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Mortality by colon, lung, esophagus, prostate, cervix and breast cancers in Brazilian capitals, 2000-2015: a multilevel analysis

Mortalidade por câncer de cólon, pulmão, esôfago, próstata, colo do útero e mama nas capitais brasileiras, 2000-2015: uma análise multinível

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Abstract *This study aimed to analyze the role of period, geographic and socio demographic factors in cancer-related mortality by prostate, breast, cervix, colon, lung and esophagus cancer in Brazilians capitals (2000-2015). Ecological study using data of Brazilian Mortality Information. Multilevel Poisson models were used to estimate the adjusted risk of cancer mortality. Mortality rate levels were higher in males for colon, lung and esophageal cancers. Mortality rates were highest in the older. Our results showed an increased risk of colon cancer mortality in both sexes from 2000 to 2015, which was also evidenced for breast and lung cancers in women. In both genders, the highest mortality risk for lung and esophageal cancers was observed in Southern capitals. Midwestern, Southern and Southeastern capitals showed the highest mortality risk for colon cancer both for males and females. Colon cancer mortality rate increased for both genders, while breast and lung cancers mortality increased only for women. The North region showed the lowest mortality rate for breast, cervical, colon and esophageal cancers. The Midwest and Northeast regions showed the highest mortality rates for prostate cancer.*
Key words *Cancer, Multilevel analysis, Mortality*

Resumo *Este estudo teve como objetivo analisar o papel de fatores temporais, geográficos e sociodemográficos na mortalidade por câncer de próstata, mama, colo do útero, cólon, pulmão e esôfago nas capitais brasileiras (2000-2015). Estudo ecológico utilizando informações brasileiras de mortalidade. Modelos de Poisson multinível foram usados para estimar o risco ajustado de mortalidade por câncer. Os níveis de mortalidade foram maiores em homens para câncer de cólon, pulmão e esôfago. As taxas de mortalidade foram mais altas nos idosos. Nossos resultados mostraram risco aumentado de mortalidade por câncer de cólon em ambos os sexos de 2000 a 2015, o que também foi evidenciado para câncer de mama e de pulmão em mulheres. Em ambos os sexos, o maior risco de mortalidade para câncer de pulmão e esôfago foi observado nas capitais do Sul. As capitais do Centro-Oeste, Sul e Sudeste apresentaram o maior risco de mortalidade por câncer de cólon tanto para homens quanto para mulheres. A taxa de mortalidade por câncer de cólon aumentou para ambos os sexos, enquanto a mortalidade por câncer de mama e de pulmão aumentou apenas para as mulheres. A região Norte apresentou a menor taxa de mortalidade por câncer de mama, colo do útero, cólon e esôfago. As regiões Centro-Oeste e Nordeste apresentaram as maiores taxas de mortalidade por câncer de próstata.*
Palavras-chave *Câncer, Análise multinível, Mortalidade*

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Background

One in eight men and one in eleven women die from cancer worldwide. Varying levels of cancer incidence and mortality may be associated with the distribution of risk factors in different countries[1].

Although the highest mortality rates are observed in developed countries, it is expected that cancer will become the leading cause of morbidity and mortality, even in developing countries over time[2]. Around 700,000 new cases of cancer per year are estimated for 2020 in Brazil. Estimates for 2020 indicate that the most incident types of cancer are prostate, breast, lung, cervix and colon and rectum. Estimates for the esophageal cancer also point high incidence rate in men[3].

Mortality rates in the last two decades of the 20th century in Brazilian capitals showed that lung cancer decreased among men, while prostate cancer increased. In women, breast cancer mortality remained stable, while cervical and lung cancer increased[4]. In the 21st century, the cervical cancer mortality rate in Brazil decreased until 2016[5]. Prostate cancer showed a small reduction in mortality in the state of São Paulo from 2000 to 2015[6]. There was an increase in esophageal cancer mortality rates in the Northeast and North of Brazil from 2000 to 2014[7]. Lung cancer mortality decreased in Brazil among men (2000 to 2015) and increased among women[8]. And colorectal cancer mortality in Brazil (1996 to 2016) increased in the North and Northeast and decreased in other regions[9].

The cancer transition begins with a change in the predominant types of cancer, changing from the predominance of infections-associated cancers to mainly non-infectious cancers, probably related to lifestyle[10].

Socioeconomic and demographic characteristics can enhance the analysis of disparities in cancer morbidity and mortality. A relationship has been detected between late cancer diagnosis and low socioeconomic status, which would increase the chances of death. Study pointed that individuals with lower family income have higher rates of lung, breast and prostate cancer[11].

Data from 2018 indicate that in countries with a low Human Development Index (HDI) the most incident cancers are: 1st) breast, 2nd) cervix and 3rd) prostate. In countries with a high HDI, the rank is: 1st) breast, 2nd) prostate and 3rd) lung[1].

This study gathered the most frequent types of cancer in men and/or women in Brazil, seeking to investigate the temporal evolution of mortality and its relationship with sociodemographic characteristics. Considering the magnitude of the disease in Brazil and in the world, addressing the dynamics of the disease over time and the factors that could identify the main risk groups, can contribute to guide health actions. Thus, we selected some of the high-incidence cancers in Brazil to investigate the pattern of mortality of the disease. This study aimed to analyze the role of period, geographic and socio demographic factors in cancer-related mortality by prostate, breast, cervix, colon, lung and esophagus cancer in Brazilians capitals from 2000 to 2015.

Methods

This is an ecological study using public access data of Brazilian Mortality Information (SIM) and Brazilian Institute of Geography and Statistics (IBGE), collected from Information Technology Department of Brazilian Unified Health System (DATASUS). State capitals were the study's analytic units. Brazil has 26 states with their respective capitals plus the Federal District.

