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Breast Cancer Mortality in Brazil: Correlation with Human Development Index

ORIGINAL

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Abstract

Background: Mortality from breast cancer has decreased in high-income countries, while countries with middle and low incomes as Brazil still have upward trend. However, large geographical variations among the federal units are observed in the country. The aim of the study was to evaluate the trend of specific mortality from breast cancer in women over 20 years old among different states of Brazil from 1996 to 2012.

Methods and Findings: Ecological study, using linear regression model for temporal analysis of specific mortality coefficient from malignant neoplasm of breast. We also checked the degree of its correlation with the HDI for the states of Brazil during the stated period. There was an increase in the specific mortality rate for malignant neoplasm of the breast in order of 33%, with range from 23.2 to 30.8/100,000 inhabitants. The states with the highest human development HDI in 2010, showed the largest specific mortality rates of breast cancer.

Conclusion: This study confirms the need for improvements in mammography coverage, following radiological lesions suspected and access to appropriate therapy.

Keywords
Breast Neoplasm; Mortality; Socioeconomic Factors.

Introduction

Breast cancer is the second most frequent cancer in the world, corresponding to 22% of new cases of cancer each year. In middle and low-income countries it is more frequent cancer in female population, followed by the cervical cancer of uterus and lung cancer [1].

In recent decades, in the high-income countries, breast cancer mortality has been on decline [2]. However, medium and low-income countries still exhibit upward trends [3]. This is explained, in part, by the demographic changes and lifestyle, that interfere with prevalence of reproductive factors such as breastfeeding for short periods of time, advanced age at first pregnancy and lower number of children [4, 5], inadequate food intake, obesity overweight and stress [5,6]. Other linked factors relate to the abusive consumption of alcohol, early menarche and late menopause [7].

In Brazil, breast cancer is the leading cause of mortality for neoplasia among women [8], with a rate of 15.8/100,000 in 2011 [8].

One of the main difficulties for the reduction of mortality for breast cancer is the diagnosis only in advanced stages of the disease, which compromises the treatment results [9], especially in low-income women [10]. Early detection of breast neoplasia is the main strategy of secondary prevention, fundamental for the good prognosis of disease [6, 11, 12].

Socioeconomic indicators are predictors of the incidence, diagnosis, treatment and prognosis of the various types of cancer in the world [13, 14]. The Human Development Index (HDI) is a composite indicator that contains information about the life expectancy at birth, educational status and the Gross Domestic Product (GDP) [15]. Despite being inversely associated with the incidence rates of cancer in general [14], is directly associated with the incidence of breast cancer [16]. Part of this relationship is explained by lifestyle and by access to early diagnosis of breast neoplasm [5, 16-19].

In developed countries, the rate of survival is higher due to early detection and, probably, to access to treatment, compared to less developed countries [18, 19]. Among the countries of Latin America, characterized by urban poverty, which exacerbates social disparities, Brazil continues to present itself as a favorable area to study geographic patterns of mortality from breast cancer.

In this study, it was decided to analyze the temporal tendency of malignant neoplasm of breast cancer in Brazil, in women older than 20 years in Federated units and administrative macro-regions for providing a national overview, in the period of 1996 to 2012, and its correlation with the HDI in the year 2010.

Methods

This is an ecological study assessing the temporal trends of breast cancer mortality in women aged over 20 years in the Brazilian States and macro-regions in the period of 1996 to 2012.

The information about the deaths was obtained from Mortality Information System of the Ministry of Health (MIS/MS) available in the database DATASUS tabulated in March 2015, through the TABWIN software (version 3.6b). The deaths were selected for inclusion using the International Classification of Diseases (ICD-10) code for breast cancer (C50) and were categorized among States by place of residence (rather than by place of occurrence). Breast cancer-specific mortality coefficients were calculated with the use of a standardized population of the World Health Organization (WHO) by age group for the year 2010, considering the proportions of the female population above 20-year-old Brazilian, extracted from the projections of the demographic census in 1996 to 2012 (DATASUS-MS, 2012).

The human development of the Brazilian States was assessed through the Municipal Human Development Index (HDI-M), as specified by the United Nations Development Programme (UNDP) in Brazil.

The IDH-M retains the dimensions of the HDI, but uses data sources and minimum and maximum values for the Brazilian reality, allowing a better comparison between the States or Brazilian municipalities. The IDH-M for the Brazilian States in 2010 was obtained from Brazilian Human Development Atlas in 2010 (http://www.atlasbrasil.org.br/2013/).

