

# Estimation of the Number of Brazilian Women Living With Metastatic Breast Cancer

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**PURPOSE** Breast cancer is the most common cancer and the leading cause of cancer-related death in women worldwide. The number of women living with metastatic breast cancer (MBC) in Brazil is unknown. The objective of this article was to use population-based data to estimate the prevalence of MBC in Brazil.

**METHODS** Using 4 different sources and cancer registries (DataSUS, Registro Hospitalar de Câncer, the Brazilian National Health Agency, and the National Geography and Statistics Institute) with data from 2008 to 2018, we built a database that represents Brazilian MBC cases. The current number of women in the model living with MBC was considered the prevalence (recurrent or de novo), and new cases in the year 2018 represented the incidence. In each of these outcomes, we were able to separate our population on the basis of cancer subtype, age, and time from diagnosis.

**RESULTS** We estimate that 44,642 women currently live with MBC in Brazil. This accounts for one in every 2,409 Brazilian women and approximately 41 women per 100,000. A total of 58% have hormone receptor–positive/human epidermal growth factor receptor 2–negative tumors, 25% are human epidermal growth factor receptor 2–positive, and 16% have triple-negative breast cancer. According to our methodology, the estimated median overall survival of Brazilian women after diagnosis of MBC is 26.2 months.

**CONCLUSION** The significant number of patients living with MBC should inform and raise the interest of the many stakeholders involved. This collaborative effort is a clear requirement to improve the lives of these patients as well as to prepare for future challenges related to the trend of a progressive increase in MBC prevalence.

JCO Global Oncol 6:307-312. © 2020 by American Society of Clinical Oncology

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## INTRODUCTION

Breast cancer is the most common cancer in women worldwide, and 70% of breast cancer deaths currently occur in women from low- and middle- income countries.<sup>1</sup> The Brazilian National Cancer Institute estimates that there were 59,700 new cases of breast cancer in 2018 and that approximately 17,000 Brazilian women die as a result of breast cancer each year.

The use of real-world data (RWD) to address clinical and policy-relevant questions is gaining increased interest. Indeed, data from cancer registries and linked treatment records can provide a unique insight into patients, treatment, and outcomes in routine oncology practice.<sup>2</sup>

Metastatic breast cancer (MBC) is an incurable form of the disease that is associated with significant health care needs and intensive resource use. MBC includes 2 distinct populations: those presenting with distant metastases at diagnosis (de novo) and those developing metastases after initial treatment of an earlier

stage (I-III) of the disease. The number of women currently living with MBC in Brazil is unknown. This information is extremely important because of the socioeconomic impact and the significant pressure on health care system costs, both in public as well as in private settings, that are associated with MBC.

Recent analyses demonstrate an increasing number of women living with MBC in developed countries, possibly because of improvements in systemic treatment but also as a result of a demographic trend of population aging.<sup>3,4</sup>

The aim of this study was to estimate the prevalence and characteristics of patients living with MBC in Brazil. In addition, we have estimated future trends in MBC prevalence.

## METHODS

### Objectives

The primary objective of this study was to estimate the prevalence of women living with MBC in Brazil.

## ASSOCIATED CONTENT

### Data Supplement

Author affiliations and support information (if applicable) appear at the end of this article.

Accepted on January 3, 2020 and published at [ascopubs.org/journal/go](https://ascopubs.org/journal/go) on February 28, 2020; DOI <https://doi.org/10.1200/JGO.19.00404>

## CONTEXT

### Key Objective

Breast cancer represents a mounting worldwide challenge that it is particularly significant for developing nations. In this study, population-based data were used to estimate the prevalence of metastatic breast cancer in Brazil.

### Knowledge Generated

We estimate that 44,642 women currently live with metastatic breast cancer in Brazil. This accounts for one in every 2,409 Brazilian women and approximately 41 women per 100,000. These patients have specific and special needs.