For each capital, we collected mortality cases from 2000 to 2015 in the population older than 19 years of age. We only collected mortality cases classified in International Classification of Diseases (10th revision) with codes C15, C18, C34, C50, C53 and C61, corresponding to deaths by esophagus, colon, lung, breast, cervix and prostate cancers, respectively. The choice of these specific types of cancer for this study took into account their high frequency of new cases in women or in men. Current statistics from 2020 from the National Cancer Institute show that prostate and breast cancer had the highest number of new cases in 2020 for men and women, respectively (about 66,000 cases, corresponding to about 30% of cases). Cervical cancer was the third with more new cases in 2020 in women and colon cancer was the second, in both genders. Lung cancer was among the four with more new cases in 2020 in men and women and esophageal cancer was the sixth with more new cases in men. Regard to mortality, data from 2018 indicate that the cancers selected for this study are among the top five in number of deaths. These values refer to both genders for lung and colon cancer, to female stratum for breast and cervical cancers and to male stratum for prostate and esophageal cancers[12].

The outcome variables were deaths by esophagus, colon, lung, breast, cervix and prostate cancers. The explanatory variables include in the

analysis were: age, gender, region of the capital, period, death year, death year squared and Gross Domestic Product per capita per 1,000 USD (GDP). The annual GDP was adjusted by deflation over time. Age was categorized into a 20-year age group. In the descriptive analysis, the year of death was categorized into 4-year periods. Gender variable was included only in the initial descriptive analysis. All subsequent analyzes were performed separately by type of cancer and gender.

Crude mortality rates over the period and age-period standardized rates per 100.000 were calculated according to the type of the cancer. For standardization, the direct method and the 2015 population of the capital "Rio de Janeiro" as a reference standard were used.

Maps were constructed with graphs of mortality rates by period according to gender and type of cancer. The digital map grid was obtained from the IBGE.

Statistical analysis

Average rates and standard deviations were calculated for each four-year period. We used chi-square tests to evaluate the association between the explanatory variables and cancer mortality.

Multilevel Poisson models were used to estimate the adjusted risks of cancer mortality (prostate, breast, cervix, colon, lung and esophageal cancers). The adjusted models included the following variables as fixed effects: age, GDP, region, year squared and year of death. Also, we included an offset with the logarithm of the population of the capital of each year studied. The variables included as random effects were capital (intercept), year squared (slope) and year of death (slope). In order to facilitate visualization and avoid very high values in the measure of effect, the models used the age group of 40 to 59 years as reference category. The South region was used as reference category, because in general, it was the region that had the highest mortality rates.

We used the software QGIS 3.12 and R-Project (version 4.0.3) to perform data analysis.

Results

From 2000 to 2015, 45,595 deaths by colon cancer, 95,555 deaths by lung cancer and 32,885 deaths by esophageal cancer were recorded in Brazilians capitals. The annual average number of deaths was 2,787.19, 5,972.19 and 2,055.31 deaths per year for colon, lung and esophageal cancers, respectively. Crude mortality rates per 100,000 over the period were 12.57, 40.24 and 9.84 for colon, lung and esophageal cancers, respectively. Age-period standardized rates per 100.000 were 11.87, 39.96 and 9.41 for colon, lung and esophageal cancers, respectively.

Women (2000-2015) recorded 23,655 deaths by cervix cancer, 65,291 by breast cancer, 24,613 by colon cancer, 37,200 by lung cancer and 5,138 by esophageal cancer in Brazilians capitals. Crude female mortality rates per 100,000 over the period were 17.07, 31.46, 11.76, 24.78 and 3.45 for cervix, breast, colon, lung and esophageal cancers, respectively. Age-period standard rates per 100,000 were 16.32, 30.15, 11.34, 23.53 and 3.32 for cervix, breast, colon, lung and esophageal cancers, respectively.

Men (2000-2015) recorded 46,623 deaths by prostate cancer, 19,982 by colon cancer, 58,355 by lung cancer and 27,747 by esophageal cancer in Brazilians capitals. Crude male mortality rates per 100,000 were 56.06, 13.40, 55.90 and 16.23 per 100,000 for prostate, colon, lung and esophageal cancers, respectively. Age-period standard rates per 100.000 were 49.51, 12.39, 50.38 and 15.50 for prostate, colon, lung and esophageal cancers, respectively.

Colon, lung and esophageal cancers showed statistically significant difference between mortality rates by gender. Men evidenced the highest mortality rates of colon, lung and esophageal cancers. Compared to women, the mortality rate in men was around twice higher for lung cancer and around four times higher for esophageal cancer. Prostate and lung cancer showed the highest rate in men (56/100,000), while breast cancer showed the highest rate in women (31/100,000) (Table 1).

All cancers investigated showed statistically significant difference in mortality rates between age groups. Regarding the 40-59 age group, rates ranged from 3.33/100,000 to 26.39/100,000 for prostate and breast cancer, respectively. The highest mortality rates were observed in the older age group, especially for prostate and lung cancers, whose values were higher than 100 deaths per 100,000 (Table 1).

For breast, colon and esophageal cancers, the higher mortality rates occurred in capitals with a GDP higher than 10,000 USD. However, regarding cervix cancer, the higher mortality rates occurred in capitals with GDP lower than 10,000 USD (Table 1).

Except for prostate cancer, there was statistical difference in mortality rate between the regions of the capitals. The highest mortality rate

of breast, colon, lung and esophageal cancers was observed in capitals from the South region. For cervix cancer, the highest mortality rate was observed in Northern capitals (Table 1).

There was statistical difference in mortality rate by colon cancer between the periods. Rates ranged from 10.46 in the 2000-2003 period to 14.04 in the 2012-2015 period (Table 1).