The temporal tendency of mortality from breast cancer was described through Prais-Winsten regression, having the year as exposure variable. On the other hand, linear regression was used to describe the relationship between breast cancer mortality and the HDI-M States in 2010.

Coropletic maps for the four years 1996-1999, 2000-2003, 2004-2008 and 2009-2012 were drawn from the ranges of specific mortality coefficients of breast cancer mortality, incorporating the proportional circle for each federated unit, following the linear scale from 10 deaths per 100,000 inhabitants with amplitude up to 50 deaths per 100,000 inhabitants. The data used in the study are aggregated and publicly available, so that it did not require the approval by the Ethics Committee.

Results

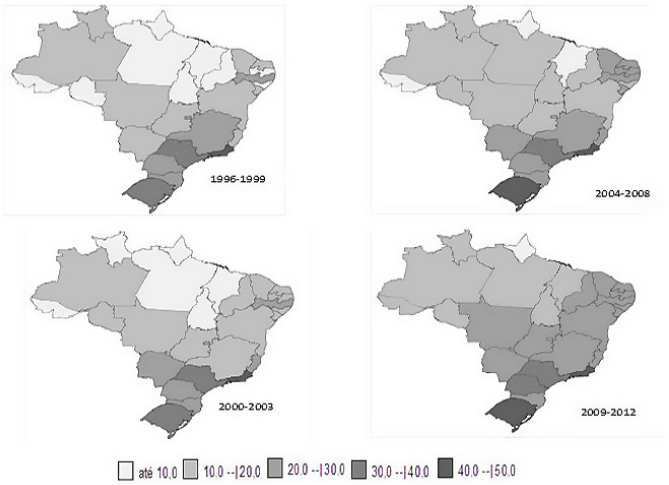
Temporal analysis of breast cancer mortality in Brazil showed an upward trend, especially after 2001, ranging from 23.2 to 30.8/100,000 inhabitants from 1996 to 2012. The increase observed was 33% in this period **(Table 1)**. This increase was observed in all States of the Federation, noting that, for the pe-

Table 1. Standardized mortality rate for breast cancer in women aged 20 years or older. Brazil. 1996 to 2012.

States	Year																
	1996	1997	1998	1999	2000	2001	2002	2003	2004	2005	2006	2007	2008	2009	2010	2011	2012
North	8.5	8.0	10.1	9.0	9.6	8.5	10.9	10.6	11.3	11.2	13.1	11.9	14.0	12.9	12.7	15.5	15.2
Rondônia	4.0	5.0	11.2	9.1	10.6	6.6	12.7	12.1	11.5	11.1	11.7	15.9	20.1	18.3	11.1	16.7	10.3
Acre	5.4	10.5	6.4	4.9	7.9	8.7	9.6	7.3	5.1	10.3	10.0	8.1	5.0	4.1	3.7	12.4	23.0
Amazonas	11.4	11.1	14.7	11.0	12.0	9.9	8.6	11.5	10.8	9.0	12.7	11.5	14.7	12.3	14.3	16.9	21.0
Roraima	16.3	13.2	7.7	7.5	11.8	9.4	3.7	5.3	12.1	16.3	15.8	10.3	5.9	13.0	11.0	16.7	25.7
Pará	9.1	8.1	9.1	9.4	8.9	8.5	12.1	10.1	11.8	13.3	13.7	12.2	14.0	13.0	13.3	14.8	12.3
Amapá	0.0	3.3	4.7	3.0	11.9	13.9	4.9	5.9	10.3	6.4	11.3	7.4	6.7	5.6	7.3	14.3	10.9
Tocantins	7.2	3.5	7.9	6.6	5.6	5.5	13.2	14.4	12.7	6.8	13.7	10.5	14.3	15.5	15.4	16.3	16.8
Northeast	12.1	12.8	14.0	13.1	13.8	13.9	15.2	16.0	17.0	18.8	21.8	20.0	21.5	21.4	22.8	23.1	24.0
Maranhão	4.4	4.1	6.1	4.4	5.7	5.1	5.4	6.0	5.4	11.0	11.4	8.2	11.2	12.6	12.9	13.8	13.6
Piauí	6.2	5.7	5.5	7.8	9.1	10.6	12.3	11.3	14.3	15.8	17.1	16.5	20.2	19.8	19.2	23.1	23.5
Ceará	14.0	16.3	17.8	18.7	17.0	16.8	20.3	20.4	21.4	21.5	25.7	23.9	25.7	23.8	26.5	26.3	26.0
Rio G. Norte	16.7	15.4	14.6	11.2	14.0	11.4	14.3	17.3	21.5	16.8	21.7	20.4	23.8	23.0	23.1	21.7	26.8
Paraíba	7.5	8.7	11.5	8.1	7.9	11.2	12.4	12.9	16.8	21.7	21.5	22.9	22.4	23.4	24.1	22.9	24.9
Pernambuco	20.0	20.8	21.6	20.2	20.2	20.3	22.3	23.9	25.2	26.5	32.0	25.9	28.1	27.5	29.8	28.0	28.6
Alagoas	5.7	10.9	9.3	10.1	11.8	12.7	10.2	11.3	11.3	19.0	16.5	17.4	17.4	19.4	20.3	21.2	22.8
Sergipe	11.3	8.4	13.5	13.6	14.9	17.8	15.0	19.3	18.7	20.0	20.4	23.4	24.4	28.9	24.0	26.8	32.4
Bahia	11.7	12.1	13.3	12.1	13.8	13.0	14.0	14.4	14.3	15.2	19.4	18.5	18.9	18.6	20.8	22.3	22.3
Southeast	31.2	32.6	32.6	33.4	30.8	32.1	32.2	32.6	34.0	33.7	33.8	32.3	34.0	33.3	34.5	35.3	36.0
Minas Gerais	19.8	21.2	20.6	20.2	18.1	19.6	19.5	22.1	23.5	22.2	24.3	22.5	24.3	23.7	25.3	28.1	28.3

