DOI: 10.1590/1413-81232024299.14782022EN

# Effects of age, period, and cohort on mortality by prostate cancer among men in the state of Acre, in the Brazilian Western Amazon

Thainá Souza Ribeiro (https://orcid.org/0000-0002-7017-3973) <sup>1</sup>
Taynāna César Simões (https://orcid.org/0000-0002-5849-343X) <sup>2</sup>
Ilce Ferreira da Silva (https://orcid.org/0000-0002-7134-3030) <sup>3</sup>
Rosalina Jorge Koifman (https://orcid.org/0000-0002-2746-7597) <sup>4</sup>
Maria Fernanda de Sousa Oliveira Borges (https://orcid.org/0000-0002-5536-6507) <sup>1</sup>
Simone Perufo Opitz (https://orcid.org/0000-0001-7124-4457) <sup>1</sup>

**Abstract** *The present study aimed to analyze the* effects of age, time period, and birth cohort on the temporal evolution of mortality rates due to prostate cancer in men from the state of Acre, Brazil, in the period of 1990 to 2019. This is an ecological study in which the temporal trend was evaluated by the joinpoint method, estimating the annual percentage variations of the mortality rates. The age-period-birth cohort effects were calculated by using the Poisson Regression method, using estimation functions. The mortality rates showed an increase of 2.20% (95%CI: 1.00-3.33) in the period studied, tended to increase with age. A relative risk (RR) of 0.67 (95%CI: 0.59-0.76) was observed between 2005 and 2009, 0.76 (95%CI: 0.67-0.87) from 2005 on, and 1.44 (95%CI: 1.25-1.68) from 2015 on. The cohorts from 1910 to 1924 presented a risk reduction (RR < 1), when compared to the reference cohort (1935). Regarding the time period, the creation of public policies and the establishment of guidelines are suggested as factors which may have contributed to more access to diagnosis, in consonance with the cohort effect. These findings can contribute to a better understanding of the epidemiological scenario of prostate cancer in regions that are more vulnerable in terms of socioeconomic conditions.

**Key words** Prostate neoplasms, Mortality, Prostate

FREE THEMES

<sup>&</sup>lt;sup>1</sup> Programa de Pós-Graduação em Saúde Coletiva, Universidade Federal do Acre. Campus da Universidade Federal do Acre. 69917-400 Rio Branco AC Brasil. thainasouzasr@hotmail.com <sup>2</sup> Instituto de Pesquisa René Rachou - Fiocruz Minas. Belo Horizonte MG Brasil. 3 Departamento de Epidemiologia e Métodos Quantitativos em Saúde, Escola Nacional de Saúde Pública, Fundação Oswaldo Cruz. Rio de Janeiro RJ Brasil.

<sup>&</sup>lt;sup>4</sup> Programa de Pós-Graduação em Saúde e Meio Ambiente Escola Nacional de Saúde Pública, Fundação Oswaldo Cruz. Rio de Janeiro RJ Brasil.

#### Introduction

Prostate cancer is a serious public health problem around the world, with incidence rates ranging from 42.0/100,000 among men in developing countries, to 100.4/100,000 among men in developed countries in 2020. This neoplasm was responsible for 375,304 deaths worldwide, with higher mortality rates in less developed regions, such as the Caribbean (26.3/100,000), South Africa (19.3/100,000), and South America (16.2/100,000) in 2020<sup>1</sup>.

In Brazil, prostate cancer is the most frequent cancer among men, not including non-melanoma skin cancer, presenting an incidence rate of 78.0/100,000 men and a mortality rate of 13.7/100,000 men<sup>1</sup>. A growth trend of 2.8% per year was observed in mortality by prostate cancer in the country, with rates ranging from 9.0/100,000 men in 1980 to 14.2/100,000 men in 2010. During the same period, the North region of the country witnessed an increase of 3.5% per year, ranging from 8.0 to 10.1/100,000 men<sup>2</sup>. In Rio Branco, Acre's state capital, Nakashima *et al.* (2011) found an increase of 3.3% per year in mortality by disease between 1988 and 2004<sup>3</sup>.

The contrasting behavior of the estimates from different countries and regions may result from different aspects, such as the increase in exposure to risk factors and access to the Prostate-specific Antigen (PSA), which has contributed to a growth in diagnosis and to an early detection of prostate cancer, including during the indolent phase, resulting in a higher incidence of the disease<sup>4</sup>; likewise, factors related to late diagnosis and less access to opportune treatment contribute to higher mortality rates<sup>5</sup>.

Acre is located in Eastern Amazon and was settled by indigenous peoples, later followed by men from the Northeast and from urban centers which migrated to the region to work in the extraction of latex from rubber trees during the first (1880 to 1920) and second (1942 to 1945) rubber cycles<sup>6,7</sup>. For many years, most of the population of Acre was composed of latex extractors, who were part of the poorest population, living in a slavery-like system. Consequently, the state of Acre has characteristics similar to those of developing countries, since the base of the male population makes up the most neglected segments of society<sup>6</sup>.

Demographically, 26.0% of Acre's men were aged 40 years or older in 2019. Even though that percentage is lower than that found for the North region as a whole (28.91%), and lower than the

national average (36.80%), in terms of proportional increase of men aged 40 or older between 1990 and 2019, the increase of this population in Acre (69.30%) was above the increase observed for the entire North region (68.40%) and for Brazil (57.90%) during the same period<sup>8</sup>.

