Future burden of prostate cancer mortality in Brazil: a population-based study

Projeções de mortalidade por câncer de próstata no Brasil: um estudo de base populacional

Proyecciones de mortalidad por cáncer de próstata en Brasil: un estudio de base poblacional

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Abstract

Prostate cancer mortality projections at the nationwide and regional levels to the year 2025 are carried out in this ecological study that is based on an analysis of Brazilian trends between 1996 and 2010. The predictions were made for the period 2011-2025 utilizing the Nordpred program based on the period of 1996-2010, using the age-period-cohort model. A significant increase was observed in the Brazilian rates between 1996 and 2006, followed by a non-significant decrease. The projections indicate a decrease in rates at a national level as well as for the Central, South and Southeast regions. Increases are expected for the North and Northeast regions. In conclusion, a reduction in the mortality rates for prostate cancer in Brazil is expected to the year 2025, as well as for the Central, South and Southeast regions. However, an increase in the absolute number of deaths in all regions is expected due to the anticipated aging of the population.

Prostatic Neoplasms; Mortality; Population Studies in Public Health

Resumo

Este estudo ecológico realiza projeções de mortalidade por câncer de próstata no Brasil e suas regiões até o ano 2025, com base nas tendências observadas no período de 1996 a 2010. As projeções foram realizadas para o período 2011-2025 mediante o programa Nordpred, baseado no período 1996-2010, usando o modelo idade-período-do-coorte. Observou-se um aumento significativo das taxas no Brasil entre 1996 e 2006, seguido de um descenso não significativo. As projeções indicam uma diminuição das taxas em nível nacional e nas regiões Centro-oeste, Sul e Sudeste, enquanto nas regiões Norte e Nordeste se espera um incremento das taxas. É esperada uma redução das taxas de mortalidade por câncer de próstata até o ano 2025 no Brasil em conjunto, assim como nas regiões Centro-oeste, e Sul e Sudeste, e um incremento nas regiões Norte e Nordeste. Contudo, prevê-se um aumento do número absoluto de mortes pela doença em todas as regiões devido ao envelhecimento populacional previsto no país.

Neoplasias da Próstata; Mortalidade; Estudos Populacionais em Saúde Pública

Introduction

Prostate cancer is considered globally to be the most prevalent and the sixth most mortal type of cancer in men. In Brazil, prostate cancer is the most common type of cancer in men and, in terms of the number of deaths, occupies second position, after lung cancer. The incidence rate is approximately 50 per 100,000 inhabitants, with more than 40,000 cases diagnosed annually. 14,500 deaths by prostate cancer are registered every year in Brazil, with rates of 16 deaths per 100,000 inhabitants per year, slightly fewer than lung cancer [1].

It has been observed that prostate cancer mortality rates have not increased at the same rate as incidence rates, probably due to improvements in treatment associated with diagnosis measures [2]. The prostate-specific antigen (PSA) test was responsible, principally after the 1980s, for causing increases in incidence and survival rates for prostate cancer, as a consequence of early diagnosis [3,4]. However, the prevalence of PSA testing is relatively low in less developed countries, where Western influenced lifestyles have caused increases in prostate cancer rates [5]. In the case of Brazil, the adjusted mortality rates increased by approximately 70% from the early 1980s to the start of the 21st century [6].

The International Agency for Research on Cancer (IARC) predicts that the number of deaths by prostate cancer in Brazil will almost double by the year 2025 [1]. However, these projections are limited, as there are no age- or region- specific data available. The detailed study presented herein is very important in a country with a high proportion of inequalities and profound regional differences such as Brazil. Furthermore, trend analysis and cancer mortality projections are very useful for planned interventions such as screening programs and therapy advances, as well as to quantify the probable burden of cancer in the future.

The objective of this study is to carry out projections of prostate cancer mortality in Brazil and its regions until the year 2025, based on the trend analysis for the period 1996-2010.

Method

This is an ecological study for which the data were obtained from the Brazilian Ministry of Health web page (Departamento de Informática do SUS. *Informações de Saúde. Estatísticas Vitais*. http://www2.datasus.gov.br/DATASUS/index.php?area=0205, accessed on 02/Jul/2013) along with population data from 1996 to 2010.