Table 1. Distribution of the mortality rate in the Brazilian capitals of the most incident cancers in the country.

	Prostate cancer		Breast cancer		Cervix cancer		Colon cancer		Lung cancer		Esophageal cancer	
	Rate/ 100,000		Rate/ 100,000		Rate/ 100,000		Rate/ 100,000		Rate/ 100,000		Rate/ 100,000	
	Mean (SD)	P-v	Mean (SD)	P-v	Mean (SD)	P-v	Mean (SD)	P-v	Mean (SD)	P-v	Mean (SD)	P-v
Gender												
Female			31.46 (29.98)		17.07 (19.01)		11.76 (16.96)	*	24.58 (30.82)	***	3.45 (6.28)	***
Male	56.06 (80.16)						13.40 (20.71)		55.90 (72.84)		16.23 (15.98)	
Age												
20-39	0.05 (0.21)	***	2.96 (1.58)	***	3.03 (2.14)	***	0.49 (0.60)	***	0.63 (0.77)	***	3.51 (4.65)	***
40-59	3.33 (2.36)		26.39 (8.37)		14.73 (9.06)		4.45 (3.17)		13.74 (7.33)		4.67 (5.12)	
≥60	164.80 (39.00)		65.03 (25.64)		33.45 (22.96)		32.78 (21.11)		106.35 (58.47)		21.33 (17.83)	
GDP												
<10,000	56.80 (81.72)	NS	29.31 (28.53)	***	18.08 (19.28)	*	10.41 (16.47)	***	39.09 (57.38)	NS	9.22 (13.61)	**
≥ 10,000	54.56 (76.99)		35.81 (32.31)		15.01 (18.30)		16.95 (22.53)		42.63 (59.38)		11.09 (13.86)	
Region												
Midwest	58.60 (82.42)	NS	32.71 (28.90)	***	14.50 (13.08)	***	15.53 (19.24)	***	39.31 (53.55)	***	11.45 (14.49)	***
North	55.60 (82.04)		21.67 (23.22)		27.01 (28.18)		6.20 (11.58)		39.56 (58.28)		7.05 (12.97)	
Northeast	58.61 (83.00)		32.00 (27.87)		15.92 (14.81)		9.42 (12.73)		35.36 (48.49)		8.35 (19.95)	
South	50.22 (72.15)		41.48 (38.55)		10.50 (8.82)		22.92 (28.53)		57.26 (82.51)		15.04 (18.26)	
Southeast	52.97 (73.98)		38.61 (33.89)		9.78 (8.05)		20.12 (24.64)		40.56 (56.85)		12.54 (14.10)	
Period												
2000-2003	55.00 (79.50)	NS	29.27 (29.09)	NS	17.25 (17.50)	NS	10.46 (17.52)	**	39.29 (60.34)	NS	10.42 (15.62)	NS
2004-2007	57.41 (82.93)		29.85 (29.07)		17.26 (18.75)		12.26 (18.64)		41.74 (59.94)		9.85 (13.69)	
2008-2011	56.61 (80.34)		32.37 (30.53)		16.53 (18.66)		13.53 (20.13)		40.28 (57.30)		9.41 (12.78)	
2012-2015	55.22 (78.16)		34.35 (31.03)		17.24 (21.04)		14.04 (19.21)		39.64 (54.60)		9.66 (12.57)	

GDP (Gross Domestic Product) = GDP/1000USD (GDP was calculated in USD using the currency exchange rate on July 1st of each year); P-v = P-value; NS = not significant. P-value significance codes: *** : < 0.001; ** : < 0.01; * : < 0.05; NS : > 0.05.

Source: Authors.

Among men, the mortality trend for: 1) esophageal cancer increased in capitals such as Manaus (North) and decreased in capitals such as Curitiba (South); 2) lung cancer increased in capitals such as Rio Branco (North) and reduced in capitals such as Curitiba (South); 3) colon cancer increased in capitals such as Recife (Northeast) and reduced in capitals such as Curitiba (South); 4) prostate cancer increased in capitals such as Manaus (North) and decreased in capitals such as Curitiba (South) (Figure 1).

Among women, the mortality trend for: 1) esophageal cancer increased in capitals such as Vitória (Southeast) and decreased in capitals such as Curitiba (South); 2) lung cancer increased in capitals such as Curitiba (South) and reduced in capitals such as Porto Velho (North); 3) colon cancer increased in capitals such as Salvador (Northeast) and stabilized in capitals such as Rio de Janeiro (Southeast); 4) breast cancer increased in capitals such as Fortaleza (Northeast) and decreased in capitals such as Curitiba (South); 5) cervical cancer increased in capitals such as Manaus (North) and decreased in capitals such as Curitiba (South) (Figure 2).

Comparing with those aged 40-59 years, men aged 20-39 years showed approximately 98% lower mortality risk for prostate and lung cancers, 90% lower for colon cancer and 8% lower for esophageal cancer. However, when men older than 59 years were compared to those aged 40-59 years, the older showed mortality risk 47 times for prostate cancer, approximately 8.5 times higher for lung and colon cancers and four times higher for esophageal cancer (Table 2).

Comparing with those aged 40-59 years, women aged 20-39 years showed approximately 95.5% lower mortality risk for esophageal and lung cancers, approximately 89% lower for colon or breast cancers and 79% lower for cervix cancer. However, when women older than 59 years were compared to those aged 40-59 years, the older showed mortality risk approximately 6 times higher for esophageal, lung and colon cancers and approximately 2.5 times higher for breast and cervix cancers (Table 3).

The death year was associated with the mortality risk in the male group for colon and lung cancers. The adjusted risk indicated that recent years showed a higher mortality risk for colon cancer and lower mortality risk for lung cancer in males (Table 2).