In the context of epidemiology, it is important to remember that in Acre there is a coexistence of high morbimortality by non-transmissible diseases and grievances, such as cardiovascular diseases, malignant neoplasms and external causes, as well as infectious and parasitic diseases, which still present rates of mortality that are high and persistent when compared to developed countries<sup>3,9-11</sup>.

Regardless of the progress in knowledge regarding the diagnosis and treatment of prostate cancer, little is known about the epidemiological behavior of the disease in less economically developed regions, nor about the possible effects of age, time period, or birth cohort in those regions, given the difficulties in access to efficient healthcare services provided to this disadvantaged population<sup>12</sup>.

Taking this into account, the age-period-co-hort (APC) approach used in the present study to determine mortality due to prostate cancer is relevant, since it may provide a better understanding of the influence of population aging, historical events, environmental issues, and exposure to risk factors, which may have an impact on mortality during distinctive periods and for different generations<sup>13-15</sup>.

Therefore, the present study proposes to analyze the effects of age, time period, and birth cohort on the temporal evolution of mortality due to prostate cancer among men in the state of Acre in the period of 1990 to 2019.

#### Methodology

This is an ecological study of temporal trend, of the mortality rates due to prostate cancer among men aged 40 years and older, in the state of Acre, in the period of 1990 to 2019, evaluating the effects of the age-period-birth cohort (APC).

The data on mortality was obtained from the Department of Informatics of the Unified Health System (*Departamento de Informática do SUS* – DATASUS), by means of the Mortality Information System (*Sistema de Informação sobre Mortalidade* – SIM), accessed in 2021. We selected the realm of deaths caused by prostate cancer (ICD 10: C61) among Acre residents between 1990 and

2019. The resident population during the period was obtained from census and intercensal estimates, according to age groups, provided by the Brazilian Institute of Geography and Statistics (*Instituto Brasileiro de Geografia e Estatística* – IBGE) and made available by DATASUS.

Deaths were corrected by the proportional reallocation method of ill-defined causes, not including external causes, as recommended by the World Health Organization (WHO)<sup>16</sup>, applying a proportional redistribution of 50% of the deaths from ill-defined causes within the group of other causes of death, given that this methodology began to be used after a validation study conducted by Mello Jorge *et al.* (2002)<sup>17</sup>.

The annual crude mortality rates were calculated (used for estimating the APC effects), specifically for age groups, followed by standardization by age. For the calculation of the rates, the numerator was the number of deaths of residents by malignant prostate neoplasm, and the denominator, the male population residing in the state or Acre in each year of the period considered. The standardization of mortality rates was conducted by the direct method, using as the standard the global population as proposed by Segi in 1960, and later modified by Doll and Hill (1966)<sup>18</sup>, in a ratio of 100,000 men/year.

To analyze the trend of mortality rates by means of annual percentage variation, the Joinpoint program, version 4.5, was used (Statistical Research and Applications Branch, National Cancer Institute, USA)19. Thus type of regression identifies points of change that are statistically significant, along with the annual percentage variation (APV) of a time series using the statistical modeling technique, which seeks to explain the relationship between two variables by means of regression lines, identifying the points that comprise those lines as inflexion or junction points. The analysis enables the adjustment of data from a time series based on the minimum number of joinpoints and tests to check if the inclusion of one or more points is significant. The annual percentage variations during different periods are determined by the number of inflexion points in the model<sup>19</sup>. Moving averages of the mortality rates, both crude and adjusted, over a five-year period, were used to determine the trend estimates.

To minimize the effect of possible self-correlations, the option: fit an autocorrelated error model based on the data was used. The final model selected was the one which best described the behavior of the series with APV, using the lin-

ear-log model for the calculation, based on the trend of each segment, in order to estimate the statistical significance (p < 0.05), using the Monte Carlo<sup>19</sup> permutation method.

For the APC analysis, the age groups, time periods, and birth cohorts were grouped in five-year intervals. The age groups of deaths ranged from 40-44 years of age to 80 and older, in a total of nine age groups. The periods were grouped into time intervals: 1990 to 1994, 1995 to 1999, 2000 to 2004, 2005 to 2009, 2010 to 2014, and 2015 to 2019, six periods in total. Although the data on mortality for the years 1980 to 1989 is available, the choice of the analysis period (1990 to 2019) is explained by the better quality of the mortality data from the 1990's on<sup>20</sup>. The birth cohorts vary from 1910 to 1979, resulting from the difference between the notification of death and the age at death.

The reference age group was 40 to 44 years of age, due to the lower risk of developing prostate neoplasms in the younger age groups. The reference period was 2000 to 2004, given that it precedes the creation of the High Complexity Oncologic Care Unit (*Unidade de Assistência de Alta Complexidade em Oncologia* – UNACON) in Acre, which has become a reference for oncologic treatment in the state. Considering that the central cohorts present more stability, the chosen reference cohort was 1935, which represents the average value of the birth cohorts.

In the age-period-cohort analysis, the models were adjusted with Poisson distribution for the answer-variable number of deaths in order to estimate the effects of age, time period, and birth cohort, which act in a multiplicative manner on the mortality rate. The offset term was the natural logarithm of the resident population. Therefore, the logarithm for the value of the rate is a linear function of the age, time period, and cohort effect<sup>13,14</sup>:

in which refers to the mortality rate expected for age i and period j. corresponds to the number of deaths in an age i and period j. is the population over the risk of death in age i and period j, a the effect average, the effect of the age group i, the effect of the period j and the effect of the cohort  $k^{13,14}$ .