All deaths registered as prostate cancer (ICD-10 code: C61) were included in the analysis. The quality of death certificates is comparable to those of developed countries, and the proportion of ill-defined death causes is lower than 13% for the overall country and lower than 6% for the capital cities (Global Health Observatory Data Repository, World Health Organization. *Demographic and Socioeconomic Statistics: Census and Civil Registration Coverage. Data by Country*. http://apps.who.int/gho/data/node.main.121, accessed on 23/Apr/2014) [7].

Analyses of mortality and predictions were performed by calculating crude and adjusted rates, expressed per 100,000 persons per year. The adjusted mortality rates were calculated by the direct method using the world standard population as reference for Brazil and its five regions (North, Northeast, Central, Southeast, and South). Adjusted rates for each year were calculated to study trends using the Joinpoint Regression Program (National Cancer Institute, Bethesda, USA). Crude rates were calculated, as well as the confidence intervals for the adjusted rates, to a confidence level of 95%. The objective was to determine whether the estimated trends were statistically significant or not. Joinpoint analysis identifies the moment in which changes in trends occur and calculates the annual percentage change (APC) in each segment. The analysis starts with a minimum number of *joinpoints* and compares whether one or more are significant to the model [8]. Birth-cohort analysis was carried out graphically and dividing data in five-year periods.

Predictions were made for the periods 2011-2015, 2016-2020 and 2021-2025, using the age-period-cohort model of the Nordpred program (Cancer Registry of Norway, Oslo, Norway), written in the statistical program R. Data were pooled into five-year blocks and the age group limit considered for analysis was the one with more than 10 cases in the combined periods. Predictions were made by geographical region and the pooled results will be referred to as total presented by age ranges (0-54, 55-74 and ≥ 75 years of age). As prostate cancer is more common in individuals over the age of 55, age groups were employed following Moller et al. [9]. Changes in the annual number of cases of the last predicted period relating to the last observed period (2006-2010) were calculated by geographical region. The proportion of this change occurring in terms of risk or change in population (size and population structure) was also calculated. These two components can be different from zero and present a positive or negative direction. The calculation can be expressed as follows [9,10]:

$$\Delta_{tot} = \Delta_{risk} + \Delta_{pop} = (N_{fff} - N_{off}) + (N_{off} - N_{ooo})$$

where: Δ_{tot} = total change, Δ_{risk} = change in function of risk, Δ_{pop} = change in function of population, N_{ooo} = number of observed cases, N_{fff} = number of predicted cases and N_{off} = number of expected cases when increasing the mortality rates in the observed period.

The Brazilian and regional population used in the projections were obtained from the website of the Brazilian Institute for Statistics and Geography (IBGE) [11].

Results

In the period 1996-2010, 139,349 deaths were registered in the Brazilian mortality database as being from prostate cancer. The Joinpoint analysis shows an initial increase in mortality rates, followed by a stable plateau after the year 2006. The same trend is found by region, with an exception for the North region, where significant increases were verified for the entire period. In the remaining regions, the initial increase occurred until the years 2005 and 2006, followed by a decrease in rates. However, the APC were not statistically significant in the second segment (Table 1).

Trend analysis for mortality by birth cohort shows an increment in rates for individuals in the age groups of 75-79 and 80-84 years of age, with a change in trends and stability for younger cohorts starting from 1933 (Figure 1).

Table 2 presents the total number of deaths and death by age group, along with rates that are adjusted to the world population, during the observed and projected periods, for Brazil and its geographic regions. For the projected period (2011-2025) an increase in the absolute number of deaths is predicted, reaching a total number of 236,086 cases. During the most recent period

under observation (2006-2010), 59,647 deaths were registered, and 91,420 cases are expected for the last projected period (2021-2025). When comparing the most recent period with the last projected period, an increase of 53.3% is predicted in the number of deaths, with 60% of these being as a result of population changes, and a reduction of 6.8% is also expected in death risk by prostate cancer.

Figure 2 shows a comparison of prostate cancer mortality rates: observed adjusted *versus* projected for the five regions of Brazil. The predicted increase can be observed in the adjusted mortality rates for the North and Northeast regions, attributed both to increases in risk as well as to population changes. Decreases are predicted for the remaining regions (South, Southeast and Central) due to reductions in risk.