Except for cervix cancer mortality, the death year was associated with the mortality risk in the female group. The adjusted risk indicated that recent years showed a higher mortality risk for breast, colon and lung cancers and lower mortality risk for esophageal cancer in females (Table 3).

Male and female cancers showed different mortality risk according to the region of the capital. In both genders, the highest mortality risk for lung and esophageal cancers was observed in Southern capitals. Midwestern, Southern and Southeastern capitals showed the highest mortality risk for colon cancer both for males and females (Tables 2 and 3).

Midwestern and Northeastern capitals showed the highest mortality risk for prostate cancer. Comparing to Southern capitals: esophageal mortality cancer in males was approximately 71% lower in Northern and Northeastern capitals and approximately 42.5% lower in Southeastern and Midwestern capitals; lung mortality cancer in males was approximately 34% lower in Northern, Northeastern, Southeastern and Midwestern capitals; colon mortality cancer in males was 61% lower in Northern capitals and 29% lower in Northeastern capitals; and prostate mortality cancer was approximately 21.5% higher in Midwestern or Northeastern capitals (Table 2).

The highest mortality risk for breast was observed in Southern capitals, while Northern capitals showed the highest mortality risk for cervix cancer. Compared with Southern capitals, breast mortality cancer was 29% lower in Northern capitals; cervix mortality cancer was around two times higher in Northern capitals; esophageal mortality cancer in females was approximately 47.5% lower in Northern and Northeastern capitals and 30% lower in Southeastern capitals; lung mortality cancer in females was approximately 27% lower in Northeastern, Southeastern and Midwestern capitals; and colon mortality cancer in females was 54% lower in Northern capitals and 27% lower in Northeastern capitals (Table 3).

Evaluating the specification of the models, it is observed that there was reduction of residual deviance and standard deviation of random effects, indicating that the adjustment contributed to explain cancer mortality. On all models, the capital (intercept) random effect showed the highest standard deviation. So that, we can interpret that the behavior of mortality rates shows significantly variation according to the specific capital (data not shown).

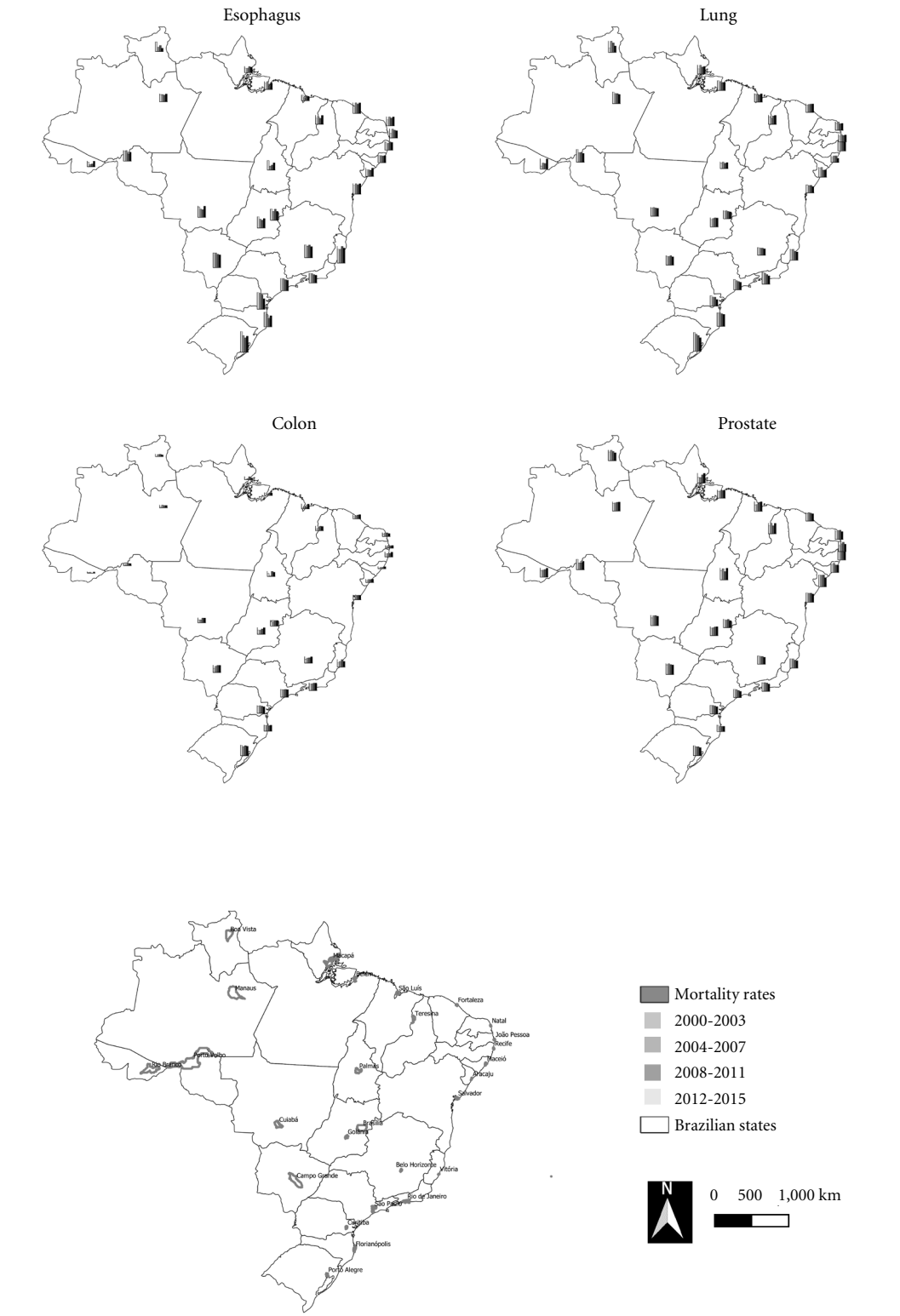

Figure 1. Trend of male mortality rate in the Brazilian capitals of the most incident cancers in the country.