The age-period-cohort effects present a linear relationship between each other, which prevents a complete estimation of the model, considering the main limitation of the APC method, known as the non-identifiability problem. To solve that limitation, several proposals have been described in literature, although without a definite

consensus regarding the best methodology to be applied  $^{13-15}$ . In the present study, we chose to estimate the parameters of age, time period, and birth cohort by using estimable functions. It is important to remember that those functions compromise the interpretation of individual effects, since only linear combinations and curvatures are estimable. However, since the curvatures (estimable functions) remain constant, regardless of the parameters used, it is possible to evaluate the contribution of these effects by comparing different models with fit linear predictors<sup>14</sup>.

The linear trend of the effects is divided into two components: drift effect, which is the sum of the linear effects of the period and of the cohort  $(\beta_L + \gamma_I)$ , and by the age effect, resulting from the sum of the age and the inclination of the period  $(\beta_{\rm T} + \alpha_{\rm T})^{13,14}$ .

The measure of association generated by the APC model is the relative risk (RR), which compares the specific risk of mortality of each birth cohort related to the reference cohort, and of each relative period, to the reference period, considering 95% confidence intervals (95%CI)<sup>21</sup>.

The comparison of the models was performed by applying the verisimilitude test, comparing the deviance statistics, considering a significance level of 5%. The statistical analysis was conducted in the R statistical software, version 3.5, by means of the *Epi* library.

#### Results

In the 1990 to 2019 period, 615 deaths by prostate cancer were registered among men from Acre, aged 40 years and older, with no correction for ill-defined causes. After the correction for ill-defined causes, the total number of deaths rose to 713. During the entire period, the mortality rates for prostate cancer, crude and age-standardized, in the 40 years of age and older group, presented a significant growth of 3.80% (95% CI: 2.90-4.70) and 2.20% (95%CI: 1.00-3.33), respectively (Fig-

When compared to the mortality rates by prostate cancer by age group, lower rates were verified among individuals under 60 years of age

When the time period was considered, the age groups of 70 to 75 years and of 80 years and over presented an increase in mortality from 2007 on; by contrast, in the other age groups, such growth began in mid-2012 (Figure 2A). In the birth cohort evaluation, a reduction in prostate cancer mortality was observed in the most recent birth cohorts, since 1940, and especially in age groups  $\leq$  50 years of age (Figure 2B).

Regarding the comparison of the APC models, a better adjustment was observed for the model with the three effects of age-period-cohort (p > 0.001 and the lowest residual deviance) (Table 2).

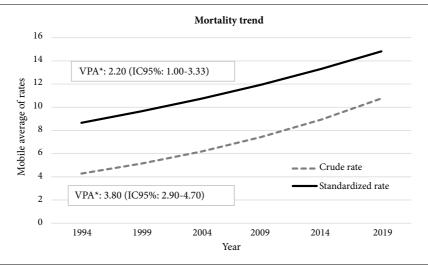
In the APC analysis, considering the age effect, the mortality rates increased in direct proportion to the increase in age, reaching a peak in the 80 years and over group (Figure 3A). In relation to the effects of time period, there was an increase in the risk of death from 2005 on, given that, since 2015, an RR > 1 has been verified, in comparison to the reference period of 2000 to 2004 (Figure 3B). For birth cohorts, a lower relative risk was observed for men born in the 1910 to 1924 cohorts (RR < 1) when compared to the reference cohort (1935), and from 1940 on, a reduction in the risk of death was verified, although this was not statistically significant. (Figure 3C).

#### Discussion

The present study identified a growing trend of mortality due to prostate cancer in the state of Acre during the analyzed period. Moreover, it was observed that the mortality rates were significantly influenced by age, time period, and birth cohort in the 1990 to 2019 period. Mortality was evaluated in two aspects, involving an analysis of the trend by annual percentage variation, and specific mortality according to the effects of age, time period, and birth cohort, resulting in more means through which to evaluate and suggest hypotheses for the behavior of mortality by prostate cancer in Acre.

The crude and adjusted rates of prostate cancer mortality indicate significant growth trends. This type of behavior was also found for the North region as a whole, as observed by Silva et al. (2020) in a study conducted with data from Brazil from the 1990 to 2017 period, when the increase in mortality rates was more evident in the North region and in countryside towns. By contrast, the South and Southeast regions presented a significant decreasing mortality trend in the last years of the analysis<sup>22</sup>.

When evaluating the rates according to age groups, the present study identified an increase in mortality for every age during the studied period. However, in places like São Paulo, located in the Southeast region, a trend of decline was



**Figure 1.** Percentage variation in crude and adjusted prostate cancer mortality rates in men residing in the state of Acre, 1990 to 2019.

Source: Mortality Information System (SIM).

**Table 1.** Age-standardized crude mortality rate of prostate cancer in men residing in the state of Acre, 1990 to 2019.

