# SOCIOECONOMIC INEQUALITY IN MORTALITY DUE TO CANCER: THE FEMALE CANCER TRANSITION IN BRAZIL

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**Background:** According to cancer transition, breast cancer, compared with cervical cancer, can be used as a marker of social inequalities in mortality. **Objective:** To analyze the transition of female cancer in Brazil according to its social indicators between 1980 and 2017. **Methods:** We performed time series analysis, spatial analysis and cluster analysis, respectively, for regional, state and municipal scales. **Results:** Time trend is rising for breast cancer in more developed regions. In less developed regions, cervical cancer persists with an increase, sometimes surpassing breast cancer. Spatial analysis detected a dependence relationship between most and least developed regions. High development group has lower cervical cancer mortality rates, higher breast cancer mortality rates, and vice-versa. **Conclusion:** There is a relationship between mostal and breast cancer in Brazil and inequalities, regardless of the scale of analysis. Brazil needs to make changes in its strategy for reaching early screening and diagnosis actions.

Keywords: Demography. Mortality. Cancer. Development. Public policy. Inequalities.

### STATEMENT OF RESEARCH QUESTION

The burden of noncommunicable diseases around the world is growing, and there is much talk about global action to curb this public health problem, especially in low-and middle-income countries, since this group of diseases currently represents 80% of deaths<sup>1</sup>. Cancer is about to become a major cause of morbidity and mortality in the coming decades in all regions of the world, regardless of the level of socioeconomic development<sup>2</sup>. This finding is intrinsically linked to the phenomenon of epidemiological transition, that assumes that countries gradually reduce the burden of infectious diseases and increase the burden of noncommunicable diseases and chronic conditions<sup>3</sup>.

In this sense, cancer transition can be considered as an extension or conclusion of Omran's theory of epidemiological transition<sup>4</sup>. Recent studies<sup>5,6</sup> explore the developmental context to explain the dynamics of incidence and mortality by specific cancers. In Brazil, social disparities are part of the scope of discussion of the National Policy for Integral Attention to Women's Health (PNAISM). The agenda of the technical area of women's health has incorporated in the last 30 years relevant aspects of the health of the female population, such as the prevention, detection and treatment of cervical and breast cancer. These two topographies of cancers, some of greatest magnitude worldwide, have heterogeneous occurrence among countries. The pattern of occurrence of these cancers, either in incidence or mortality, shows that cervical cancer is more significant than breast cancer for low and middle-low income countries, and the opposite for high and medium-high income countries<sup>7</sup>.

The study on the relationship between cancer incidence and mortality and social inequalities has gained notoriety in recent years, and recently the International Agency for Research on Cancer (IARC) has published some research findings on cancer registries from around the world<sup>8</sup>. Considering the existing social inequality in Brazil, as well as the remarkable disparity between the Brazilian regions in relation to social development, the following questions are asked to be answered: 1) At what stage of the cancer transition Brazil is? 2) Are there differences in the stages of this transition according to regions? 3) How has the distribution of breast and cervical cancer cases in Brazil been spatially distributed over the last 35 years? 4) Is there any correlation between differences in mortality cancer rates and social development? Therefore, the objective of the present study is to analyze the transition of female cancer in Brazil according to its social development between 1980 and 2017.

## DATA AND RESEARH METHODS Background

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It is an ecological study, whose units of analysis are the federation units (FUs), in a total of 27. The FUs are subnational entities with a certain degree of autonomy (self-government, self-regulation and self-collection) and endowed with their own government and constitution<sup>9</sup>. They are made up of 26 states and one federal district, located in 5 major regions. Like what has happened in many countries on all continents, the constraints of regionalization processes that account for territorial transformations in Brazil follow demographic, economic, political and social criteria. It is important to emphasize, however, that this process is equally marked by the increase of inequalities between social classes and territories. Thus, despite the Brazilian progress in the social and economic areas, these federative units maintain considerable heterogeneity with respect to indicators of poverty, inequality, income and social development<sup>10</sup>.

#### Data source

We used population data from the Brazilian Demographic Census of 1991, 2000 and 2010, collected by the Brazilian Institute of Geography and Statistics Foundation (IBGE), according to age in Brazil, disaggregated by FU. Additionally, the following social indicators were extracted from the Brazilian Human Development Atlas<sup>11</sup>:

a) Human Development Index (HDI): This is a summary measure of long-term progress in three basic dimensions of human development: income, education and health.

b) Gini Index: is a measure of inequality that evaluates the concentration of income in a population.

c) Proportion of extremely poor: Proportion of individuals with per capita household income equal to or less than ¼ of the minimum wage.

d) Average income per capita: average income of each resident of a given FU. This is the sum of the income of all residents divided by the number of inhabitants.

Population data also allowed the calculation of the following demographic indicators:

i) Crude Birth Rate (TBN): number of live births per thousand inhabitants;

ii) Crude Mortality Rate (TBM): total number of deaths per thousand inhabitants.

Breast and cervical cancer mortality data were obtained from the Mortality Information System (SIM), and the denominators were estimated through the inter-population projections of the Brazilian Institute of Geography and Statistics (IBGE), calculated through linear interpolation. The deaths from 1980 to 1995 were obtained considering the codification of the Manual of the International Statistical Classification of Diseases, Injuries and Causes of Death (ICD-9), through codes 174 (breast) and 180 (cervix); from 1996 to 2017, the International Statistical Classification of Diseases and Related Health Problems (ICD-10), through codes C50 (breast), and C53 (cervix), classified under these codes after the death correction process.