Source: Authors.

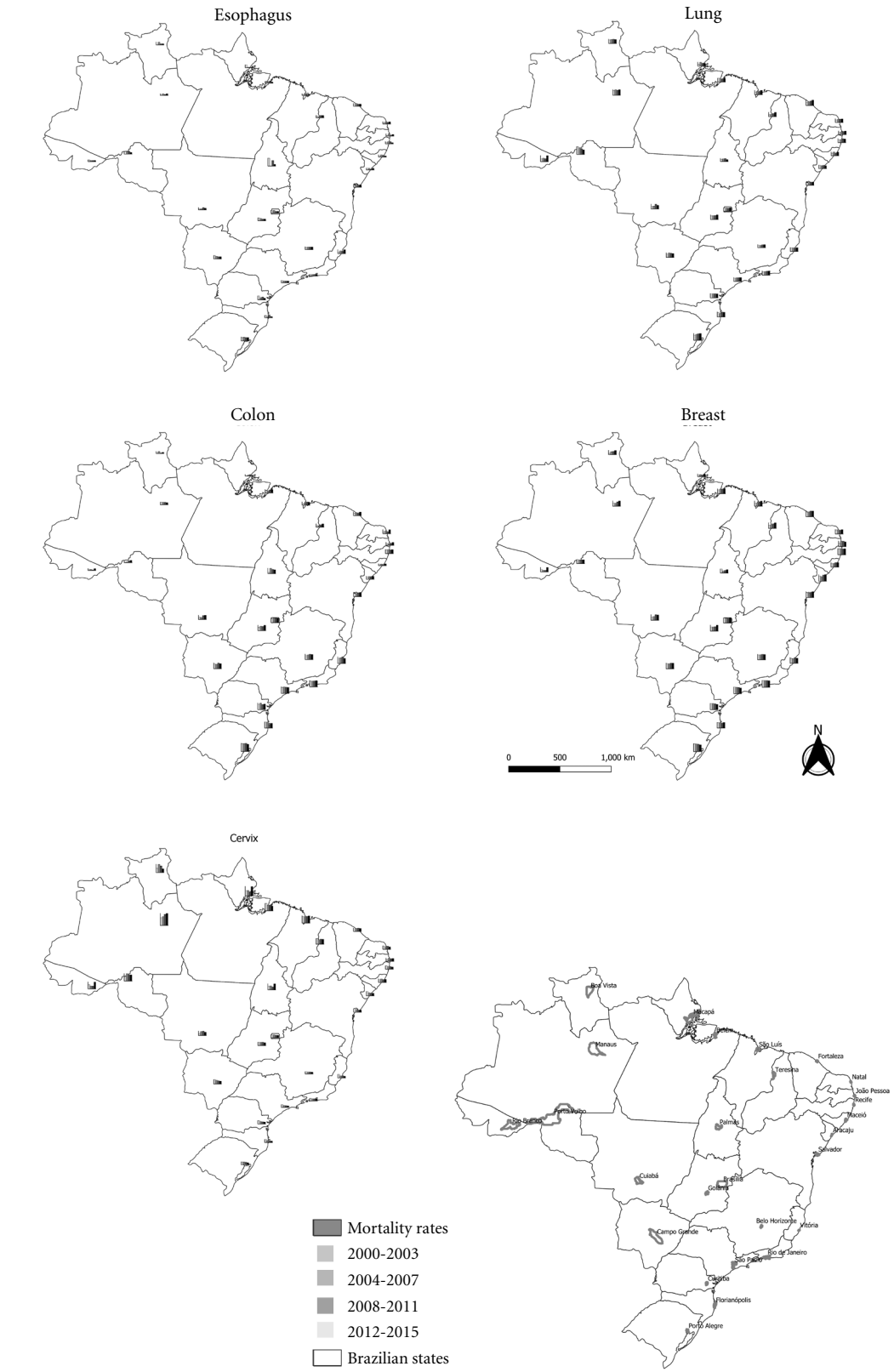

Figure 2. Trend of female mortality rate in the Brazilian capitals of the most incident cancers in the country.

Source: Authors.

Table 2. Unadjusted and adjusted rate ratio for a set of factors associated with cancer mortality in men.

	Prostate cancer				Colon cancer				Lung cancer				Esophageal cancer			
	Unadjusted		Adjusted		Unadjusted		Adjusted		Unadjusted		Adjusted		Unadjusted		Adjusted	
	RR	P-v	RR	P-v	RR	P-v	RR	P-v	RR	P-v	RR	P-v	RR	P-v	RR	P-v
Fixed effect																
Age																
20-39	0.01	***	0.01	***	0.10	***	0.10	***	0.03	***	0.03	***	0.92	***	0.92	***
40-59	1		1				1				1				1	
≥60	46.57	***	46.59	***	8.51	***	8.50	***	8.64	***	8.64	***	3.78	***	3.78	***
GDP	1.00	NS	1.00	NS	1.04	NS	0.99	NS	1.02	NS	1.00	NS	1.05	**	1.00	NS
Year	1.02	***	1.00	NS	1.05	***	1.04	***	1.01	NS	0.99	**	1.01	**	1.00	NS
Year^2	1.00	NS	0.999	**	1.00	NS	0.998	***	1.00	NS	0.999	***	1.00	NS	1.00	NS
Region																
South	1		1		1		1		1		1		1		1	
Southeast	1.05	NS	1.06	NS	0.87	NS	1.00	NS	0.65	**	0.65	***	0.60	***	0.62	***
Midwest	0.98	NS	1.23	*	0.58	**	1.07	NS	0.59	***	0.70	**	0.46	***	0.53	***
Northeast	0.92	NS	1.20	*	0.33	***	0.71	**	0.48	***	0.62	***	0.27	***	0.31	***
North	0.69	**	1.14	NS	0.18	***	0.39	***	0.40	***	0.64	***	0.23	***	0.27	***

RR = Rate Ratio; P-v = P-value; ref = reference; GDP (Gross Domestic Product) = GDP/1000USD (GDP was calculated in USD using the currency exchange rate on July 1st of each year); P-value significance codes: *** : < 0.001; ** : < 0.01; * : < 0.05; NS : > 0.05.

