ORIGINAL ARTICLE

Observational Study

Trends and predictions for gastric cancer mortality in Brazil

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Abstract

AIM: To analyze the effect of age-period and birth cohort on gastric cancer mortality, in Brazil and across its five geographic regions, by sex, in the population over 20 years of age, as well as make projections for the period 2010-2029.

METHODS: An ecological study is presented herein,

which distributed gastric cancer-related deaths in Brazil and its geographic regions. The effects of age-period and birth cohort were calculated by the Poisson regression model and projections were made with the age-period-cohort model in the statistical program R.

RESULTS: Progressive reduction of mortality rates was observed in the 1980's, and then higher and lower mortality rates were verified in the 2000's, for both sexes, in Brazil and for the South, Southeast and Midwest regions. A progressive decrease in mortality rates was observed for the Northeast (both sexes) and North (men only) regions within the period 1995-1999, followed by rising rates.

CONCLUSION: Regional differences were demonstrated in the mortality rates for gastric cancer in Brazil, and the least developed regions of the country will present increases in projected mortality rates.

Key words: Gastric neoplasms; Brazil; Projections; Mortality

Core tip: Currently there are no detailed predictions in Brazil per geographic region and this study will provide the means for the elaboration of public health actions. This study presents a high citation potential, due to the innovative methodology and to the scientific development of Brazil, which is among the countries with most publications nowadays.

INTRODUCTION

Gastric cancer incidence has been decreasing globally since 1950[1], however its aggressiveness, malignity and, consequently, its prognosis, remain unaltered. Gastric cancer is currently one of the main causes of cancer-related deaths worldwide, and appears as the fourth most frequent cancer in men and sixth in women, being the fifth cancer-related cause of death for both sexes in the world[1].

Regarding risk factors for the development of gastric cancer, a higher incidence is verified in men than in women, in a 2:1 proportion, approximately[2]. Also, researchers remark that the main etiological factors related to the development of gastric cancer are infection by *Helicobacter pylori* (*H. pylori*) and diet, as the elevated consumption of salted foods (preserved or smoked), meat, and refined carbohydrates is directly associated with the risk of developing this neoplasm, while a diet based on fiber, vegetables and fresh fruit presents the inverse association[3,4].

Gastric cancer is usually also associated with low socioeconomic conditions[5], an aspect that highlights the importance of analyzing mortality along with the geographic distribution of the population, especially in countries characterized by high socioeconomic inequalities.

Given the epidemiological importance of gastric cancer, essential measures to support public policy actions include the analysis of the age-period and birth cohort on the distribution of mortality and mortality rate projections. These analyses enable the evaluation of the role of risk factors as well as modifications in therapeutics and diagnosis methods in the evolution of mortality rates[6,7].

Brazil presents demographic and socioeconomic heterogeneity across its five geographic regions, which translates to different mortality and morbidity patterns due to non-transmissible chronic diseases. Addressing cancer, both in prevention and attention to patients, requires differentiated responses that should be adapted to each specific region. Monitoring the trends of incidence and mortality rates, as well as risk factor prevalence, is paramount for vigilance actions and planning of prevention and treatment policies. The objectives of this manuscript are to analyze the effect of age-period and birth cohort in gastric cancer mortality, for Brazil and its five geographic regions, by sex, for the population over the age of 20, and make projections for the period 2010-2029.

MATERIALS AND METHODS

Study design and population
An ecological study is presented herein, on the distribution of deaths by gastric cancer, in Brazil and its five geographic regions, per sex. The study included deaths classified as 151 (stomach neoplasm) and C16 (malignant stomach neoplasm) in the 9th and 10th edition of the International Classification of Diseases (ICD), respectively. The study population included Brazilian men and women over 20 years of age. Mortality data were obtained from the Mortality Information System (MIS/DATASUS). Population data were obtained from the Informatics Department of the Unified Health System (DATASUS), based on the population censuses of 1980, 1991, 2000 and 2010. Inter-census projections for populations on July, 1st of the inter-census years were estimated by the Brazilian Institute of Geography and Statistics (BIGS).

Study variables
After extraction, data were corrected, redistributing 50.0% of the registries classified as ill-defined causes (codes 780-789 in ICD-9, and R00-R99 in ICD-10),

utilizing the redistribution methodology of the World Health Organization (WHO)[8]. After redistribution of ill-defined registries, deaths with incomplete diagnosis were redistributed proportionally by year and age group[9] (Mello *et al*[8], 2002). Herein gastric cancer deaths were corrected by two death groups with incomplete diagnosis: incomplete diagnosis for general cancer and incomplete diagnosis for gastric cancer. The following codes were considered as incomplete diagnosis for general cancer: C-77 to C-80 and C-97 in ICD-10; and codes 195, 197 to 199, 238 to 239 in ICD-9. For incomplete diagnosis of gastric cancer, the following codes were considered: 150 in ICD-9 and C-26 in ICD-10.

Once death data were corrected, mortality rates for gastric cancer were calculated per 100000 inhabitants, adjusted by the world population[10]. Age groups, periods and birth cohorts were grouped in five-year intervals, totaling 13 age groups (20-24 years of age to over 80 years of age), six periods (1980-1984 to 2005-2009) and 20 birth cohorts (1895-1899 to 2005-2009).