States	Year																
	1996	1997	1998	1999	2000	2001	2002	2003	2004	2005	2006	2007	2008	2009	2010	2011	2012
Espírito Santo	17.6	21.8	15.1	17.0	17.0	20.0	23.9	26.1	27.3	25.6	25.3	22.6	27.1	25.4	28.0	30.7	30.7
Rio de Janeiro	40.6	43.5	43.5	43.9	40.8	42.7	41.6	41.4	44.2	42.7	44.3	45.8	46.7	46.7	45.4	44.5	46.7
São Paulo	33.6	34.0	35.0	36.4	33.5	34.5	34.8	34.3	35.1	36.0	34.6	32.2	33.9	32.9	34.8	35.3	35.6
South	27.5	29.5	32.1	31.6	30.8	31.1	32.6	32.6	33.0	33.2	34.2	32.2	32.6	33.8	35.7	37.3	37.0
Paraná	22.6	24.6	24.2	26.0	25.2	27.0	29.0	26.5	27.6	29.3	29.5	27.6	28.8	29.8	30.3	33.1	33.7
Santa Catarina	21.3	24.5	26.3	24.2	25.3	23.6	25.8	25.7	24.2	26.8	26.1	25.6	25.4	28.7	30.1	32.1	33.2
Rio Gr. do Sul	34.7	36.2	41.6	39.9	38.4	38.6	39.1	41.3	42.1	39.8	42.5	39.8	39.9	40.3	43.8	44.1	42.3
Central-West	14.2	17.9	18.4	19.7	18.1	18.5	17.5	21.1	19.9	20.8	23.3	19.5	22.3	23.1	24.0	25.0	26.8
Mato G. do Sul	12.0	17.0	18.1	26.1	18.6	21.9	20.9	31.3	24.3	28.2	30.2	18.7	32.8	27.2	29.9	26.8	28.4
Mato Grosso	11.3	13.6	11.6	15.3	13.9	14.2	13.6	11.0	13.7	14.4	17.0	17.6	18.8	18.3	20.3	20.7	25.4
Goiás	12.8	17.1	18.6	16.8	16.1	16.3	16.2	18.5	18.9	18.6	19.8	18.1	18.7	22.7	22.2	25.2	25.3
Dist. Federal	22.4	25.0	25.4	24.8	26.5	25.0	21.6	28.3	24.6	25.5	31.3	25.1	24.8	25.3	26.5	27.7	30.2
Brazil	23.2	24.5	25.4	25.4	24.2	24.8	25.5	26.1	27.0	27.4	28.7	26.8	28.3	28.1	29.3	30.2	30.8

Figure 1: Coefficient of specific mortality by breast cancer accumulated quadrennial in women over 20 years in de Brazilian states, Brazil, 1996-2012.



