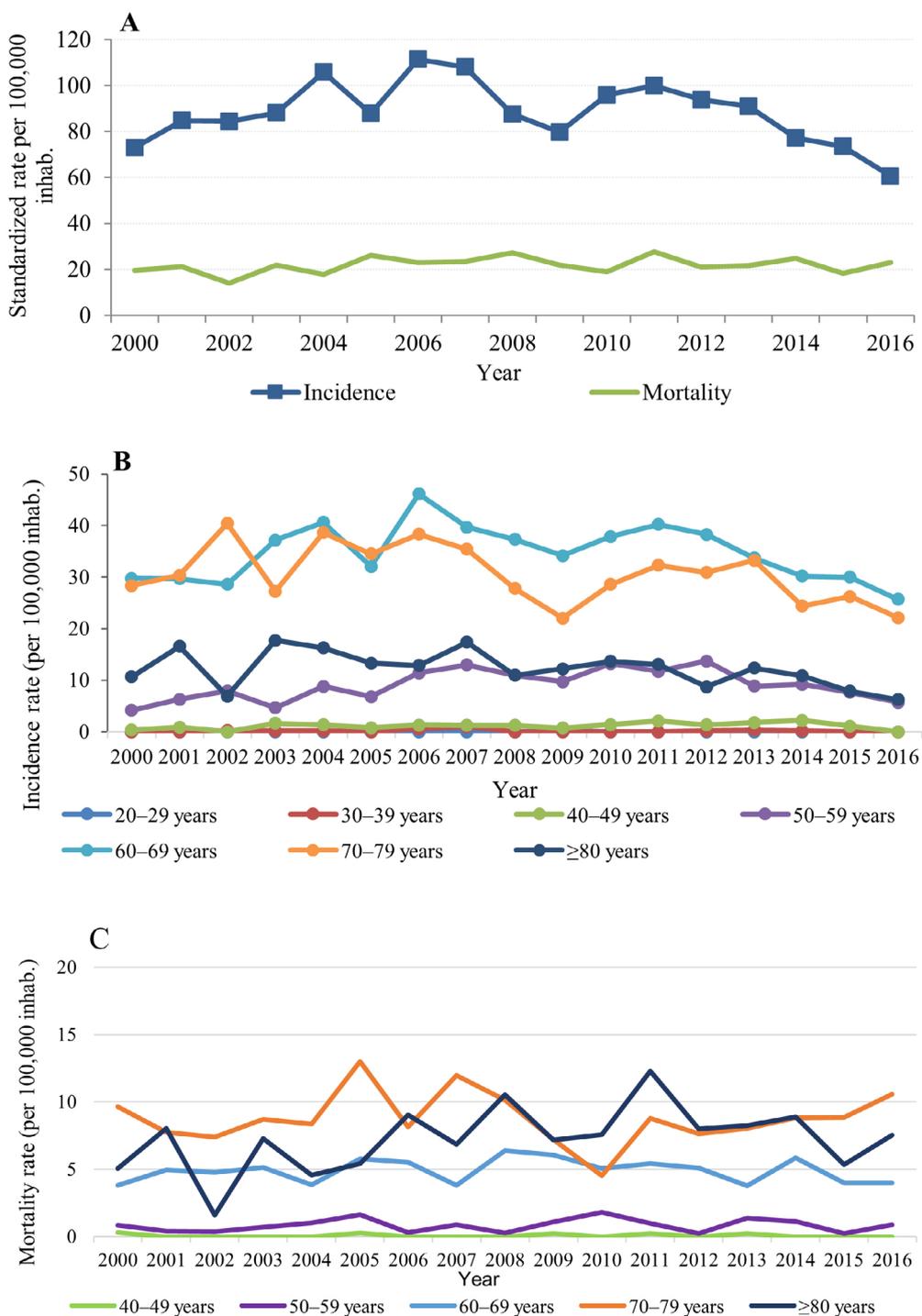


Figure 2. Standardized prostate cancer incidence and mortality rate for the total population (A) and incidence rate (B) and mortality rate (C) by age group, Cuiabá and Várzea Grande, 2000 to 2016.

Table 1. Trends in prostate cancer incidence and mortality rates according to age group between 2000 and 2016, Cuiabá and Várzea Grande.