Data projections were made by sex for the periods 2010-2014, 2015-2019, 2020-2024 and 2025-2029 based on the three observed periods (1995-1999, 2000-2004 and 2005-2009), with results being presented in three age groups (0-39, 40-59 and $\geqslant$ 60 years of age) as well as the total result.

Statistical analysis

Age-period and birth cohort (APC) effects were calculated by the Poisson regression method. In this model, effects act in a multiplicative manner on the rates and the logarithm of the expected rate value is a linear function of the effect of age, period and cohort[6,7].

$$ln(E[r_{ij}]) = ln(\theta_{ij}/N_{ij}) = \mu + \alpha_i + \beta_j + \gamma_k$$

Where is the mortality rate expected for age *i* and period *j*, θ_{ij} is the number of deaths for age *i* and period *j*, and N_{ij} expresses the population under risk of death in age *i* and period *j*; μ represents the average of the effect, α_i represents the effect of group age *i*, β_j represents the effect of period *j*, and γ_k is the effect of cohort *k*.

The greatest limitation with the estimation of APC effect parameters is the linear relationship between the factors age, period and cohort, which hinders the estimation of the complete model. Methodologies have been proposed to address this issue; however, there is still no consensus in literature[6,7]. The APC effect parameters were estimated by estimable functions: deviations, curvatures, and *drift*, a method proposed by Holford[6,7].

A reference age group was selected (50-54 years of age), along with a reference period (1990-1994), and a reference cohort (which was the median value, as central cohorts are more stable). This manuscript utilized the 1930-1934[6,7] cohort as reference. The adjustment of the model was evaluated by the statistical function deviance, defined as twice the logarithm of the likelihood of the complete model in relation to the logarithm of the likelihood function of the estimated model. The contribution of effects was evaluated by the comparison between the deviance of the model with the specific effect in relation to the complete model (age-period-cohort). The results with $P \leqslant 0.05$ were considered statistically significant.

The association measurements, respective confidence intervals (95%CI), and the adjustments of the models were calculated by statistics program R version 3.2.1, with the Epi 1.1.18 library (R Foundation for Computational Statistics, Viena, Austria http://www.r-project.org).

Projections were made for each period utilizing the age-period-cohort model of the Norpred program, inscribed within the program R. Data were compiled in 5-year blocks and the limit age group considered for analysis was the first with more than 10 cases for the combined period. The results of the projections are presented by the observed and expected deaths for each period, for each Brazilian state. Also, for each period, adjusted mortality rates were calculated based on the standard world population to enable comparison with international data, expressed per 100000 inhabitants per year (ASW/100000 inhab). Variations between the number of cases in the last projected year (2025-2029) and the last observed period (2005-2009) were calculated, considering the proportion of variation that occurred in terms of changes in risk or demographics (size and structure of population). Both components can be different from zero and present a positive or negative direction. Calculation is expressed as follows[11]:

Δ tot = Δ risk + Δ pop= (Nfff - Noff) + (Noff - Nooo)

Where Δ tot is the total change, Δ risk is change in function of risk, Δ pop is change in function of population, Nooo is the number of observed cases, Nfff is the number of projected cases, and Noff is the number of expected cases when mortality rates increase throughout the observed period.

RESULTS

Within the period 1980-2009, there were 314445 deaths registered in Brazil, corresponding to an average standardized mortality rate of 11.71 deaths per 100000 inhabitants. After correction of the number of deaths, there was an increase of 30.8% in the number of deaths (411558), representing an average mortality rate of 15.32 deaths per 100000 inhabitants for gastric cancer, in individuals over 20 years of age. It must be highlighted that, throughout the country, the highest proportion of deaths occurred in the male sex. Also, the highest mortality rates for gastric cancer were observed for the male sex in Brazil and in all geographic regions of the country.
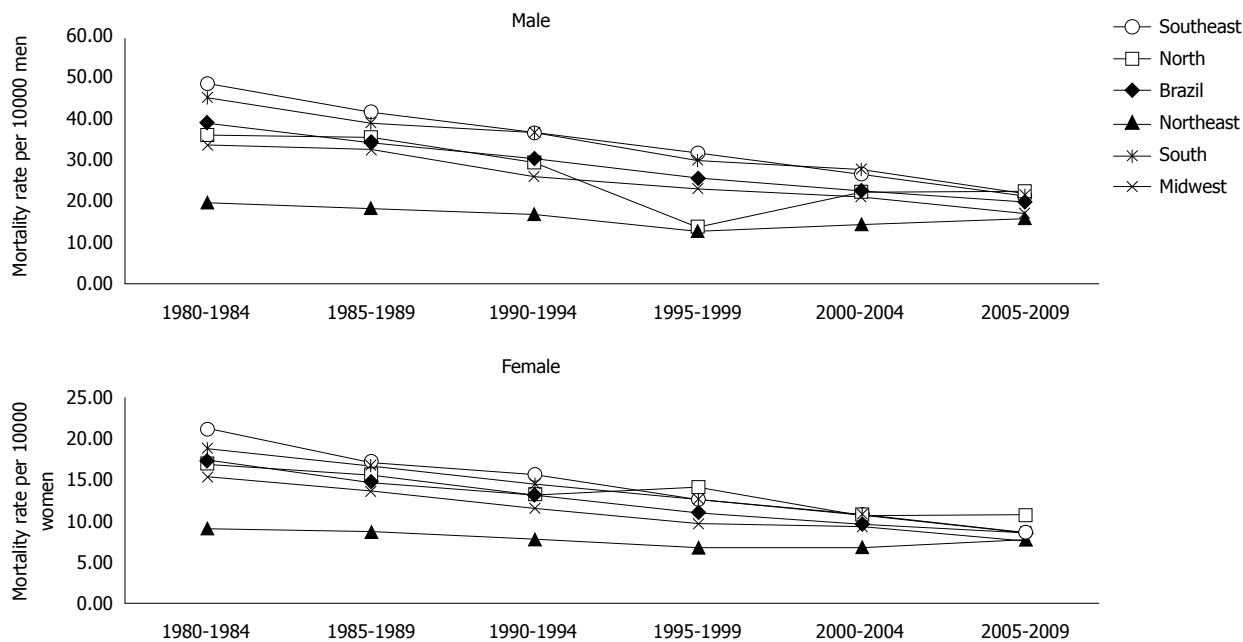
Figure 1 Mortality from gastric cancer according to sex and geographical regions, in Brazil, 1980 to 2009.