Age	1990-1994	1995-1999	2000-2004	2005-2009	2010-2014	2015-2019
< 50	0.00	0.00	0.00	1.32	1.06	0.89
50 to 54	0.00	0.00	0.00	5.49	0.00	1.23
55 to 59	23.39	7.72	6.17	4.75	5.53	7.73
60 to 64	10.63	18.57	18.87	12.42	14.79	31.89
65 to 69	32.46	44.58	24.42	32.68	27.41	39.85
70 to 74	77.58	72.02	92.72	37.00	73.49	108.65
75 to 79	121.38	145.40	158.70	146.82	108.02	256.15
≥80	254.51	215.98	276.91	206.78	426.63	538.01

<sup>\*</sup> Crude rates expressed per 100,000 men/year.

Source: Mortality Information System (SIM).

observed in the 2000 to 2015 period, for all age groups, which were, respectively, -2.33 (50 to 59 years), -2.84 (60 to 69 years), -1.93 (70 to 79 years), and -1.92 (80 years and over)<sup>23</sup>.

These findings corroborate with the context of geographic polarization in Brazil, where contrasting epidemiological characteristics co-exist, with the rates in the South and Southeast regions being similar to those of the most developed countries, while the North and Northeast regions showed rates at the level of underdeveloped countries<sup>24</sup>. Specific factors, such as the

quality of healthcare, more training in diagnosis, improvements in treatment, and increase in the survival of cancer patients may contribute to lower mortality, as can be observed in the more developed regions of the country<sup>2</sup>. The results revealed that mortality increases in the older age groups, regardless of birth cohort and period of death, showing higher numbers among the oldest; such results are expected considering that prostate cancer is cancer that tends to be more common among the elderly. Other national studies also verified a progressive increase in mor-

<sup>\*</sup>Annual percentage variation.

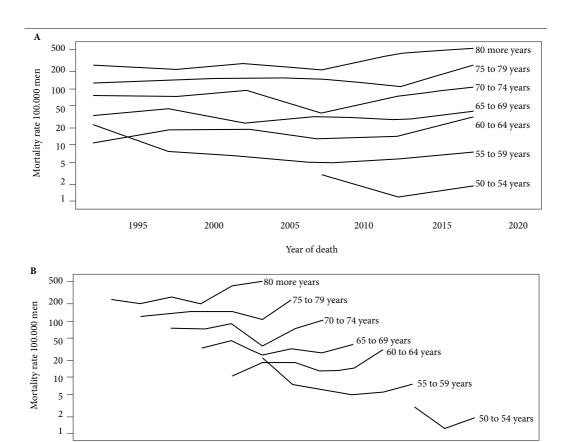


Figure 2. Mortality rates due to prostate cancer, specific to the period of death and to the birth cohort, according to age groups, among men residing in the state of Acre, 1990 to 2019.

1940

Birth cohort

1950

1960

1970

Source: Mortality Information System (SIM).

1910

1920

1930

Table 2. Comparison of the models of the age-period-cohort effect, for prostate cancer mortality, among men residing in the state of Acre, 1990 to 2019.

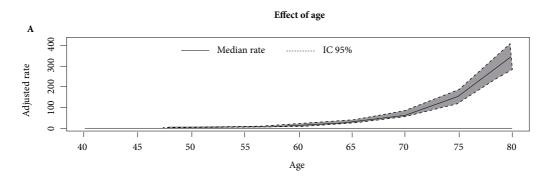
Models	Degrees of freedom	Residual deviance	p-value
Age	50	50139. 82	
Age-drift*	49	49105. 31	< 0.001
Age-cohort	46	4693. 29	0.007
Age-time period-cohort	44	4451.03	< 0.001
Age-time period	47	4771.65	< 0.001
Age-drift**	49	49105. 31	< 0.001

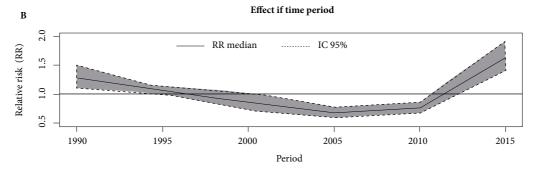
<sup>\*</sup> Linear trend of the algorithm of specific rates according to age over time is equal to the sum of the inclinations of the time period plus the cohort ( $\beta L + \gamma L$ ), where  $\beta L$  and  $\gamma L$  are the linear trends of the time period and the cohort, respectively; \*\* longitudinal trend according to age is equal to the sum of the age plus the inclination of the time period.

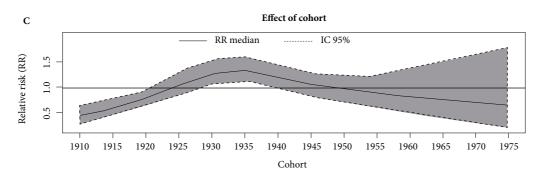
Source: Mortality Information System (SIM).

tality by malignant prostate neoplasm with the increase in age, especially among men who are 80 and older<sup>2,25,26</sup>.

The effect of age is widely known as a non-modifiable risk factor for the development of fatal prostate cancer, since aging reduces adap-







**Figure 3.** Adjusted rates and estimates of relative risks for prostate cancer mortality, according to age (A), period of death (B), and birth cohort (C), among men residing in the state of Acre, 1990 to 2019.