Trend	Year	APC	95%CI	AAPC	95%CI
Incidence					
Age group					
50 to 59 years	2000–2016	2.2	(-1.6–6.2)	2.2	(-1.6–6.2)
60 to 69 years	2000–2016	-0.5	(-2.5–1.5)	-0.5	(-2.5–1.5)
70 to 79 years	2000–2016	-2.1	(-4.1–0.0)	-2.1	(-4.1–0.0)
80 years or older	2000–2016	-3.0*	(-5.7--0.3)	-3.0*	(-5.7--0.3)
All ages	2000–2006	5.4	(-2.2–13.5)	-0.1	(-3.1–3.0)
	2006–2016	-3.2*	(-6.1--0.3)		
Mortality					
Age group					
50 to 59 years	2000–2016	0.7	(-6.6–8.5)	0.7	(-6.6–8.5)
60 to 69 years	2000–2009	3.2*	(0.2–6.2)	-0.2	(-2.7–2.2)
	2009–2016	-4.5	(-9.1–0.4)		
70 to 79 years	2000–2007	5.8	(-0.7–12.6)	1.8	(-6.9–11.2)
	2007–2010	-17.0	(-49.8–36.9)		
	2010–2016	7.8	(-0.7–16.9)		
80 years or older	2000–2016	3.9	(-0.6–8.6)		
All ages	2000–2016	1.0	(-0.8–2.7)	1.0	(-0.8–2.7)

APC: annual percent change; AAPC: average annual percent change; 95%CI: 95% confidence interval; *(p<0.05).

The probability of specific survival at five years decreased with increasing age, being 96.3% (95%CI 76.5–99.5) in men younger than 50 years and 46.0% (95%CI 37, 2–54.4) in those aged 80 or over (Figure 3). The risk of death was statistically higher among those aged 70 to 79 years (HR=2.43; 95%CI 1.5–3.9) and 80 years or older (HR=7.20; 95%CI 4.5–11.5) when compared to those 50 to 59 (Table 2).

DISCUSSION

The results of the present study reveal that in the period between 2000 and 2016 in Cuiabá and Várzea Grande, the incidence rate of prostate cancer showed a decreasing trend from 2006 for all ages and among the elderly 80 and over. As for the mortality rate, specifically in the age group 60 to 69 years old, there was an upward trend between 2000 and 2009,

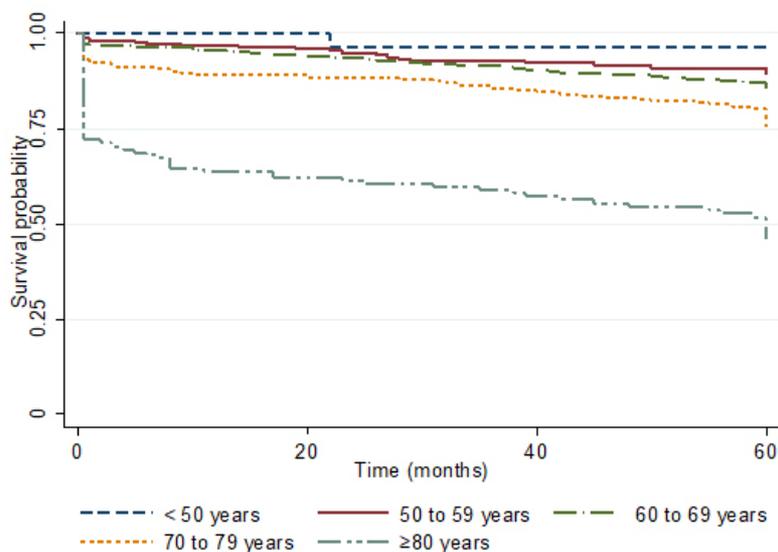


Figure 3. Prostate cancer survival curve by age group, Cuiabá and Várzea Grande, 2008 to 2012.

Table 2. Cases, deaths and survival of prostate cancer in general and by age group, Cuiabá e Várzea Grande, 2008 to 2012.

	New cases		Deaths		Survival - 60 months	HR (95%CI)
	n	%	n	%	(95%CI)	
Age group						
<50 years	28	2.4	1	3.6	96.3 (76.5–99.5)	-
50 to 59 years	219	18.6	23	10.5	89.4 (84.5–92.8)	1.00
60 to 69 years	447	38.0	63	14.1	85.5 (81.8–88.5)	1.39 (0.9–2.2)
70 to 79 years	334	28.4	74	22.2	75.6 (70.3–80.1)	2.43 (1.5–3.9)*
80 years or older	148	12.6	73	49.3	46.0 (37.2–54.4)	7.20 (4.5–11.5)*
All ages	1,203	28.4	234	19.4	79.6 (77.2–81.9)	

HR: hazard ratio; 95%CI: 95% confidence interval; *($p < 0.05$).

but that was not enough to change the general trend of stability observed throughout the series. The specific five-year survival was 79.6% considering all ages and showed a negative association with age, such as lower survival from 70 years onwards.