The correction of death records from breast and cervical cancer was performed by redistributing deaths due to ill-defined causes (ICD-9 codes 780-799 and ICD-10 R00-R99). Specific mortality rates were calculated by five-year ranges and then standardized by the direct method, adopting as standard population the world population proposed by Segi<sup>12</sup> and modified by Doll et al<sup>13</sup>.

## Data analysis

#### Time series analysys

We performed time series analysis with data from the five Brazilian regions. We assume that because it is a chronic disease, there is no seasonality effect. Initially, we verified the non-stationary occurrence of the series through the Wald-Wolfowitz test. Then, in order to obtain a first idea of the evolution of the values of the series rates, evaluating the effect of the trend, the Cox-Stuart test was performed. Finally, the trends were analyzed by the polynomial model, whose dependent variable (Y) is represented by mortality rates, and the independent variable (X) is represented by calendar years. For trend analysis, dispersion diagrams were constructed between the rates and the years of study to visualize the function that could express their relationship and choose the order of the polynomial. The choice of the best model depended on the scatter plot analysis, the coefficient of determination (R<sup>2</sup>) value and the residual analysis (especially for ratifying the homoscedasticity assumption). When two models were similar from a statistical point of view, the simplest model was chosen, that is, of a smaller order, that is, the most parsimonious model was chosen. And a significant trend was the one whose estimated model presented p value less than 0.05. Residual analysis was performed and, for all models, the assumption of homoscedasticity and adherence to normal distribution was evaluated.

#### Spatial analysis

We consider three periods as markers for women's health actions in Brazil: 1983, year of the creation of the Women's Health Program (PAISM); 2003, creation of the National Policy for Integral Attention to Women's Health (PNAISM); and 2013, publication of the National Cancer Prevention and Control Policy. Thus, for each year we take the 5-year average rate from the time-markers: 1983-1987; 2003-2007 and 2013-2017.

From the calculated rates, we performed a georeference by state, and the units were divided into quartiles. To assess spatial dependence, we used Moran's global autocorrelation index. Also, the local Moran index (LISA) was used to determine the data dependence on its neighbors. For this analysis, we constructed the BoxMap and MoranMap for Breast and Cervical Cancer Mortality and Incidence rates.

## **Cluster analysis**

In order to minimize the occurrence of bias due to the low occurrence of cancer in the population, we selected all Brazilian municipalities with at least 50 thousand inhabitants, distributed into five Brazilian regions. Considering that the study seeks to observe indicators that are a proxy of the contextual effect of the social situation, we chose to work in municipal households.

From this set of social indicators, the municipalities were gathered through cluster analysis, performed by the K-means method. From the cluster classification, the average mortality rates adjusted for cervical and female breast cancer in the clusters were compared. To test the study hypotheses, the Mann Whitney test was used, and its U statistic was evaluated at a significance level of 5%. To analyze the variability of the indicators, we calculated Spearman bivariate correlation as the objective of evaluating the relations that are smoothed when comparing the averages between the groups of municipalities.

## FINDINGS

## Temporal trend by regions

There is a downward trend in the rate of cervical cancer mortality in Brazil and regions, except for the north and northeast. The mortality rate for breast cancer is increasing in Brazil and regions. It is noteworthy that, in the northern region, except for the others, mortality from cervical cancer is systematically higher than the mortality rate from breast cancer.

We fit models for all-time series. The Midwest region obtained better fit for its series (cervical and breast cancer) with the linear model. For the nonsignificant series mentioned in the Cox-Stuart test, the adjustment with inclusion of the quadratic term was adequate and significant. For the others, although the linear adjustment was satisfactory, there was an improvement in the explanation of the model, and we used the second-degree polynomial, thus opting for this adjustment. For Brazil, we observed a change in the magnitude of the decreasing trend in the rate of cervical cancer mortality from 2004, the year following the implementation of the National Policy for Integral Attention to Women's Health, whose reduction in cancer morbidity and mortality. Cervical and breast cancer has become a health priority.

## Spatial Analysis by Federation Unit

The spatial distribution of cervical and breast cancer mortality rates in women in Brazil demonstrates strong inequality between states. There is a concentration for cervical cancer of the highest rates in the north and northeast regions; For breast cancer, by contrast, the concentration of the highest rates occurred in the southern and southeastern regions.

Spatial autocorrelation was observed for both topographies in the three years of observation. It is noteworthy that autocorrelation, as measured by the Moran Global Index, is systematically higher for breast cancer. However, there is a trend towards a reduction in spatial estimation over time, showing a reduction in spatial dependence in the period from 1983 to 2017.

#### **Municipal clusters**

The first concentrated the largest number of cities and shows a population with better human development, lower social inequality, and a higher degree of urbanization. Most of its cities (59.3%) are concentrated in southeastern Brazil. The second group presents a worse performance in human

development, a pattern of greater social inequality), and lower degrees of urbanization. In contrast to the previous group, most of the cities in this group (78.6%) are concentrated in the northeast region.

The highest average cervical cancer mortality rate is in the second group, which has the worst performance on social indicators; In contrast, the highest average mortality rates for female breast cancer are observed in the first group, which presents the best performance in social indicators. This pattern confirms that these two cancer topographies behave inversely according to the developmental pattern of cities, with female breast cancer mortality being more frequent in places of greater social development, and cervical cancer mortality. more frequent in cities with lower level of social development.

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