Source: Mortality Information System (SIM).

tive and innate immunity, thus generating a higher susceptibility to infections and, consequently, to the inflammatory response. The changes may generate Prostatic Intraepithelial Neoplasia (PIN) and even lead to prostate cancer. Another contributing factor is that the levels of testosterone reduce with age, due to the decline in the number and activity of the *Leydig* cells, which are responsible for testosterone production. This decline contributes to the risk of developing prostate cancer<sup>27,28</sup>.

In a study regarding the effects of age, time period, and birth cohort on the trend of mortality due to prostate cancer between 1990 and 2017, conducted in China, a significant increase in mortality rates due to the effect of age was observed for individuals 55 years of age and older<sup>29</sup>. In Taiwan, a study was conducted with the same methodology, which evaluated mortality by prostate cancer between 1964 and 1994. The authors observed a strong age-related effect, which was stronger than the effect of the time period and

of the birth cohort, indicating aging as the main reason for the increase in mortality<sup>30</sup>. In France, an ecological study with data on mortality specifically caused by prostate cancer from five administrative areas, from 1982 to 1996, found that age seems to account considerably for the evolution of mortality by this neoplasm<sup>31</sup>.

In terms of the time period effects, an increase in the risk of death was observed from 2005 on, as compared to the reference period (2000 to 2004), regardless of age and birth cohort. This increase in mortality due to the disease may be related to improvements in diagnosis capability and in identifying prostate cancer since the 2000s, resulting from the implementation of a series of guidelines, policies, and programs for cancer control, such as the creation of the National Program for Controlling Prostate Cancer in 2001. Its guidelines were aimed at training health professionals in the areas of prevention and early detection of cancer. Since then, a series of publications has been made available by the José de Alencar National Cancer Institute (INCA), with the purpose of providing updated information regarding this malignant neoplasm and prescribing actions<sup>32-34</sup>.

Additionally, in Brazil, important public health policies were implemented, such as the National Policy of Oncological Care in 2005<sup>35</sup> and the National Policy of Integral Care for Men's Health (Política Nacional de Atenção Integral à Saúde do Homem - PNAISH) in 200836, which promoted the organization of lines of care for individuals with cancer at all levels of care.

When evaluating the behavior of the rates according to age groups in relation to the period of death, it was observed that, since 2007, the oldest age group (≥ 80 years) showed an increase in mortality rates due to prostate cancer. A factor which may have contributed for this finding may well have been the implementation of UNA-CON, in 2007, in the state capital of Acre<sup>10</sup>. This may have brought improvements in diagnosis and recording capability and may have increased survival by providing more access to treatment and oncological care for elderly prostate cancer patients who, in previous years, would have died from the disease before reaching an advanced age, thus reflecting an increase in mortality for men aged 80 years and older.

Further on, from 2015 to 2019, a relative risk of 1.64 was observed (95%CI: 1.41-1.91), in comparison to the reference period of 2000-2004. This result may be related to the improvements in diagnosis and recording of prostate cancer, which was most likely improved with the implementation of UNACON in Acre.

In addition to the previously discussed hypotheses, it is also important to mention that since 2016 the radiotherapy service of the Acre UNACON had been suspended due to a breakdown and need for maintenance of the cobalt therapy equipment. The process of substitution of the equipment and the structural criteria required for the implementation of a linear accelerator were only be concluded in 202137,38. Therefore, the lack of radiotherapy services during that period consisted of the access of many patients who needed the treatment, and had to be sent, by means of the Treatment out of Place of Residence, to Rondonia, a neighboring state. Those delays may have resulted in an average waiting time of nearly five months for the start of the treatments. Considering that radiotherapy is recommeded for men with prostate cancer of low, moderate, and high risk, the delay in treatment may have affected the prognosis, partially explaining the increase in mortality in the 2015-2019 period<sup>38,39</sup>.

As far as the effect of the birth cohort is concerned, the older generations showed a lower risk of death in comparison to the reference cohort (1935), regardless of age and period of death. This type of behavior was also observed in a national study, with similar results for Brazil and for its geographic regions, especially the North region, where the state of Acre is located<sup>25</sup>. On the other hand, countries with more socioeconomic development presented higher mortality rayes in older cohorts<sup>40,41</sup>.

In Brazil, until 1990, the diagnosis of prostate cancer was based exclusively on digital rectal examination<sup>42,43</sup>. That exam may often be seen with prejudice and the belief that it may interfere negatively in one's masculinity<sup>44</sup>. Moreover, poor socioeconomic conditions, lower levels of education, and difficulties in access to healthcare services may be related to not having this exam<sup>44,45</sup>.

The oldest cohorts from Acre were mostly made up of Northeastern migrants trying to escape the droughts ravaging the Northeast and seeking prosperity working as latex extractors for the rubber industry. Besides the lack of access to basic sanitary conditions, they also had no access to education<sup>6</sup>. Therefore, the cultural barriers and limitations of the health services in the region increased the difficulty of access to healthcare services for the oldest cohorts. Following this reasoning, it is possible that deaths caused by prostate cancer were not attributed to this cause, resulting in underreporting in those cohorts<sup>46</sup>.