Analysis of the evolution of gastric cancer mortality rates for the last 30 years indicated a progressive decrease in rates in the 1980's, with higher and lower rates in the 2000's for both sexes in Brazil and the South, Southeast and Midwest regions. In the Northeast region, for both sexes, and in the North region for the male sex, there was a progressive decrease in mortality rates until 1995-1999, followed by rising rates (Figure 1).

In Brazil, as well as in all geographic regions and both sexes, the mortality rates for gastric cancer increased considerably after the age group 55-59 years of age. The highest mortality rates were verified in the age group over 80 years of age. Analysis of mortality according to study periods evidenced decreasing trends for both sexes in the South, Southeast and Midwest regions.

Regarding the mortality rates per age group according to birth cohorts, decreasing trends were observed in the evolution of mortality rates, for both sexes, in Brazil and in the Midwest, Southeast and South regions. This reduction occurred after the 1920 birth cohort, and was observed in all age groups. However, in the North region, increasing mortality rates were identified, for both sexes, in the age groups 75-79 years of age and over 80 years of age, starting from the 1919-1924 birth cohort. A similar profile was verified in the Northeast region, for both sexes, in individuals born after the 1910-1914 cohort for age groups after 65-69 years of age.

Regarding death risk in the analyzed periods, Brazil presented a protection risk (relative risk, RR, under 1) when compared to the reference period 1990-1994. Analysis of death risk per geographic region pointed towards disparities between the Brazilian geographic regions. The South and Southeast regions showed decreases in death risks due to this neoplasm, with a protection effect (RR ⩽ 1) especially in the period 2005-2009 for both sexes. The Midwest region presented a very specific profile, as despite RR was above 1 in all periods in relation to the reference period, there was a progressive reduction in death risk due to gastric cancer in the analyzed periods (Figure 1). The North and Northeast regions presented decreases in death risks for the period 1995-1999, but in the following periods there was an increase in risk (RR ⩾ 1), for both sexes (Figure 2).

Brazil and the Midwest, North, Southeast and South regions presented reductions in death risks for gastric cancer for both sexes, with a protection effect for birth cohorts after 1940-1944, when compared to the reference cohort. This reduction was more expressive in the South and Southeast regions (Figure 2).

Table 1 shows the deviance changes in the sequential construction of APC models. In the evolution of rates for both sexes, in Brazil and its geographic regions, the model with three factors (APC) presented best fit, except for the Midwest region and female sex, for which the most explanatory model was age-cohort (AC).