The mean incidence rate observed in this study (87.96 per 100,000 inhabitants) was similar to that found in more developed regions or countries^{1,12}. According to a systematic

review carried out by Dasgupta et al.¹³, men who live in socially favored and urban areas generally have greater access to the prostate-specific antigen (PSA) test, used for the diagnosis of the disease, which contributes to the increased incidence rates for prostate cancer. This may explain, at least in part, the high incidence rates of prostate cancer in the cities studied, especially among the elderly between 60 and 79 years, since Cuiabá and Várzea Grande are highly urbanized and enjoy greater availability of specialized services and diagnostic support.

Regarding the incidence trend, considering all ages, the rate was decreased from 2006. A study that evaluated the burden of prostate cancer based on data from population-based registries in 13 countries in Central and South America found for Brazil a growing trend of 2.8% between 2003 and 2007, explaining this result as a possible difference in the means of diagnosis, access to health and early detection¹⁴. Another study evaluated the temporal trends (from 1980 to 2012) in the incidence of prostate cancer in 44 countries based on population records and found a decrease or stability of rates in many of them, especially in developed countries¹². In Brazil, a similar result was found with data from the cancer registry of Goiânia State: the incidence rate of prostate cancer showed a reduction of 4.1% in the period of 2008 to 2012.

For the elderly 80 and older, there was a downward trend in the incidence rate in the period. Analogously to the findings of the present study, Etxeberria et al.¹⁵, reported for the period of 1975 to 2013, that only men over 75 years old had a reduced incidence rate of prostate cancer. Global estimates show that across all age groups, the incidence began to decline in 2008, with the biggest drop between 2011 and 2012, which might have been associated with reduced PSA¹ screening. Also, in a study carried out in Estonia (1995–2014), it was observed that most of those diagnosed with prostate cancer were between 65 and 74 years old, and that the incidence of cancer increased until 2011, stabilizing in the following years, probably thanks to increased PSA testing¹⁶.

However, there is no consensus on whether the PSA test is indicated as a screening strategy for prostate cancer since studies demonstrate an imbalance between the possible risks and benefits of performing this test¹⁷⁻¹⁹. In Brazil, INCA does not recommend the use of PSA for screening, and if the man wishes to have this test done, individual circumstances and professional opinion must be observed, highlighting the benefits and harms of this strategy¹⁷.

The nature of the mortality rate in the cities studied differs from that observed in all of Brazil in the period of 1980 to 2010, in which the mortality rate from prostate cancer showed an upward trend²⁰. A similar pattern of stability was observed in other early series, such as those from 1996 and 2006²¹ and from 1990 to 2015²². In the Central-West region, for the set of inland municipalities, a growing trend was observed in the period of 1980 to 2017 and a drop in rates for the capitals between 1997 and 2017²³. Differences in mortality trends can be attributed to methodologies used to calculate rates, such as the redistribution of ill-defined causes²⁰⁻²³.

In the world, the temporal trend of reduced mortality from this type of cancer has been observed in high-development countries, such as Ireland, France and Australia (-5%)

and Germany and the United Kingdom (-2.0%)¹². These decreases have been associated, above all, with early detection and advances in forms of treatment (radical prostatectomy for localized tumors and increased hormone therapy, among others) and greater access to them. However, the contribution of PSA screening in reducing mortality is still controversial, as PSA level tends to increase in benign prostatic hyperplasia and not only in prostate cancer. In addition, PSA results are heterogeneous, and there is no unanimity in its use by the medical community^{13,17-19}.

For the age group 60 to 69 years, there was an inflection point in the trend of the mortality rate from prostate cancer, which showed a rise from 2000 to 2009 and stability from 2009 to 2016, and for the other age groups, there was stability. A result different from that observed for the whole of Brazil and for the Central-West region in the period of 1980 to 2010²⁰, which showed a growing trend for all age groups from 60 years onwards. The improvement in the mortality indicator for this age group may indicate an improvement in access to early cancer diagnosis and treatment at an early stage. A study carried out in the Central-West region²⁴ between 2005 and 2009 found a negative correlation between prostate cancer mortality rate and the proportion of the population that had annual medical check-ups and the proportion of the population covered by health insurance, which may somehow reflect the better coverage of the health care network and access.