In the 90's, the PSA exam was introduced in Brazil as a measure of complementary diagnosis of prostate cancer, considering the limitations of digital examination alone, resulting in more sensitivity and specificity in tracking and diagnosis<sup>42</sup>. However, its use became controversial, considering that it is a prostatic-specific marker and not tumor-specific, generating a large number of false-positives, which, although in benign conditions, such as the case of prostatitis and hyperplasia, also provoke a high PSA. This characteristic raises questions regarding overdiagnosis and overtreatment, which may result in complications, such as hospitalization, infections, urinary incontinence, erectile dysfunction, and actinic proctitis. It is likely that those cancers would most likely not evolve throughout the life of those individuals, and those men would have died of other causes unrelated to prostate cancer<sup>47,48</sup>. However, the overgeneralization of the idea that the introduction of PSA exams alone or together with digital exams as a measure for tracking reduces mortality is questionable and should be considered with caution<sup>23,46,49</sup>.

Another important consideration is that a reduction in mortality rates due to prostate cancer was observed in more recent birth cohorts, since 1940, and especially in the  $\leq 50$  years of age groups. These results suggest that health care has been improved, through the early identification of cancer and better treatment conditions, which may have contributed to a decrease in mortality rates among younger elderly people.

However, the results presented in this study are subject to limitations related to the quality of the SIM data, especially due to the high proportion of ill-defined causes among the elderly<sup>50</sup>. However, seeking to reduce that limitation, we conducted a proportional reallocation of the deaths among the ill-defined causes. Abreu *et al.* (2016) identified that, in Brazil, there is an underreporting of deaths caused by prostate neoplasms, and after the redistribution by ill-defined causes, the deaths caused by prostate cancer increased by 22.2% in 1996 and 6.2% in 2011, proving the importance of this methodology<sup>51</sup>.

Another limitation is related to the APC models, since there is no consensus in the literature concerning the most efficient method to correct the identification problem in the complete model. However, in the present study, the models were evaluated by means of estimable functions, a methodology which is more recommended by studies that compare classic statistical methods<sup>13-15</sup>.

The present investigation was the first conducted with APC methodology to analyze mortality rates due to prostate cancer in the state of Acre, and has the benefit of having evaluated 29 years of specific mortality according to SIM records. Moreover, it used the redistribution of ill-defined causes to attenuate the absence of information regarding the basic cause of death.

The findings from this study must be analyzed with caution, since this is an ecological study using secondary data; however, the present study allowed for the development of hypotheses, including the idea that mortality due to prostate cancer increases with age (I), which supports the premise that prostate cancer is a third-age cancer. Considering that Brazil is experiencing population aging, there is a need to intensify the public health measures aimed at the early diagnosis and treatment of this neoplasm in the country, especially in the North region.

Furthermore, our results allow us to hypothesize that issues such as difficulty in access to healthcare services, low availability of efficient tracking and diagnosis systems, and unfavorable socioeconomic conditions contributed to the underreporting of deaths caused by prostate cancer in older cohorts (II); the increase in mortality observed since 2005, when compared to the reference period, may be related to better diagnosis conditions (III); and finally, the effect of the birth cohorts on the behavior of mortality due to prostate cancer confirms the improvements in diagnosis and access to health care (IV), given that, since the 1930 cohort, a decrease was observed in mortality rates due to prostate cancer among younger age groups, as compared to older cohorts. It is important to remember that differences in prostate cancer care have also been connected to sociodemographic and clinical variables<sup>52</sup>.

## Conclusion

In the present study, an increase in mortality rates was observed as age increased, and the impact of the time period showed increasing behavior from 2005 on. Meanwhile, the older birth cohorts presented a lower risk of death by prostate cancer. Age is a risk factor for prostate cancer, which is widely known and was also verified in the present study. The behavior of the time period factor may be related to the implementation of public policies and more access to diagnostic services, increasing the reporting of mortality due to prostate cancer. Moreover, the identification of a signifi-

cant risk of death from 2015 on may also be related to difficulties in access to oncological services, especially radiotherapy, since it coincides with the period when the service was not available at the High Complexity Oncology Care Unit, the only specialized service of this nature in the state. It is possible to assume that the older cohorts had less access to diagnostic services, resulting in a lower number of deaths attributed to prostate cancer.

It is important to highlight that efforts must be prioritized in order to ensure access to diagnosis and adequate treatment for prostate cancer, in due time, so that positive impacts can be felt in terms of a decrease in mortality rates. To avoid fallacious conclusions, complementary studies are warranted, which should include the collection of primary data and analytical designs that enable a deeper understanding of the epidemiological profile of the prostate cancer cases, of survival, and of the factors associated with the risk of death by this neoplasm in the state of Acre.

### **Collaborations**

TS Ribeiro: scientific writing of the article. MFSO Borges, SP Optiz and IF Silva: review of the article and writing contributions. RJ Koifman: review of the article and contributions to the writing, as well as mentor on the topic covered. TC Simões: article review and writing contributions, as well as statistical analysis.