When comparing the evolution of standardized mortality rates for gastric cancer, increases were observed for the male sex in the North and Northeast regions, and in the female sex in the Northeast region. The projections for the Midwest, South and Southeast regions as well as the pooled analysis for Brazil indicated a reduction in mortality rates for the male sex and stability for the female sex. The number of cases per region, the adjusted rates for the observed period, and projections per sex are presented in Table 2.
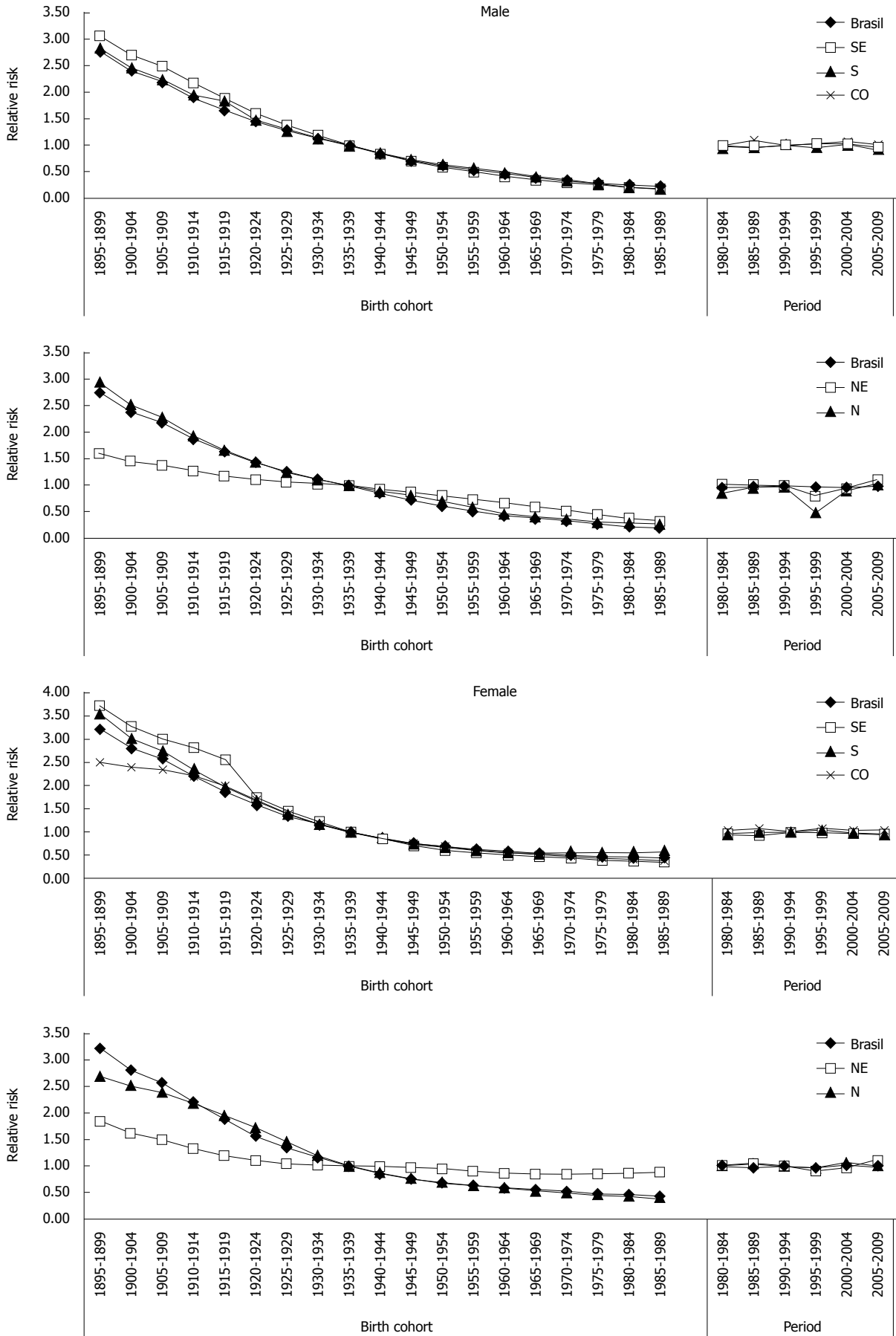
Figure 2 Results of the Age-period-cohort model, adjusted for gastric cancer mortality, according to to sex and geographical regions, in Brazil, 1980 to 2009.

Table 1 Deviance changes in the sequential construction of age-period and birth cohort models

Models	Brazil					
	Female			Male		
	Resid.DF	Res.Dev	*P* value	Resid.DF	Res.Dev	*P* value
Age	72	9069.3		72	15752.0	
Age-drift	71	661.6	< 0.00001	71	515.1	< 0.00001
Age-cohort	67	390.5	< 0.00001	67	403.0	< 0.00001
Age-period-cohort	64	372.5	0.001	64	370.6	< 0.00001
Age-period	68	642.8	< 0.00001	68	485.9	< 0.00001
Age-drift	71	661.6	0.001	71	515.1	< 0.00001
Midwest						
Models						
Age	72	399.77		72	899.91	
Age-drift	71	88.88	< 0.00001	71	116.80	< 0.00001
Age-cohort	67	72.14	0.002	67	111.94	0.302
Age-period-cohort	64	66.18	0.200	64	95.83	0.003
Age-period	68	83.03	0.002	68	100.13	0.366
Age-drift	71	88.88	0.210	71	116.80	0.002
North						
Models						
Age	72	325.04		72	1310.75	
Age-drift	71	140.37	< 0.00001	71	779.28	< 0.00001
Age-cohort	67	129.65	0.030	67	751.44	< 0.00001
Age-period-cohort	64	110.22	0.001	64	178.57	0.003
Age-period	68	121.64	0.022	68	194.68	< 0.00001
Age-drift	71	140.37	0.001	71	779.28	< 0.00001
Northeast						
Models						
Age	72	566.75		72	1038.52	
Age-drift	71	405.46	< 0.00001	71	656.22	< 0.00001
Age-cohort	67	269.65	< 0.00001	67	597.78	< 0.00001
Age-period-cohort	64	142.85	< 0.00001	64	155.70	< 0.00001
Age-period	68	230.83	< 0.00001	68	208.92	< 0.00001
Age-drift	71	405.46	< 0.00001	71	656.22	< 0.00001
South						
Models						
Age	72	1903.85		72	3090.98	
Age-drift	71	219.90	< 0.00001	71	207.96	< 0.00001
Age-cohort	67	152.41	< 0.00001	67	189.07	0.001
Age-period-cohort	64	124.92	< 0.00001	64	129.74	< 0.00001
Age-period	68	200.58	< 0.00001	68	143.44	< 0.00001
Age-drift	71	219.90	0.001	71	207.96	< 0.00001
Southeast						
Models						
Age	72	6993.8		72	11604.0	
Age-drift	71	447.6	< 0.00001	71	399.5	< 0.00001
Age-cohort	67	278.8	< 0.00001	67	290.5	< 0.00001
Age-period-cohort	64	217.6	< 0.00001	64	209.5	< 0.00001
Age-period	68	389.4	< 0.00001	68	284.7	< 0.00001
Age-drift	71	447.6	< 0.00001	71	399.5	< 0.00001

For Brazilian men, an increase is expected in the number of deaths (30203) when comparing the last observed period with the last projected period, representing a 62% growth, of which 101% is due to population increase and -39% is due to reduction in risk. For women, the expected increase in the number of deaths is 20308, with 99% growth due to changes in population and -23% in reduction of risk. Figure 3 shows the changes in the number of deaths, in function of risk and population increase, when comparing the last observed period and the last projected period for gastric cancer in the Brazilian regions.