Discussion

From 1996 onwards, a significant increase in Brazilian prostate cancer mortality rates was observed, followed by a slight decrease in the period after 2006. The projections of this study indicate decreases in mortality rates from prostate cancer in Brazil, as well as in the South, Southeast and Central regions, until the year 2025. In contrast, an increase is predicted in the rates of less developed regions of the country, in the North and particularly in the Northeast region. Nevertheless, it must be mentioned that it is expected that the absolute number of deaths from prostate cancer increases in all regions due to the population aging process in Brazil. This increase in mortality is predicted to be smooth in the South and Southeast regions, as a consequence of the reduction in risk or increased effectiveness of early diagnosis, while for the North and Northeast regions

Table 1

Number of deaths, annual percentage change (APC), 95% confidence intervals (95%CI) and joinpoint year by geographical region.

Geographical region	Deaths	APC1	95%CI	Joinpoint	APC2	95%CI
North	5,106	3.9 *	2.9; 4.8	-	-	-
Northeast	31,633	7.3 *	5.5; 9.0	2006	-2.9	-26.4; 28.1
Central	8,742	2.2	-0.2; 4.8	2006	-2.7	-8.4; 3.3
Southeast	67,680	0.9	-0.8; 2.6	2005	-4.1	-7.9; 0.0
South	26,191	1.9	-0.1; 3.9	2005	-4.1	-8.7; 0.7
Brazil	139,349	2.5 *	1.4; 3.6	2006	-2.3	-6.6; 2.1

* Statistically significant values (p-value < 0.005).
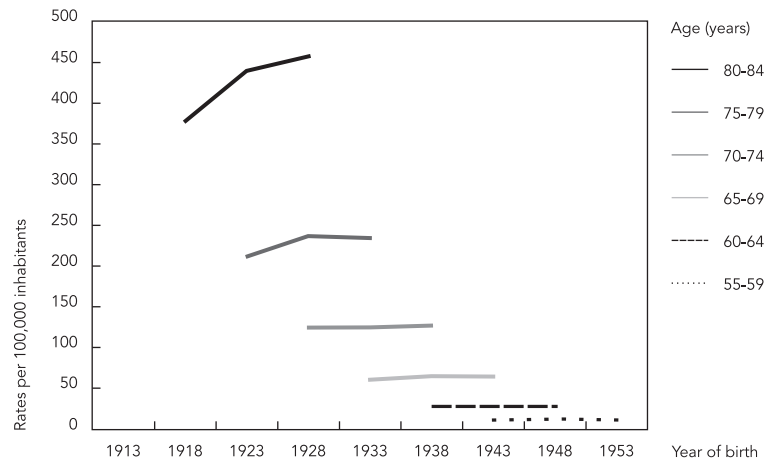
Figure 1

Mortality trends by birth cohort.

Table 2

Observed and predicted average number of deaths by age and crude rate (CR), world age-standardized rates (ASW) and 95% confidence interval (95%CI) in Brazil.

Geographic region	Observed				Predicted	
	1996-2000	2001-2005	2006-2010	2011-2015	2016-2020	2021-2025
North						
Age (years)						
0-54	53	63	59	133	178	215
55-74	478	686	967	1,827	2,339	2,815
≥ 75	524	809	1,462	2,978	3,876	4,831
Total	1,055	1,558	2,488	4,937	6,393	7,861
CR	3.4	4.3	6.4	12.3	15.4	18.5
ASW (95%CI)	7.1 (6.0; 8.0)	8.2 (7.2; 9.1)	10.1 (9.1; 10.9)	11.9 (11.1; 12.6)	12.9 (12.1; 13.6)	13.2 (12.5; 13.9)
Northeast						
Age (years)						
0-54	192	193	299	550	718	1,067
55-74	2,613	3,322	5,292	8,471	11,462	13,510
≥ 75	3,345	5,753	10,620	15,771	22,368	28,788
Total	6,150	9,268	16,211	24,792	34,548	43,365
CR	5.4	7.6	12.4	18.0	25.0	30.0
ASW (95%CI)	6.9 (6.5; 7.3)	8.7 (8.3; 9.2)	12.9 (12.4; 13.4)	17.5 (16.9; 17.9)	20.3 (19.8; 20.8)	21.2 (20.8; 21.7)
Central						
Age (years)						
0-54	61	61	88	100	102	103
55-74	968	1,201	1,514	1,805	2,086	2,482
≥ 75	1,081	1,570	2,915	2,865	3,243	3,778
Total	2,110	2,832	3,797	4,770	5,431	6,362
CR	7.6	9.1	11.1	13.4	14.8	16.9
ASW (95%CI)	14.0 (12.6; 15.3)	14.7 (13.4; 16.0)	13.7 (12.7; 14.7)	12.9 (12.1; 13.8)	12.3 (11.6; 13.1)	12.1 (11.3; 12.7)