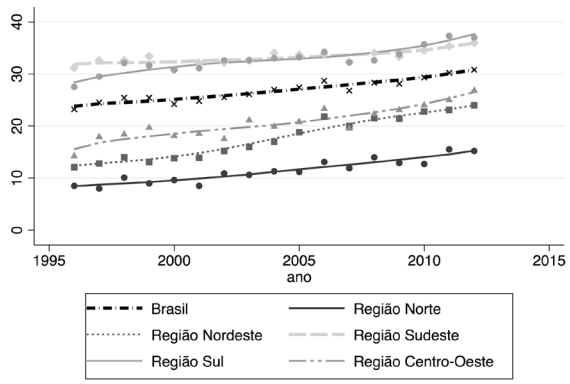
riod 2009-2012, all States had mortality rates above 20 deaths/100,000 inhabitants **(Figure 1)**.

The macro-regions South and Southeast presented coefficients higher than national values for the period of 1996 to 2012 **(Figure 2)**.

In this period the yearly increase in the mortality rate was 0,41 (IC95% 0,33-0,50). The macro-regions with highest increases were the Northeast with 0.79 (IC95% 0.66-0.92) and the Central-West with 0.56 (IC95% 0.43-0.69), followed by the South and North with 0.47 (IC95% 0.30-0.64) and 0.43 (IC95% 0.36-0.49), respectively, and the Southeast with 0.21 (IC95% 0.11-0.31 **(Figure 2)**.

In 2010, the states with the highest mortality rates were Rio de Janeiro (44.3/100,000 inhab.) and Rio Grande do Sul (43.8/100,000 inhabitants.), in the Southeast and South Regions, respectively. In the North the highest rates were in the states of Amazonas (14.3/100,000 inhab.) and Pará (13.3/100,000 inhabitants.); in the Northeast, the states of Pernambuco (29.8/100,000 inhab.) and Ceará (26.5/100,000 inhabitants.); in the Central-

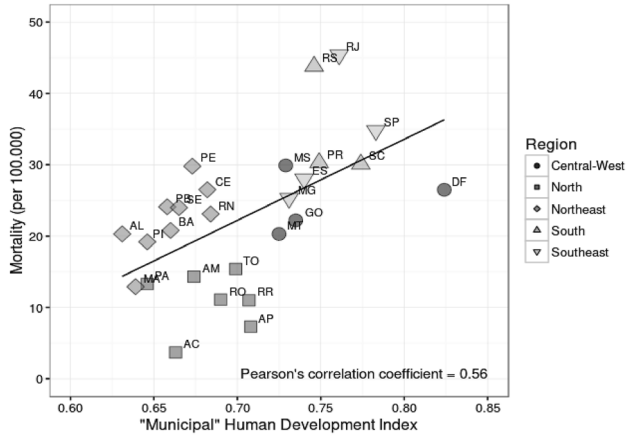
Figure 2: Mortality rate for breast câncer in women over 20 years by Brazilian regions, Brazil; 1996-2012.



West Region, in Mato Grasso do Sul (29.9/100,000 inhab.) and the Federal District (26.5/100,000 inhabitants.). These states exceeded the respective regions coefficients **(Table 1)**.

Regarding the HDI-M, during the year 2010, the States with the highest HDI were those with higher mortality from breast cancer. Each 0.1 additional point HDI-M was associated with an increase in 11.4 (95% CI 4.4 to 18.3) in the standardized coefficient of breast cancer mortality, explaining 31.4% of its variability between States. The States of the North Region had breast cancer mortality rate substantially lower than that of the Northeast States, although they had a similar HDI-M **(Figure 3)**.

Figure 3: Realationship between the Municipal Human Development Index (HDI-M) and the standardized coeficiente of specific mortality from breast câncer among aged 20 years or older in Brazilian states in 2010.



Discussion

The study showed increasing breast cancer mortality behavior in Brazil in 1996 to 2012.