DISCUSSION

This study evidenced disparities in the evolution of mortality rates due to gastric cancer in Brazilian geographic regions, within the analyzed periods. There was an increase in death risk by this neoplasm in the North and Northeast regions starting from the 2000's, when compared to the reference period.

Gastric cancer, despite the decrease presented in incidence and mortality rates, is still one of the main cancer-related causes of death globally[12]. This disease presents a bad prognosis, with 5-year survival rates

Table 2 Observed and predicted number of deaths by age and world age-standardized rates in Brazil

| Males			Observed			Predicted			
			1995-1999	2000-2004	2005-2009	2010-2014	2015-2019	2020-2024	2025-2029
Males									
North	Age	0-39	99	126	156	200	243	277	296
		40-59	700	818	929	1119	1247	1478	1670
		≥ 60	1287	1597	2151	2792	3579	4332	5195
	Total		2086	2541	3236	4110	5069	6087	7160
	ASW		13.6	13.3	14.3	15.0	15.2	14.8	14.2
Northeast	Age	0-39	310	332	405	388	377	366	365
		40-59	1662	2041	2633	3226	3745	4135	4155
		≥ 60	4086	5624	7020	9070	11415	14018	16827
	Total		6058	7997	10058	12685	15537	18519	21347
	ASW		7.5	8.7	9.8	10.9	11.4	11.6	11.4
Midwest	Age	0-39	94	98	102	102	105	97	92
		40-59	684	707	753	779	813	941	1126
		≥ 60	1404	1705	1827	2039	2371	2784	3362
	Total		2182	2510	2682	2920	3289	3821	4580
	ASW		13.5	12.2	10.6	9.3	8.4	7.9	7.8
Southeast	Age	0-39	801	616	660	563	576	619	524
		40-59	6255	6404	6304	5748	5629	6052	7537
		≥ 60	16611	16790	14648	14316	15277	17650	21598
	Total		23667	23810	21612	20627	21482	24320	29658
	ASW		18.7	15.5	12.0	9.6	8.3	7.9	8.3
South	Age	0-39	250	235	241	188	137	120	108
		40-59	2245	2356	2403	2361	2410	2444	2649
		≥ 60	5515	6052	6062	6392	7041	8199	9745
	Total		8010	8643	8706	8941	9588	10762	12502
	ASW		18	16.2	13.6	11.5	10.3	9.7	9.5
Brazil	Age	0-39	1660	1403	1567	1796	2105	2502	2736