We used Poisson multilevel modeling, with the following random effects: capital (intercept), year squared (slope) and year of the death (slope). The response variables of the unadjusted and adjusted models were mortality by prostate cancer, colon cancer, lung cancer and esophageal cancer. The adjusted models were adjusted with the following fixed effects: age and GDP, region, year squared and year of death. Also, we included an offset with the logarithm of the population of the capital.

Source: Authors.

Table 3. Unadjusted and adjusted rate ratio for a set of factors associated with cancer mortality in women.

	Breast cancer				Cervix cancer				Colon cancer				Lung cancer				Esophageal cancer			
	Unadjusted		Adjusted		Unadjusted		Adjusted		Unadjusted		Adjusted		Unadjusted		Adjusted		Unadjusted		Adjusted	
	RR	P-v	RR	P-v	RR	P-v	RR	P-v	RR	P-v	RR	P-v			RR	P-v			RR	P-v
Fixed effect																				
Age																				
20-39	0.12	***	0.12	***	0.21	***	0.21	***	0.10	***	0.10	***	0.05	***	0.05	***	0.04	***	0.04	***
40-59	1		1	***	1		1				1				1				1	
≥60	2.64	***	2.64	***	2.05	***	2.05	***	6.76	***	6.75	***	5.31	***	5.31	***	5.91	***	5.91	***
GDP	0.99	NS	0.99	NS	0.98	NS	1.01	NS	1.03	NS	0.98	NS	1.02	*	1.00	NS	1.04	**	1.01	NS
Year	1.03	***	1.02	***	1.00	NS	0.99	NS	1.03	***	1.03	***	1.03	***	1.02	***	1.01	NS	0.99	**
Year^2	1.00	NS	1.00	NS	1.00	NS	1.00	NS	1.00	NS	1.00	NS	1.00	NS	0.999	*	1.00	NS	0.998	*
Region																				
South	1		1		1		1		1		1		1		1		1		1	
Southeast	0.98	NS	1.00	NS	0.93	NS	0.89	NS	0.98	NS	1.10	NS	0.76	NS	0.73	*	0.66	**	0.70	*
Midwest	0.83	NS	0.93	NS	1.12	NS	1.26	NS	0.55	*	1.02	NS	0.60	**	0.76	*	0.55	***	0.76	NS
ortheast	0.84	NS	0.92	NS	1.23	NS	1.42	NS	0.35	***	0.73	*	0.57	***	0.70	**	0.43	***	0.58	**
North	0.54	***	0.71	**	1.71	**	2.27	***	0.16	***	0.46	***	0.47	***	0.81	NS	0.28	***	0.48	***

RR = Rate Ratio; P-v = P-value; ref = reference; GDP (Gross Domestic Product) = GDP/1000USD (GDP was calculated in USD using the currency exchange rate on July 1st of each year); P-value significance codes: *** : < 0.001; ** : < 0.01; * : < 0.05; NS : > 0.05.

We used Poisson multilevel modeling, with the following random effects: capital (intercept), year squared (slope) and year of the death (slope). The response variables of the unadjusted and adjusted models were mortality by breast cancer, cervix cancer, colon cancer, lung cancer and esophageal cancer. The adjusted models were adjusted with the following fixed effects: age and GDP, region, year squared and year of death. Also, we included an offset with the logarithm of the population of the capital.

Source: Authors.

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Discussion

In Brazil, about 70% of the population depends on public health[13], and there are difficulties in accessing cancer diagnosis and treatment in public health services. The pattern of access to health services in Brazil is influenced by the social condition of people and the place where they live. The Unified Health System (SUS) has contributed to reducing social inequalities in access to health care, however, geographical inequalities still remain. In 2003, people living in the Southeast and South regions in Brazil, had the highest chances of using health services, while the chances of using them in the North, Northeast and Midwest were 45%, 40% and 23% smaller, respectively[14].

Primary care service is main route for the early diagnosis of cancer in Brazil. Over the years, there has been an increase in the population covered by the Family Health Strategy in Brazil reaching 64,7% in 2020.The growth occurred in both urban and rural areas[15].

There are still some barriers to the early diagnosis of cancer in Brazil. Among these barriers we can highlighted: the opportunistic screening, performed only when the patient in the risk group comes to the health service; and the difficulty of starting cancer treatment in 60 days, as required by Brazilian law[16]. The consequences of these problems are the worsening of the disease and the high numbers of preventable deaths.

Breast, cervix and colon cancer have a cure rate of around 95% when diagnosed early[17]. Mortality from breast and colon cancer continues to increase in Brazilian capitals, while mortality from cervical cancer remains stable, unlike what occurs in developed countries, whose mortality for these cancers is decreasing. The situation of prostate cancer is not different. The chance of cure for this cancer is 90% in the early stages[17]. Mortality rates for this type of cancer have remained stable in Brazilian capitals, while in developed countries mortality has been decreasing[18].