#### References

- International Agency for Research on Cancer. Global Cancer Observatory: Cancer Today [Internet]. 2018. [cited 2022 abr 10]. Available from: https://gco.iarc. fr/today
- Conceição MBM, Boing AF, Peres KG. Time trends in prostate cancer mortality according to major geographic regions of Brazil: an analysis of three decades. Cad Saude Publica 2014; 30(3):559-566.
- Nakashima J de P, Koifman S, Koifman RJ. Cancer mortality trends in Rio Branco, Acre State, Brazil, 1980-2006. Cad Saude Publica 2011; 27(6):1165-1174.
- Marcos Dall'Oglio, Alexandre Crippa, Miguel Srougi. Câncer de próstata. Santos: Livraria Santos Editora LTDA; 2013.
- Neupane S, Bray F, Auvinen A. National economic and development indicators and international variation in prostate cancer incidence and mortality: an ecological analysis. World J Urol 2017; 35(6):851-858.
- Bezerra MJ. Invenções do Acre: de território a estado

   um olhar social [tese]. São Paulo: Universidade de São Paulo: 2006.
- Instituto Socioambiental. Povos do Acre: história indígena da Amazônia Ocidental [Internet]. 2002. [acessado 2023 jun 11]. Disponível em: https://acervo. socioambiental.org/acervo/documentos/povos-do-acre-historia-indigena-da-amazonia-ocidental
- Instituto Brasileiro de Geografia e Estatística (IBGE). Censo Demográfico, Estimativas da População [Internet]. [acessado 2021 nov 16]. Disponível em: https://www.ibge.gov.br/
- Bezerra PCL, Monteiro GTR. Trends in overall mortality and from diseases of the circulatory system in elderly individuals in Rio Branco, Acre, 1980-2012.
   Rev Bras Geriatr Gerontol 2018; 21(2):143-154.
- Nakashima J, Koifman RJ, Koifman S. Incidência de câncer na Amazônia ocidental: estimativa de base populacional em Rio Branco, Acre, Brasil, 2007-2009. Cad Saude Publica 2012; 28(11):2125-2132.
- Ribeiro TS, Ramalho AA, Vasconcelos SP, Opitz SP, Koifman RJ. Tendência temporal da mortalidade em idosos em municípios no estado do Acre. Rev Bras Geriatr Gerontol 2020; 23(3):e200018.
- Araújo JD. Polarização epidemiológica no Brasil. Epidemiol Serv Saude 2012; 21(4):533-538.
- Holford TR. The estimation of age, period and cohort effects for vital rates. *Biometrics* 1983; 39(2):311-324.
- Holford TR. Understanding the effects of age, period, and cohort on incidence and mortality rates. Annu Rev Public Health 1991; 12:425-457.
- Robertson C, Boyle P. Age-period-cohort analysis of chronic disease rates. Stat Med 1998; 17(12):1305-1323
- Mathers CD, Bernard C, Iburg KM, Inoue M, Ma Fat D, Shibuya K, Stein C, Tomijima N, XU H. Global burden of disease in 2002: data sources, methods and results. Geneva: WHO; 2003.
- Jorge MHPM, Gotlieb SLD, Laurenti R. O sistema de informações sob mortalidade: problemas e propostas para o seu enfrentamento I – mortes por causas naturais. Rev Bras Epidemiol 2002; 5(2):197-211.
- Doll R, Muir CS, Waterhouse JAH. Cancer incidence in five continents: volume II – 1970. Berlin, Heidelberg: Springer Berlin Heidelberg; 1970.

- 19. Kim HJ, Fay MP, Feuer EJ, Midthune DN. Permutation tests for joinpoint regression with applications to cancer rates. *Stat Med* 2000; 19(3):335-351.
- Frias PG, Szwarcwald CL, Lira PIC. Avaliação dos sistemas de informações sobre nascidos vivos e óbitos no Brasil na década de 2000. Cad Saude Publica 2014; 30(10):2068-2280.
- Cartensen B. Demography and epidemiology: age-period-cohort models in the computer age. Copenhagen: University of Copenhagen; 2005.
- Silva GA, Jardim BC, Ferreira VM, Junger WL, Girianelli VR. Mortalidade por câncer nas capitais e no interior. Rev Saude Publica 2020; 54:126.
- Luizaga CTM, Ribeiro KB, Fonseca LAM, Neto JE. Tendências na mortalidade por câncer de próstata no estado de São Paulo, 2000 a 2015. Rev Saude Publica 2020; 54:87.
- Araújo JD. Polarização epidemiológica no Brasil. Epidemiol Serv Saude 2012; 21(4):533-538.
- Braga SFM, Souza MC, Cherchiglia ML. Time trends for prostate cancer mortality in Brazil and its geographic regions: an age-period-cohort analysis. *Cancer Epidemiol* 2017; 50(Pt. A):53-59.
- Fonseca LAM, Eluf-Neto J, Wunsch Filho V. Tendências da mortalidade por câncer nas capitais dos estados do Brasil, 1980-2004. Rev Assoc Med Bras 2010; 56(3):309-312.
- Decaroli MC, Rochira V. Aging and sex hormones in males. *Virulence* 2017; 8(5):545-70.
- Vaidyanathan V, Karunasinghe N, Jabed A, Pallati R, Kao C, Wang A, Marlow G, Ferguson LR. Prostate cancer: is it a battle lost to age? *Geriatrics* 2016; 1(4):27.
- Liu X, Yu C, Bi Y, Zhang ZJ. Trends and age-periodcohort effect on incidence and mortality of prostate cancer from 1990 to 2017 in China. *Public Health* 2019: 172:70-80.
- Chang CK, Hong Jeng Yu, Kin Wei A Chan, Ming Keun Lai. Secular trend and age-period-cohort analysis of prostate cancer mortality in Taiwan. *J Urol* 1997; 158:1845-1848.
- Chirpaz E, Colonna M, Menegoz F, Grosclaude P, Schaffer P, Arveux P, Lesec'h JM, Exbrayat C, Schaerer R. Incidence and mortality trends for prostate cancer in 5 French areas from 1982 to 1996. *Int J Cancer* 2002; 97(3):372-376.
- Brasil. Ministério da Saúde (MS). Lei 10.289 de 20 de setembro de 2001. Institui o Programa Nacional de Controle do Câncer de Próstata. *Diário Oficial da União* 2001; 20 set.
- Instituto Nacional de Câncer (INCA). Programa nacional de controle do câncer da próstata: documento de consenso. Rio de Janeiro: INCA; 2002.
- 34. Instituto Nacional de Câncer (INCA). *Detecção precoce do câncer*. Rio de Janeiro: INCA; 2021.
- Brasil. Ministério da Saúde (MS). Portaria nº 741, de 19 de dezembro de 2005. Institui a Política Nacional de Atenção Oncológica. *Diário Oficial da União* 2005; 19 dez.
- Brasil. Ministério da Saúde (MS). Portaria nº 1.944, de 26 sw agosto de 2009. Institui a Política Nacional de Atenção Integral a Saúde do Homem. Diário Oficial da União 2009; 27 ago.