The findings confirm the upward trend of the mortality from malignant neoplasm of the breast in agreement with other studies [20, 21]. Zapponi and Melo [20] conducted a study on the mortality of women for breast cancer in the period from 2003 to 2007, with the use of the database and checked a higher concentration of deaths for this specific cause in the South and Southeast regions, with emphasis to Rio de Janeiro, São Paulo and Rio Grande do Sul. In this study, the highest concentration of deaths among married women and race/ethnicity white. In the Southeast have observed an increase in the rate of the order of 12%, 6% and 22% for São Paulo, Rio de Janeiro and Minas Gerais, respectively. Girianelli et al. [21], analyzing data aggregated from 30 years (1980-2010) breast cancer mortality, observed tendencies of increasing mortality from breast cancer in the whole period in the five regions of the country. However, perceived tendency of decline of the coefficients in the capitals from the late 1990 [21].

Considering the Brazilian context, in the city of Aracajú it was found that there was a positive correlation between breast cancer incidence and level of income of the area [22]. In the period from 1996 to 2006, the standardized incidence of breast cancer has increased over the years, especially for women 45 to 64 years of age. On the other hand, mortality only increased between 55 and 64 years of age [22].

In addition, there was an increase in breast cancer mortality in the municipality of Juiz de Fora, Minas Gerais, in the period from 1980 to 2006, where female with the disease showed more than 81% survival in five years. These data suggest increased incidence of the disease similar to that observed in most studies conducted in Brazil [23].

The higher chances for breast cancer mortality occurred in women over 60 years and with low level of schooling in the study conducted in the municipality of Maringá, Paraná, which is statistically significant association [24]. This study also showed highest concentration of deaths among married women and race/ethnicity white.

The effect of the trace in reducing breast cancer mortality in Brazil is less than what happens with cervical cancer [21]. A set of factors has pointed to a low impact tracking measures in breast cancer mor-

tality in Brazil: the low mammography coverage, inadequate tracking of suspicious radiological findings and the limited access to surgical treatment [19]. Azevedo e Silva et al. [19], analyzing the number of biopsies compared to the number of cases that would require follow-up to diagnostic clarification, concluded that only 27% of women between 50 and 59 years with mammograms with BI-RADS 4 and 5 performed biopsy and 63% of those with 60-69 years.

In this study, which lasted until 2012, our units of note were the States and analysis of the data shows an increase in the specific coefficient of mortality from breast cancer in all Brazilian regions and Federal District **(Figure 2)**. The South and Southeast regions continued to show the highest coefficient of specific mortality for breast cancer, and the States of Rio Grande do Sul (43.8/100,000 inhab.) and Rio de Janeiro (45.4/100,000 HAB.) presented higher coefficients of the values of the respective regions **(Table 1)**.

In Brazil, has taken place the logic of combating disease from the degree of economic development in South and Southeastern regions have the highest rates of breast cancer and are the ones that guarantee access to examinations and treatments considered of high complexity [21].

Azevedo e Silva noted that in South and Southeast regions there is a higher concentration of accredited services to SUS (national health system) in chemotherapy and radiotherapy. Noted that only in the State of Rio de Janeiro, 44% of the cases of breast cancer were diagnosed in advanced stage [19].

In the study conducted by Azevedo e Silva et al. [19], the authors argued that the North, Northeast and Central-West, as well as less developed, have younger populations and showed smaller mortality rates, even after standardizing for age. Also, found an almost total absence of accredited services to SUS (national health system) in chemotherapy and radiation therapy in the North region, which can affect the prognosis of women affected by the disease outside the major centers of the country [19].

Studies show the variation in the occurrence of breast cancer among the countries according to the degree of socio-economic development. The high-income countries boast much higher rates to low and medium-income [16-19]. However, in the richest countries the rate of survival is higher because breast cancer is detected early and women have more access to treatment, what does not happens in other emerging and poor countries [18, 19].

Our study showed positive correlation between breast cancer mortality and the HDI in all macroregions and for Brazil as a whole. The apparent contradiction may be because the indicator of development are covered by the socioeconomic components of education and health services availability. Furthermore, this Brazilian pattern could be showing some demographic, social, nutritional, epidemiological and cultural characteristics of each Region.

In high-income countries, an observed decrease in a breast neoplasm mortality is attributed to access to diagnosis and treatment by employing new technologies such as endocrine therapy, in addition to increased social interest in the theme for breast cancer prevention [5-27], in the Brazilian scenario, the divergence, in the extent of coverage achieved was not sufficient to influence the reduction of mortality coefficient.