Lung cancer has more chance of cure when detected in the early stages, 56%[17]. Esophageal cancer is difficult to detect early. In most cases, the signs and symptoms only appear in more advanced stages of the disease. There is no well-established evidence on the benefits of screening for this type of cancer[17].

Despite the advance in knowledge about cancer, not all countries seem to benefit from this advance. This is the case of low- and middle-income countries, where a significant portion of the population does not have access to diagnosis and treatment, decreasing their chances of survival. Cervical cancer mortality rates in developed countries, for example, have decreased by at least 70% after the implementation of cervical cancer screening (1970s). Interventions such as vaccination against Papilloma Virus (HPV) and cervical cancer screening could also be implemented, even in low-income countries, where the mortality rate is still high (19).

Scientific literature indicates that colon, esophageal and lung cancers mortality rates are consistently higher in men than in women. Our results corroborate the literature, pointing to higher male mortality rates for these types of cancer.

From 2000 to 2015, we detected high lung cancer mortality rate in Brazilians capitals: 60/100,000 and 25/100,000 for males and females, respectively. Our findings pointed to a reduction in mortality in men and an increase in women. As in many other countries, lung cancer is the leading cause of cancer death in Brazil (20). Recent data indicate a reduction in lung cancer incidence and mortality in developed countries. From 2000 to 2017, the United State had a general reduction both in incidence (from 69.9/100,000 to 55.2/100,000) and in mortality (from 55.8/100,000 to 36.7/100,000)[21]. In Brazil, mortality by lung cancer increased 78.4% in men and 8.2% in women from 1979 to 2004[22]. More recent Brazilian study corroborates the findings of this study, indicating that between 1996 and 2011, there was a reduction in mortality by lung cancer in males and an increase in females[23].

The main risk factor for lung cancer is tobacco consumption, which is higher for males[24]. Tobacco consumption has been decreasing, and this decline may have contributed in some way to reducing lung cancer mortality in men over time[19].

The most significant reductions in smoking rates have occurred in countries that have implemented more advanced tobacco control laws, such as the United Kingdom, Australia and Brazil. Forecasts indicate that cigarette consumption will increase up to 2025 in many countries with a lower Human Development Index (HDI).

Regarding to sex, the rate of reduction in smoking has been slower among women[19].

In the same period, we detected a colon cancer mortality rate in Brazilians capitals around 12/100,000 for people older than 19 years old. Colon cancer is one of the three leading cancer death causes in Brazil. From 1996 to 2015, Bra-

zilian mortality by colon cancer increased by around 7% in both genders[25].

The incidence of colon cancer varies in different countries, with a predominance in developed countries, such as North America, Northern Europe, New Zealand and Australia. South America, Southwest Asia, Equatorial Africa and India have lower incidences[26]. Our results pointed to an annual increase of about 3.5% in colon cancer mortality rates. Dutra *et al.*, 2018, also reported a significant increasing trend of colon cancer mortality in both genders from 1996 to 2015, which are higher for men than for women[25].

One of the main risk factors for colon cancer is the high consumption of red meat[27]. However, others factors like sedentary lifestyle, tobacco and alcohol use have also been associated with colon cancer[28].

Obesity is an important risk factor for many types of cancer, including colon cancer. The increase in colon cancer levels is associated with an increase in the Body Mass Index (BMI)[29]. The magnitude of this relationship appears to be somewhat greater in men according to meta-analysis study[30].

In Brazil, the obesity prevalence estimates, available at VIGITEL, point to a reduction in the percentage of obesity in men from 20.2% to 14.4% from 2006 to 2010, and an increase in women from 12.7% to 15.5% in the same period. These results suggest obesity in women may have contributed to an increased risk of colon cancer in this specific group. However, more recent data estimated an increase in the incidence rates of colon cancer in Brazil, both for men and for women, from 2014 to 2020. In Brazilian capitals, estimates in the same period indicated a reduction in the colon cancer incidence rates in men from 2014 to 2020, while in women there was an increase from 2014 to 2018 and a reduction from 2018 to 2020[3].

Colon cancer mortality can be prevented when detected in the early stages, which justifies efforts to be made for early detection by screening for asymptomatic patients at higher risk. Countries like the United States, Luxembourg, Switzerland, Norway and the Netherlands screen for colon cancer[31], however, some middle-income countries provide only opportunistic tests for groups at risk when these people attend health services.

Global trends indicate that middle- and lower-income countries are not only experiencing rapid growth in the incidence of colorectal cancer, but also in mortality. High-income countries, on the other hand, have stabilized or reduced their incidence and mortality rates[32]. Since 2003, rapid annual increases in the incidence of colorectal cancer of up to 2% have been recorded in middle-income countries, such as Brazil and Costa Rica. Others middle-income countries like Philippines and Belarus, also experiment significant increases in colorectal cancer mortality rates[33].

In the 2000-2015 period, our results showed that the esophageal cancer mortality rate in Brazilians capitals was around 9/100,000. In the 2012-2016 period, the United States showed a rate of 4/100,000 for esophageal mortality cancer[34]. Studies evidenced a growing increase of esophageal cancer mortality in the Southern and Southeastern Brazilian regions, where the rates are similar to highly industrialized countries[7].

The main risk factors for esophageal cancer are the high intake of hot drinks[35], alcoholic beverages and tobacco, low ingestion of fruit and vegetable and exposure to occupational agents like benzene, silica and asbestos[36].

Just like colon cancer, epidemiological and biological data also link obesity to the development of esophageal adenocarcinoma[29]. Although the present study does not show evidence that points to an increase in esophageal cancer mortality in the study period, the increase in obesity in women over time deserves careful observation.