(continues)

Table 2 (continued)

Geographic region	Observed			Predicted		
	1996-2000	2001-2005	2006-2010	2011-2015	2016-2020	2021-2025
Southeast						
Age (years)						
0-54	408	479	543	419	436	398
55-74	8,111	9,205	9,976	8,897	9,577	11,031
≥ 75	9,792	13,089	16,075	14,742	16,117	18,292
Total	18,311	22,773	26,594	24,059	26,131	29,720
CR	10.8	12.3	13.6	11.7	12.4	13.7
ASW (95%CI)	14.7 (14.2; 12.2)	15.0 (14.5; 15.4)	12.9 (12.5; 13.3)	11.3 (10.9; 11.6)	10.2 (9.9; 10.2)	9.7 (9.4; 9.9)
South						
Age (years)						
0-54	157	168	195	141	120	109
55-74	3,019	3,635	4,024	3,357	3,578	4,008
≥ 75	3,713	4,944	6,332	6,197	6,853	7,689
Total	6,889	8,747	10,551	9,694	10,550	11,805
CR	11.5	13.6	15.5	13.7	14.4	15.7
ASW (95%CI)	15.9 (15.0; 16.8)	17.1 (16.2; 17.8)	14.8 (14.1; 15.4)	13.0 (12.3; 13.6)	11.8 (11.2; 12.3)	11.0 (10.5; 11.5)
Brazil						
Age (years)						
0-54	871	964	1,184	1,183	1,159	1,179
55-74	15,189	18,040	21,773	23,893	27,720	32,050
≥ 75	18,458	26,171	36,690	41,457	49,256	58,191
Total	34,518	45,184	59,647	66,533	78,134	91,420
CR	8.6	10.3	12.8	13.7	15.6	17.8
ASW (95%CI)	12.0 (11.7; 12.3)	13.0 (12.7; 13.3)	13.1 (12.8; 13.3)	13.1 (12.8; 13.3)	12.8 (12.6; 12.9)	12.5 (12.3; 12.5)

the changes in risk and population may almost double the number of deaths by the year 2025.