It is well established that breast cancer survival varies according to socioeconomic status and region of residence and that the delay in diagnosis may reduce survival. In the study conducted by Mclaughlin et al. [10], the waiting time for initiation of treatment was associated with increased risk of 85% in death among low-income women in North Carolina [10]. The clinical stage of disease at diagnosis is a prognostic factor key [28].

In the study by Montella et al. [29], the diagnostic phase depended on subjective variables, such as the patient's age, level of education, income and residence, as well as the specialization of the doctor and the dissemination of mammography exams as a preventive practice. According to these authors, the survival rate of breast cancer is probably an expres-

sion of complex and varied components connected to the characteristics of the patients (for example, premenopausal or postmenopausal), the stage of the tumor, the location of the lesion, the consciousness and attention of primary care caregiver, the fulfillment of a trace, the competence of the medical professionals involved in the treatment of patients (for example , radiologist, surgeon) and in public hospitals, the waiting list for admission of people diagnosed with breast cancer [29].

In the study by Bouchardy et al. [30], when comparing patients of various social classes, those of low social class, showed an increased risk of dying as a result of breast cancer (HR 2.4, 95% CI: 1.6 -3.5), even after adjusting for conservative surgery, radiotherapy, chemotherapy and lymph involvement (HR 1.8 , IC 95%: 1.2 -2.6).

In Europe, international or regional differences in survival could be at least partly attributable to cultural differences which influence the phase when the disease is diagnosed, as well as to the different ways in which national health systems are organized.

Following various measures that have been introduced for prioritization of early diagnosis and immediate and universal access to ideal treatment [28], Europe has shown a progressive reduction in the number of patients with advanced breast cancer at diagnosis [29]. However, Gatta et al. [26], point to a linear correlation (0.8) between health spending and access to diagnosis with 5-year survival among breast cancer in the European countries.

Thomson et al. [31], in a study conducted in Scotland, concluded that the survival of poor women with breast cancer was 10% lower than the rich, and the difference of estrogen receptor status only explained part of that difference.

Between women from all over Norway, breast cancer mortality is weakly associated with education, with lower mortality among women with less schooling. This difference did not change between the 1970s and 1990s [32].

In the United States, disparities in breast cancer mortality are evident by State, socioeconomic status and race/ethnicity. Although they have noticed significant decreases in the same over the past ten years, in 36 States and the District of Columbia, in fourteen States mortality remained unchanged. The decrease in mortality rates began later and was slower among women living in poor areas. Further progress in the control of breast cancer will require support and increase efforts to provide high-quality screening, diagnosis and treatment to all segments of the population [33].

Studies have reported a more advanced stage of breast cancer diagnosis in racial and ethnic subgroups, especially among African-American women, Hispanic, American Indian and women of native cultures of Hawaii. Several factors may be associated with advanced stage at diagnosis in multicultural populations. These range from basic biological characteristics at the molecular and cellular level, to social issues, such as access to care, socioeconomic conditions [34] and education [35].

Schneider & d Orsi [36], in Brazil, found that the survival rate of breast cancer is lower in women under 30, with less education, and with more advanced clinical stages. The study population were patients enrolled in CACONs (Specialized Oncology treatment Center), and the analysis followed a tiered model [36].

We emphasize also the genetic heterogeneity of familial breast cancer and it is known that a significant portion of disease is associated with inheritance of highly penetrant mutations in the BRCA 1/2 genes [37], whose estimated prevalence for people with mutations in BRCA1/2 are respectively 0.11% and 0.12% in the general population and between 12.8%-16% in high-risk families with three or more cases of breast cancer or ovary [38]. Their impact is influenced by exogenous exposure to carcinogenic factors, the type and position of the mutation and reproductive history, and these genes responsible for about 20% of the familial risk, while the other 80% are due to a combination of the effects produced by mutations in genes known high penetrance [37].

Limitation of this study stem from the fact that it was based on the SIM – an information system characterized by regional differences in completeness, coverage, and quality of information. However, even though the calculations may include a small number of incorrectly defined death causes, the system used contains the best data available in Brazil.

Contributions of this study is the analysis of breast cancer-specific mortality by the year 2012, as well as its analysis by States, which allowed us to observe the growth of this coefficient in all States of Brazil, even though recent study point to a trend of decline of this coefficient in the capitals from the late 1990 [21].

This study confirms the need for improvements in mammography coverage, following radiological lesions suspected and access to appropriate therapy.

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Competing interests

None.

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