		40-59	13382	12196	12944	13909	15114	16962	19978
		≥ 60	32344	31439	34145	37297	41994	48255	56146
	Total		47386	45038	48656	53002	59213	67718	78861
	ASW		16.7	13.3	12.2	11.2	10.4	10.0	10.0
Females									
North	Age	0-39	110	122	127	159	163	174	180
		40-59	324	375	460	557	659	790	909
		≥ 60	678	792	1040	1327	1739	2244	2870
	Total		1112	1289	1627	2044	2561	3208	3959
	ASW		7.1	6.4	6.8	6.9	7.0	7.1	7.0
Northeast	Age	0-39	274	314	380	460	554	527	524
		40-59	943	1114	1394	1773	2105	2490	2754
		≥ 60	2551	3152	4318	5723	7392	9309	11348
	Total		3768	4580	6092	7955	10051	12326	14626
	ASW		4	4	4.7	5.2	5.6	5.8	5.9
Midwest	Age	0-39	82	92	96	93	87	82	79
		40-59	277	333	382	442	547	634	717
		≥ 60	603	771	875	1028	1217	1515	1947
	Total		962	1196	1353	1562	1850	2232	2743
	ASW		5.8	5.3	4.7	4.3	4.0	3.9	3.9
Southeast	Age	0-39	576	652	675	674	685	627	562
		40-59	2413	2778	3008	2983	3140	3569	4168
		≥ 60	8058	9652	9619	9950	10667	12047	14398
	Total		11047	13082	13302	13606	14493	16243	19127
	ASW		6.8	6.4	5.4	4.6	4.2	4.1	4.2
South	Age	0-39	215	217	258	257	280	238	220
		40-59	984	949	1052	1150	1283	1546	1857
		≥ 60	3005	3106	3143	3268	3578	4111	4939
	Total		4204	4272	4453	4675	5142	5895	7016
	ASW		7.6	6.2	5.3	4.7	4.4	4.4	4.6
Brazil	Age	0-39	1313	1376	1511	1811	2107	2268	2515
		40-59	5540	5458	6274	7075	8168	9879	11902
		≥ 60	16991	17450	18982	20635	23267	27116	32678
	Total		23844	24284	26767	29522	33542	39263	47095
	ASW		6.9	5.6	5.2	4.8	4.7	4.7	4.9
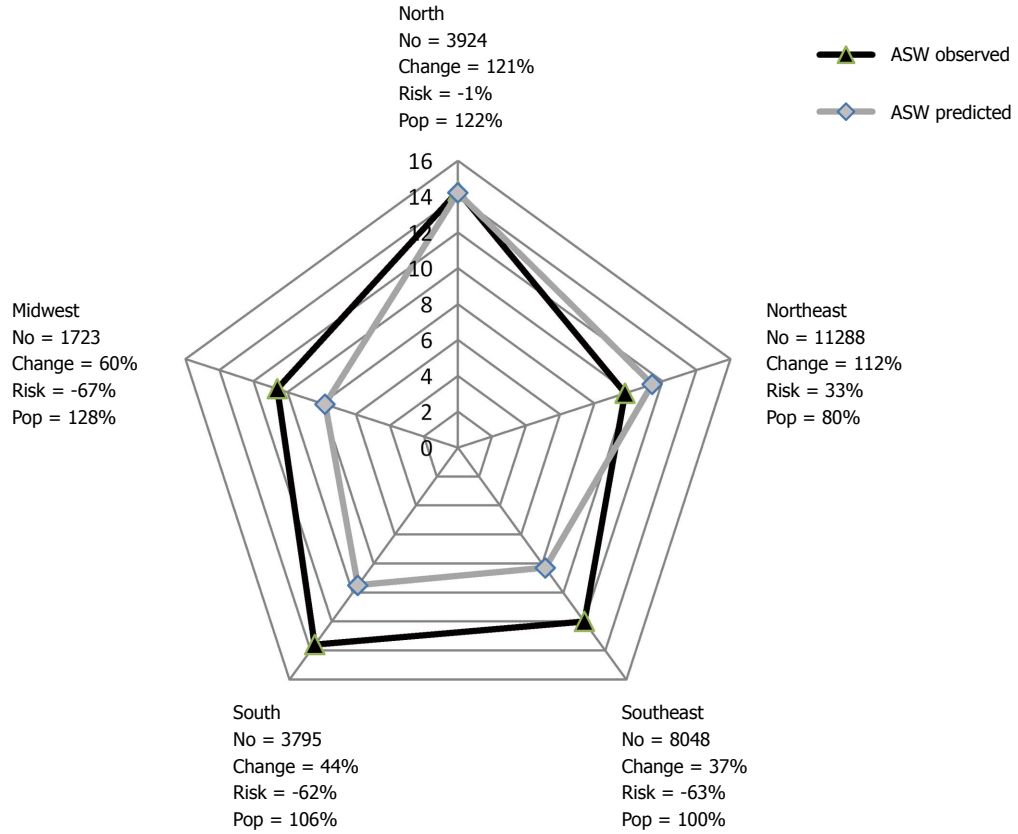
ASW: Age-standardized rates.
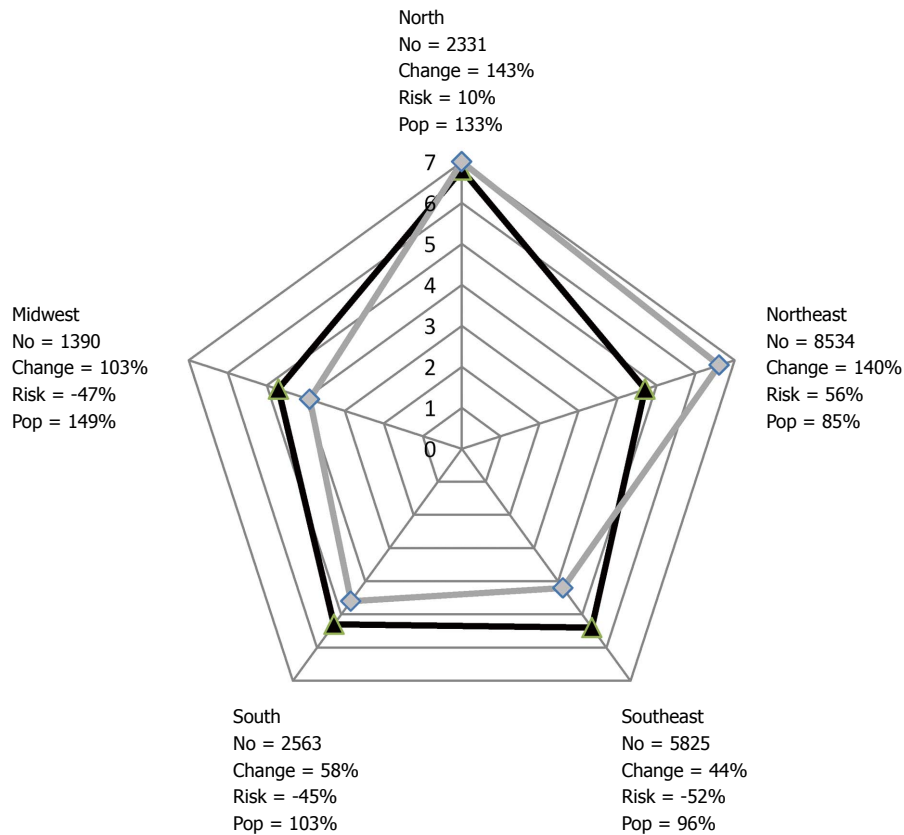
Figure 3 World age-standardized rates, changes in numbers of deaths relative change due to risk and changed population, between 2005-2009 (observed) and 2025–2029 (predicted) of gastric cancer mortality in Brazil. ASW: Age-standardized rates; Pop: Population.

under 20%[13].