When analyzing cancer projections two situations must be distinguished, which could influence the number of deaths: changes in death risk by cancer and changes in the exposed population itself. Population changes can occur due to population increases and structural changes [12,13]. In Brazil, the global phenomenon of population aging is picking up speed, due to the quite steep decline in fecundity rates, decreases in mortality, and increases in life expectancy [13]. The number of individuals over the age of 60 is expected to increase by approximately 60% from the period 2006-2010 to 2021-2025 [11]. This trend will particularly affect the case of prostate cancer, as age is known to be one of the main risk factors associated with incidence and mortality from this disease [14,15].
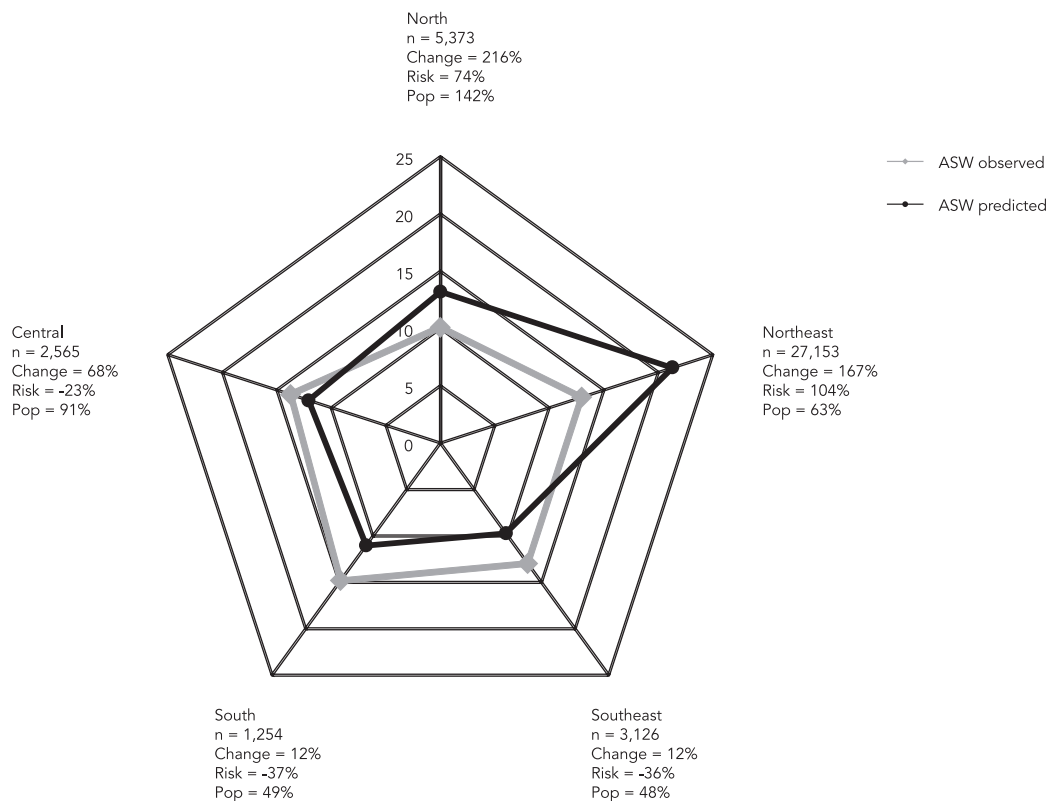
Regarding cancer mortality rates, there are three factors that could exert an influence: changes in risk factors for the development of the disease, screening programs and advances in treatment [16]. Currently it is known that non-modifiable risk factors, such as family-genetic factors

and especially age, play an important role in the development of prostate cancer. However, these factors do not affect the analysis presented herein because this study analyzed age-adjusted rates and at a collective level, where there is a low influence of family-genetic factors. Regarding modifiable risk factors, such as obesity and the consumption of tobacco and alcohol, which have already been established for other types of cancer, the association remains little known for prostate cancer [15]. For this reason, it is not possible to explain the influence of these factors in the regional differences in mortality rates encountered herein.

An explanation for the change from an initial increase to the stable plateau observed in this study could be a result of the improvements in screening programs and therapeutic measures in the more developed regions of Brazil. Prostate cancer screening has not been systematically applied in Brazil, and there is an inequality in the availability of diagnostic tests with regard to socio-demographic and socioeconomic levels. In this way, the difficulty of accessing diagnosis and treatment services for individuals in conditions

Figure 2

World age-standardized rates (ASW), changes in numbers of deaths (n), total change (change), relative change due to risk (risk) and changed population (pop), between 2006-2010 (observed) and 2021-2025 (predicted) of prostate cancer mortality in Brazil.

North
n = 5,373
Change = 216%
Risk = 74%
Pop = 142%

Northeast
n = 27,153
Change = 167%
Risk = 104%
Pop = 63%

Central
n = 2,565
Change = 68%
Risk = -23%
Pop = 91%

South
n = 1,254
Change = 12%
Risk = -37%
Pop = 49%

Southeast
n = 3,126
Change = 12%
Risk = -36%
Pop = 48%

ASW observed
ASW predicted

of poverty could explain the higher prostate cancer mortality rates observed in the low stratum [17]. This difficulty in accessing diagnosis services seems to occur with a greater frequency in the North and Northeast regions, where the projections of this study reveal increasing mortality rates. Therefore some studies show that prostate cancer tracking is less prevalent in men under the age of 70, with less years of schooling, and of low-income [17,18]. An ecological study carried out in Brazil has found that approximately 57% of the individuals with a higher education level related diagnostic practices such as digital rectal exam or PSA, while for individuals with less years of schooling the percentage was only 35% [17].