- 37. Anute D. Unacon oferece radioterapia e melhora a qualidade de vida dos pacientes no Acre [Internet]. 2021. [acessado 2022 jan 21]. Disponível em: https:// agencia.ac.gov.br/unacon-oferece-radioterapia-e-melhora-a-qualidade-de-vida-dos-pacientes-no-acre/
- 38. Rodrigues I. Único aparelho de radioterapia do Acre está quebrado há um ano, diz Unacon [Internet]. G1 2018. [acessado 2022 jan 21]. Disponível em: https:// g1.globo.com/ac/acre/noticia/2018/10/18/unico-aparelho-de-radioterapia-do-acre-esta-quebrado-ha--um-ano-diz-unacon.ghtml
- Conselho Federal de Medicina do Estado do Acre. CRM-AC fiscaliza Hospital do Câncer e flagra falta de radioterapia e salas improvisadas [Internet]. 2019. [acessado 2021 dez 2]. Disponível em: http:// www.crmac.org.br/index.php?option=com\_content&view=article&id=21285:2019-09-11-21-23-59&catid=3
- Niclis C, Pou SA, Bengió RH, Osella AR, Díaz MP. Prostate cancer mortality trends in Argentina 1986-2006: an age-period-cohort and joinpoint analysis. Cad Saude Publica 2011; 27(1):123-130.
- 41. Oberaigner W, Siebert U, Horninger W, Klocker H, Bektic J, Schäfer G, et al. Prostate-specific antigen testing in Tyrol, Austria: prostate cancer mortality reduction was supported by an update with mortality data up to 2008. Int J Public Health 2012; 57(1):57-62.
- Instituto Nacional de Câncer (INCA). Monitoramento das ações de controle do câncer de próstata. Rio de Janeiro: INCA; 2014.
- Konert J, Sentker L, August C, Hatzinger M. The long journey from palpation to biopsy: the history of diagnosing prostate câncer. Urol Ausg A 2021; 7:943-949.
- 44. Lima AP, Lini EV, Giacomazzi RB, Dellani MP, Portella MR, Doring M. Prevalência e fatores associados à realização de exames de câncer de próstata em idosos: estudo de base populacional. Rev Bras Geriatr Gerontol 2018; 21(1):55-61.
- 45. Amorim VMSL, Barros MBA, César CLG, Goldbaum M, Carandina L, Alves MCGP. Fatores associados à realização dos exames de rastreamento para o câncer de próstata: um estudo de base populacional. Cad Saude Publica 2011; 27(2):347-356.

- 46. Welch HG, Albertsen PC. Reconsidering prostate cancer mortality - the future of PSA screening. N Engl I Med 2020; 382(16):1557-1563.
- 47. Carlsson SV, Vickers AJ. Screening for prostate cancer. Med Clin North Am 2020; 104(6):1051-1062.
- 48. Ilic D, Djulbegovic M, Jung JH, Hwang EC, Zhou Q, Cleves A, Agoritsas T, Dahm P. Prostate cancer screening with prostate-specific antigen (PSA) test: a systematic review and meta-analysis. BMJ 2018; 362: k3519.
- Steffen RE, Trajman A, Santos M, Caetano R. Rastreamento populacional para o câncer de próstata: mais riscos que benefícios. Physis 2018; 28(2):e280209.
- Jorge MHPM, Laurenti R, Lima-Costa MF, Gotlieb SLD, Chiavegatto Filho ADPC. A mortalidade de idosos no Brasil: a questão das causas mal definidas. Epidemiol Serv Saude 2008; 17(4):271-281.
- Abreu DMX, Guimarães MDC, Franco GC, Lana GC, Ishitani LH, França EB. O impacto da correção dos dados na mortalidade prematura por câncer de próstata, Brasil, 1996-2011. Rev Bras Cancerol 2016; 62(2):147-154.
- Sacramento RS, Simião LJ, Viana KCG, Andrade MAC, Amorim MHC, Zandonade E. Association of sociodemographic and clinical variables with time to start prostate cancer treatment. Cien Saude Colet 2019; 24(9):3265-3274.

Article submitted 30/05/2023 Approved 01/09/2023 Final version submitted 03/09/2023

Chief editors: Maria Cecília de Souza Minayo, Romeu Gomes, Antônio Augusto Moura da Silva