The mortality rates presented in Brazil, in all regions and for both sexes, are located at intermediate levels, similar to the rates of Venezuela and Argentina, but still superior to those of developed countries such as the United States, Spain, France and Canada. However, Brazilian rates are lower than the mortality rates verified for China, Japan and South Korea[12-20].

This neoplasm can be classified according to its location, in cardia and non-cardia gastric cancer. These diseases present different risk factors and population distributions. While non-cardia gastric cancer presents main risk factors such as *H. pylori* infection, consumption of salt-preserved food, low consumption of fruit and vegetables, consumption of alcohol and use of tobacco, cardia gastric cancer (esophagogastric junction adenocarcinoma) is a pathology related to obesity, gastroesophageal reflux and Barrett esophagus. Besides, this disease is more common in developed countries and white race individuals, while non-cardia gastric cancer is more incident in Afro-Americans and in developing countries[19,21,22]. There have been important global reductions in incidence and mortality rates for non-cardia gastric cancer; however, an increasing trends have been observed for esophagogastric junction adenocarcinoma, which represents currently 50% of new diagnosed cases of gastric cancer. The prognosis of this type of cancer is worst than non-cardia gastric cancer, as esophagogastric junction adenocarcinoma can disseminate to the abdominal region as well as to the lymph nodes of the thoracic region. Due to the absence of symptoms at the beginning of the disease, esophagogastric junction adenocarcinoma is usually diagnosed in advanced stages[23].

As in other parts of the world, the Brazilian and per region rates for the male sex were approximately twice higher than mortality rates for the female sex[19,21,22]. Some authors believe that this difference is due to the co-existence of other risk factors and that there is unequal exposition according to sex[5,21]. Other authors mention that this reality is related to the fact that women are more aware of health issues than men[18].

Mortality due to this neoplasm in Brazil and in the Midwest, South and Southeast regions presented decreasing trends, along with France, Italy, Spain, Germany, South Korea, Japan and China[1,14]. In the United States and United Kingdom, half of gastric cancers are located in the cardia area, and in the last 30 years, globally, incidence of this disease has increased between 5 and 6 times[22].

A reduction in death risk was evidenced in Brazil and in the South and Southeast regions, starting from the 1990's, and increased risk was observed in the North and Northeast regions after the 2000's. Changes in mortality rates of diseases can reflect changes in exposition to risk factors (environmental and/or associated with lifestyle), as well as improvements in diagnosis, treatment, verification and certification of deaths. The differences presented between the North-Northeast regions and other regions of Brazil, especially in the 2000's, can be a result of the period effect, due to improvement in death registry data and better access to health services. Due to an increase in the possibilities of diagnosing this neoplasm, even if in advanced stages of the disease, these regions presented higher mortality rates in the 2000's.

Regarding birth cohorts, a progressive reduction in death risk was verified starting in the XX century, in all regions and for both sexes. This result was similar to the results of South Korea, Japan, United States, and Spain[15,17,24,25]. This reality can be explained by the prevalence reduction of *H. pylori* infection, use of refrigerators (which increased the consumption of fruit and vegetables)[26-29], besides the reduction in the consumption of salt-preserved foods[30] and better sewage collection and treatment, which contributes to reducing the transmission of *H. pylori*, especially in children and teenagers[19,22]. Reduction of mortality can also be related to new therapeutic strategies implemented within the last decade for the treatment of gastric cancer. These are based on neoadjuvant/ adjuvant chemotherapy treatment, which can be associated with radiotherapy[31]. A literature review study with meta-analysis evidenced that patients treated with adjuvant chemotherapy presented better global survival (HR = 0.82; 95%CI: 0.76-0.90; *P* < 0.001) and disease-free survival (HR = 0.82; 95%CI: 0.75-0.90, *P* < 0.001) when compared to patients submitted to surgical treatment only[32]. However, there is still no consensus within literature on the best treatment to be utilized, and no studies were found in Brazil that evaluated the implementation of these new therapeutic measures on the survival of patients.

Survival rates are affected by early diagnosis, standardized surgery techniques, nutritional therapy, availability of beds in intensive care units, and the existence of specialized health teams for cancer treatment[13,17]. In this way, the pronounced inequity between Brazilian geographic regions (large urban centers *vs* the interior) regarding access to cancer diagnosis and treatment services can influence the evolution of mortality rates for this disease. The study by Oliveira *et al*[33] evidenced sanitary gaps related to breast cancer treatment, especially in North Brazil, with half of health assistance concentrated in few capital cities. The cities of Rio de Janeiro and São Paulo (Southeast Brazil) were responsible for one fifth of attendances, mostly for the resident population. Brazil has a public and universal health system that faces limitations regarding funding and access to diagnosis and treatment services. This reality should not be exclusive to breast cancer treatment and highlights the difficult access to health services that most cancer patients suffer in Brazil[34].