Breast cancer is the most common malignancy worldwide[37]. From 2002 to 2004, mortality by breast cancer in Porto Alegre (South of Brazil) in the age group of 40-49-years was 26/100,000[38]. Breast cancer mortality increased from 1991 to 2010 in Brazil. The significant elevation occurred in the Northeastern region (106%)[39]. According to the present study, breast cancer mortality rates in Brazilian capitals in the 2000-2015 period were around 30/100,000 for women older than 19 years. We detected an annual increase of 2% in mortality rates from this type of cancer over the period.

Family history is one of the most important breast cancer risk factors[40]. However, there are many other risk factors, such as aging, genetic mutations, reproductive history, dense breasts, past history of breast disease, previous treatment with radiotherapy, sedentary lifestyle, overweight or obesity after menopause, alcohol intake, use of hormones and some oral contraceptives[41].

Like colon cancer, breast cancer mortality can be prevented through early diagnosis by screening in asymptomatic women, which is already done in Brazil for women aged 50-69. Although, in general, the incidence of breast cancer in low-

and middle-income countries is lower than in developed countries, the mortality rate has been increasing in low- and middle-income countries, indicating inadequate screening for early detection and inadequate treatment[42]. Overall, 5-year survival rates for high-income countries, such as the United Kingdom, Canada, Australia, Northern Europe and Western Europe, are estimated at more than 85%, while in low- and middle-income countries the survival rates are much lower - examples: South Africa (53%), Algeria (38.8%), India (60%) and Brazil (58.4%)[43].

Our findings indicated that cervix mortality rates from 2000 to 2015 were around 16/100,000 for women older than 19 years. Cervix cancer is the third leading cause of death among women worldwide[44]. In Brazil, this is the fourth most common type of cancer[45]. Correcting and redistributing all the deaths classified as "malignant neoplasm of uterus, part unspecified" for "deaths due to cancer of cervix uteri and corpus uteri", it can become the second leading cause of death in the Brazilian female population[46]. Some Brazilian capitals recorded declining trend in cervix cancer mortality. In Pernambuco (Northeast of Brazil), the mortality rate by cervix cancer fell from 7.6/100,000 in 2000 to 6.8/100,000 in 2012[47].

Cervix cancer risk factors are associated with the risk of Human Papillomavirus (HPV) infection. High number of pregnancies and no regular preventive colpocytology are pointed out as risk factors to cervix cancer[48]. Brazilian research detected that around 7% of females have never submitted to cervical cancer screening, around 11% have done so late (over 36 months) and 19% do not have any guidance about the need of regular cervical cancer screening[49].

Many cancer risk factors are related to development. While morbidity and mortality of some cancers are higher in more developed countries, for other types, like cervical cancer, the rates are higher in middle and low income countries[1]. In this study, the highest rate of cervix cancer was detected in Northern capitals, which show one of the lowest Human Developing Index of Brazil.

Given that cervical cancer and its mortality are considered preventable conditions, accessibility to health services for the screening of this cancer and its precursor lesions is a fundamental condition to reduce its mortality. The coverage and frequency of Papillomavirus test are conditioned by socioeconomic and demographic disparities, with opportunistic screening predominating in countries with lower socioeconomic levels[50]. However, there are also studies that point out problems in cervical cancer screening. A study carried out in Minas Gerais (Southeastern Brazil) highlights high rates of non-performance of Papillomavirus tests and the high frequency of cases detected in advanced staging[51].

Prostate cancer mortality rates over the study period were around 50/100,000 for men older than 19 years. This type of cancer is the sixth leading cause of death worldwide[52]. Brazil and Latin America have a special position regarding the incidence and mortality of prostate cancer. In Brazil, prostate cancer is the second male mortality cause. From 1980 to 2010, there was an annual increase of 2.8% in prostate mortality rates in Brazil[53].

The main risk factors associated to this type of cancer are age, ethnicity, family history[54], lifestyle and dietary habits[55]. As with other types of cancer, diet is considered an important risk factor to explain the differences found in prostate cancer rates between different countries.

Like several cancers mentioned above, prostate cancer mortality can be prevented through early diagnosis and screening. The global trend suggests that the routine method for screening prostate cancer, Prostate Specific Antigen (PSA), is increasing worldwide[18]. However, there is still controversy regarding the benefits of screening for this type of cancer[56].

The results found in this study must be interpreted with caution, as our findings are derived from secondary data. Problems like underreporting and data coverage can differ by capital and region and can conceal the actual number of cancer mortality cases. These problems are more significant in the Northern and Northeastern Brazilian regions.

On the other hand, this study was able to analyze some of the cancers with the highest mortality rate in Brazil, differentiating them by gender. Trends were analyzed, both for cancers whose death could be prevented by screening, early diagnosis and appropriate treatment (breast, cervix, prostate and colon cancers), as well as those that are more difficult to detect early, such as esophageal and lung cancer. Our findings indicated that mortality from colon and lung cancer continues to increase between males and females, and mortality from breast cancer also increases in women.

Conclusion

Many deaths could be prevented if the Brazilian health system were more agile in detecting the

disease in its early stages and promptly provide adequate treatment to the diagnosed cases.

These study findings help to measure the magnitude of mortality from the main types of cancer in Brazil in the different subgroups and are important for planning actions in the Brazilian health system.

Collaborations

Study conception and design: NCP Rodrigues, G O'Dwyer, MKN Andrade, DLM Monteiro, IN Reis, VC Frossard and VTS Lino. Acquisition of data: Rodrigues. Analysis and interpretation of data: Rodrigues. Drafting of manuscript: Rodrigues Andrade. Critical revision: NCP Rodrigues, G O'Dwyer, DLM Monteiro, IN Reis, VC Frossard and VTS Lino. Final approval of the manuscript: NCP Rodrigues, G O'Dwyer, MKN Andrade, DLM Monteiro, IN Reis, VC Frossard and VTS Lino.

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