A pronounced inequity between the regions of Brazil remains regarding access to prostate cancer treatment. The different mortality trends encountered herein can be partially attributed to that fact that therapeutic services are much more limited in less developed regions of Brazil (the North and Northeast). In municipalities in the interior of these areas, Silva et al. [19] have found increases in cancer rates twice as high as those registered in capital cities of the country. In these regions, low-income individuals that use the public health system occasionally suffer as a result of late diagnoses, precariousness of services and tardiness in beginning treatment, which compromises prognostics. In addition, a much higher offer of chemotherapy and radiotherapy services is concentrated in the South and Southeast regions, where there is a higher proportion of individuals who can afford private health plans [18,19].

The evolution observed in the rates of this study for the more developed regions of Brazil is similar to that found in the majority of European

countries and the USA. In these countries, mortality rates have declined during the last two decades, probably due to early diagnoses facilitated by the PSA testing and improvements in prostate cancer treatment [4,5,20]. Such a trend has also been observed in other South American countries, as is the case of Chile and Argentina. Nevertheless, it is worth highlighting that in these countries, the adjusted rates are higher than the Brazilian rates, with changes occurring earlier, at the end of the 1990s (International Agency for Research on Cancer; World Health Organization. *Cancer Mortality Database*. http://www-dep.iarc.fr/whodb/whodb.htm, accessed on 30/Jul/2013) [21,22].

As a limitation of this study, the period for which the projections apply – just 15 years – is short. Regarding the national registry of deaths by cancer in Brazil, it must be mentioned that in the past there were issues with data reliability, particularly in the North and Northeast regions, but improvements have been made since the 2000s [6]. Cancer projections must be considered with caution, as the actual diagnosis and treatment conditions might change in the future, and consequently modify the mortality trends. However, the methods currently used have certified validity and some authors point to small differences of between 10 and 20% in estimations [2].

In conclusion, an initial increase in prostate cancer mortality rates was herein demonstrated, followed by a slight decrease in rates that is predicted to take place until the year 2025 in the entire country. However, in the North and Northeast regions increases in mortality are expected, attributed to changes in risk and the aging of the population. The results of the projections presented herein clearly show the inequities present in prostate cancer mortality rates per geographic region, which must be considered for the development of public policies and for the planning of health services.

Resumen

Este estudio ecológico presenta proyecciones de mortalidad por cáncer de próstata en Brasil y sus regiones para el año 2025, en base a las tendencias observadas en el período 1996-2010. Las proyecciones se realizaron para el período 2011-2025, mediante el programa NORDPRED*, con base en el período 1996-2010, utilizando el modelo edad-período-cohorte. Hubo un aumento significativo en las tasas en Brasil entre 1996 y 2006, seguido de una disminución no significativa. Las proyecciones indican una disminución de las tasas, tanto a nivel nacional, como en las regiones Centro-oeste, Sur y Sudeste, mientras que en las regiones Norte y Nordeste se espera un incremento de las tasas. Se prevé una disminución de la mortalidad por cáncer de próstata para el año 2025 en Brasil en su conjunto, así como en las regiones Centro-oeste, Sur y Sudeste, y un aumento en las regiones Norte y Nordeste. Sin embargo, se espera un aumento del número absoluto de muertes de la enfermedad en todas las regiones, debido al envejecimiento de la población previsto en el país.*

Neoplasias de la Próstata; Mortalidad; Estudios Poblacionales en Salud Pública

Contributors

J. Jerez-Roig conceived and planned the study, analyzed and interpreted the data and collaborated in the writing of the article. D. L. B. Souza and P. F. M. Medeiros conceived and planned the study, analyzed and interpreted the data, collaborated in the writing of the article and approved the final version. I. R. Barbosa, I. C. C. Costa and K. C. Lima guided the research, contributed in the writing of the article, made the critical review and approved the final version of the manuscript. M. P Curado collaborated in the writing of the article and approved the final version.

Conflicts of interest

None declared. This article does not contain any studies with human or animal subjects performed by the any of the authors.

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