Despite the stability, it is noteworthy that the mortality rate level was similar to that observed in less developed regions^{1,12} and exceeds that observed for the Central-West Region in the period of 2000 to 2011 and for the State of Mato Grosso between 2000 and 2011²⁰. Higher mortality rates from prostate cancer may reflect, among other factors, the underlying incidence trends, the influence of harmful health behaviors and the precariousness of the cancer care network for the population in general^{4,5,25}. Considering the local reality, it is possible that the stability of the mortality rate at higher levels is associated with the difficulties of diagnosis and treatment and the precariousness of the care network, which still shows structural problems, which can hinder the time needed for treatment^{22,23}.

The specific survival of prostate cancer in Cuiabá and Várzea Grande was higher than that observed in all of Brazil, that is 70%, according to data from Brazil's National Oncology Base (Base Onco) from 2002 to 2003 and in the different regions: South (62%), Central-West (68%), North and Northeast (71% in both) and Southeast (72%)²⁶. In developed countries, such as the United States, net survival up to five years after diagnosis was 96.7%²⁷, and survival in the 2010–2014 quadrennium was 90.2% in Austria and 93.6% in Canada²⁸. This result can be attributed to advances in the diagnosis and treatment of prostate cancer, which may result in a higher cure rate or survival time.

In a population-based cohort study conducted in central Denmark, the estimated five-year survival was 65% and, when assessing the age group, a reduction in this indicator was noted from 70–79 years onwards²⁹. Regarding age, it is known that the higher the age group, the greater the risk of developing cancer and having a worse prognosis of survival. Likewise, when analyzing the age group, a study carried out in the United States based on the Surveillance, Epidemiology, and End Results Program (SEER) database,

with 24,054 patients, observed that the worst survival results were found in men 65 or over³⁰. In addition, other studies also show that the greater the age, the lower the probability of patient survival³¹⁻³³.

Survival is the parameter used to evaluate the results of cancer diagnosis and treatment, with observations obtained from health records. Although in Brazil there is little information available about survival in cancer patients, survival studies are important in assessing the distribution of resources and in identifying the main prognostic factors in a given region and population³⁴.

As limitations of the research, we point out the lack of population-based data on staging at the time of diagnosis of prostate tumors in the state of Mato Grosso, which could raise hypotheses about early detection and advances in the treatment of the disease. Furthermore, the absence of information on the life table for the municipalities of Cuiabá and Várzea Grande made it impossible to calculate net survival^{35,36}.

The coverage and quality of SIM data have improved over the years^{37,38}. In Cuiabá and Várzea Grande, ill-defined causes accounted for 4.76% of all deaths, rising from 9.51% in 2000 to 2.73% in 2016; in addition, their distribution was similar between age groups³⁹. For prostate cancer, the Cuiabá RCBP showed, for all the years analyzed, a microscopic verification greater than 70% and a percentage of cases registered only by the death certificate less than 20%, according to the International Agency for Cancer Registry⁴⁰.

In the period from 2000 to 2016, there was a fluctuation in incidence rates, which might have been related to data quality, differences in diagnostic practice and death certification procedures^{14,41}. Improvements in the coverage and quality of the RCPB and SIM are needed to provide robust statistics on the cancer burden.

The present study only evaluated age, but other factors also explain incidence, mortality and survival, such as ethnicity, heredity, marital status, place of residence and type of treatment⁴²⁻⁴⁵. Despite the limitations, the relevance of using a recent historical series and the possibility of simultaneously evaluating the indicators of incidence, survival and mortality are not extinguished.

This study made it possible to describe the decreasing trend in the incidence and the stability of mortality and also to estimate the survival of men with prostate cancer in Cuiabá and Várzea Grande. It was possible to identify that the age groups 60 to 69 years and 70 to 79 years were the ones with the highest incidence and mortality rates, respectively. In turn, those aged 70 years and over had the worst survival probability. Knowledge of incidence, mortality and survival contributes to understanding the magnitude of cancer and to targeting prostate cancer prevention and control measures.

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ETHICAL APPROVAL

Ethics Committee of Hospital Universitário Júlio Muller (CEP-HUJM), Certificate of Presentation for Ethical Assessment (CAAE) 98150718.1.0000.8124, approval No. 3,048,183, of November 20, 2018, and of the Research Ethics Committee of Mato Grosso State Health Department (SES-MT), CAAE: 98150718.1.3003.5164, approval No. 3.263.744, of April 12, 2019.

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