The projections indicated that the least developed

regions of Brazil (North and Northeast) will present increments in gastric cancer mortality rates. These regions present structural challenges in oncology services[34-36]. Also in the North and Northeast regions of the country, the increased mortality can be explained by higher difficulty in the access to diagnosis and treatment services. The ratio medical doctor/inhabitant is lower in the North and Northeast regions (in 2010, approximately 1 doctor per 1000 inhabitants) than in the South and Southeast regions (respectively 2.5 and 2.0 doctors per 1000 inhabitants). The distribution of oncology specialists and oncology hospitals is also unbalanced[37]. Also, there is concentration of oncology services in large urban centers, as a consequence of internal migration and development of these areas. The search for appointments with specialists and access to diagnosis and treatment services generates dislocation from rural areas to large urban centers, which delays diagnosis and therefore, entail in worst prognosis for these patients[32].

A limitation to be considered in the study is the impossibility of separating cardia and non-cardia locations for gastric cancer, which seem to present different behaviors according to most recent studies, as the Brazilian Mortality Information System does not differentiate gastric cancers according to histological type[21]. Another important fact to consider is the lack of historical series for risk factor prevalence, which could aid in the analysis of the observed changes. Finally, it must be highlighted that this is an ecological population study, and intra-regional differences can be found in Brazil due to its large continental dimensions, especially regarding the quality of death registries, which the authors attenuated after correcting death data. Limitations related to the APC models must also be mentioned, as these are still under development and there is no consensus in literature on the best methodology to correct the issue of non-identification of the complete model[6,7].

The projections made must be interpreted with caution, as the diagnostic and therapeutic conditions can change in the future, and consequently the mortality trends could be slightly modified. The projection of mortality rates is very important to support the planning of public health measures, as well as to control modifiable risk factors at short and long terms, on the burden of the disease to the population[33]. The main objective of the projections made herein was to provide the required information for health planning purposes, aiming at the selection of vigilance actions for gastric cancer.

COMMENTS

Background
The evolution of gastric cancer mortality has evidenced decreasing trends for Brazil in the South, Southeast and Midwest regions of the country, for both genders. However, after the 1990's, increasing trends were observed in the Northeast (both genders) and North (in men only) regions. After the 1940-1944

birth cohort, reduction in death risk was observed for this neoplasm, in both genders, for Brazil and its South, Southeast and Midwest regions. The opposite situation was verified for the Northeast region, which presented a progressive death risk for cohorts born from the 1940-1944 cohort. Regarding mortality projections until 2030, increased mortality rates were evidenced for both genders, in the North and Northeast regions of the country.

Research frontiers
The study evidenced a progressive reduction in risk of death from gastric cancer in birth cohorts after the 1940's, in the most developed regions of Brazil, with the opposite occurring in the poorer geographic regions. These findings are similar to those in studies carried out in South Korea, Denmark, Japan, United States, England, Italy, Switzerland and Spain, and evidences the important role played by basic sanitation and access to health services in gastric cancer mortality.

Innovations and breakthroughs
In most epidemiological studies, trend analysis of mortality rates is based on the evaluation of mortality by age group and death date. The present study analyzed the effect of age-period-birth cohort on the evolution of gastric cancer mortality rates and enabled the evaluation of factors related to age and period as well as whether modifications in mortality trends for this disease were associated to changes in exposition to long-term risk factors (birth cohort effect).

Applications
The results suggest flaws in gastric cancer prevention and control measures in the North and Northeast regions of Brazil. The findings will help plan Brazilian public policies directed to the promotion of primary, secondary and tertiary prevention, to reduce mortality rates for gastric cancer in Brazil and its geographic regions.

Terminology
South region: this Brazilian geographic region presents the best human development indices. This region includes the states of Rio Grande do Sul, Santa Catarina and Paraná. Southeast region: this is the most populous and rich region of the country, and 85% of industry-related jobs are located in this region. This region comprehends São Paulo, Minas Gerais, Rio de Janeiro and Espírito Santo. Midwest region: the main economic activity of this region is farming and livestock. This region presents the second lowest demographic density of the country, and is constituted by Mato Grosso, Mato Grosso do Sul, Goiás and Distrito Federal. Northeast region: this Brazilian region presents one of the worst human development indices, and is characterized by the presence of a semi-arid region within its territory, and is one of the poorer areas of the country. This region comprises nine states: Alagoas, Bahia, Ceará, Maranhão, Paraíba, Pernambuco, Piauí, Rio Grande do Norte and Sergipe. North region: this Brazilian region presents the lowest demographic density, as well as the second worst human development index. This region spans the Amazon Forest, which is an important ecosystem for the world, and includes the states of Amazonas, Amapá, Pará, Tocantins, Roraima and Rondônia. Age effect: evaluates the influence of age on the evolution of mortality rates. Period effect: evaluates the impacts of changes in diagnostic methods, treatment protocols, as well as changes in death certification and improvement of mortality information systems on the evolution of mortality trends. Birth cohort effect: analyzes whether modifications in mortality trends were associated with changes in exposition to long-term risk factors.

Peer-review
In this study the authors report trends in the incidence and mortality of gastric cancer over the last decades and make a prediction on the mortality in the upcoming years. All in all the study is well conducted and has interesting results, needs some minor revisions.

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