### Relevance

This information should call attention to the magnitude of the problem and has direct implications for the development of health care strategies necessary to prepare for the numerous issues faced by this population.

Secondary objectives were to estimate the prevalence of MBC according to tumor subtype, patient age, and time interval from diagnosis and to estimate median overall survival (OS) and 5-year OS after the diagnosis of MBC.

### Data Sources

To estimate the total number of women with MBC in Brazil, we created a database with information collected from 1 main source (DataSUS) and 3 auxiliary sources (Registro Hospitalar de Câncer [RHC], the Brazilian National Health Agency [ANS], and the National Geography and Statistics Institute [IBGE]). DataSUS,<sup>5</sup> the information technology department of the Brazilian Unified Health Care System, collects and manages health information (health indicators, epidemiologic and morbidity information, health care network information, vital statistics, demographic and socioeconomic information) and financial information (National Health Fund transfers to municipalities, credits to health service providers and declared States', Federal Districts', and Municipalities' public health budgets). Furthermore, the data set is publicly available and covers in- and outpatient procedures for all public institutions dealing with high complexity care. For all therapeutic actions in oncology, a specific form called an authorization for high-complexity procedure is registered and is requested for reimbursement. Each authorization for high-complexity procedure is composed of code that is specific for every tumor, stage, and type of treatment.<sup>6</sup>

The RHC also plays a relevant role in the cancer information system in Brazil. This is a source of information about patients with a confirmed diagnosis of cancer attended in a certain hospital unit. Its quality is guaranteed by the obligation of its update by Brazilian Unified Health Care System hospitals qualified as Specialized Oncology Services. Conversely, ANS provides information about private market patients, with data collected from 4,027 municipalities. Finally, IBGE (the National Geography and Statistics Institute) publishes data about the Brazilian population and its future trends, which were used in our projections of breast cancer incidence for the coming years.

Each of the database sources had a specific role in the construction of our model: (1) DataSUS was responsible for the core database (public health care system patients treated with chemotherapy); (2) RHC fed the model with patients who did not receive chemotherapy; (3) ANS added information from private health care plans; and (4) IBGE gave future Brazilian population projections.

With the application of a specific collection and analytical methodology to all these sources, this robust database allows for the generation of information on prevalence and incidence with a high level of accuracy and statistical value. Furthermore, it generates data at a more granular perspective, which allows us to study more disease characteristics, such as subtypes, age, and time since diagnosis. For a comprehensive description of methods and statistical analysis, see the Data Supplement.

### Prevalence and Incidence Estimate

The prevalence of MBC was calculated directly from the data set, considering the unique patient ID of each woman diagnosed with breast cancer from January 2008 to December 2018, using as a period measure the date that each patient's ID appeared in the system. De novo and recurrent breakdowns were calculated by searching back through the data set for the longitudinal history of each unique patient ID for those with confirmed stage IV in 2018. Therefore, patients identified in the historical data set with stage I, II, or III were classified as having recurrent disease and the others, de novo MBC. To determine the incidence, the total number of new MBC cases (an ID's first appearance) in each year was calculated. The prevalence and incidence projections for 2019 to 2023 were calculated over the final data set generated by the model from 2008 to 2018 through a linear regression exponential smoothing method.

The estimation of the prevalence and incidence by subtype was performed using the procedure proxy approach. The DataSUS chemotherapy database presents treatment information segmented by disease subtype. Consequently, patients were grouped into 3 different subtypes: hormone

receptor (HR)-positive/human epidermal growth factor receptor 2 (HER2)-negative, HER2+ (regardless of HR status), and triple-negative breast cancer (TNBC). We were also able to separate the cases on the basis of age group and time since diagnosis (given the high level of granularity of the database).

### Survival

OS was calculated as the time from the date of MBC diagnosis to death from any cause; patients who were alive or who were lost to follow-up were censored at the date of last information available. OS curves were estimated using Kaplan-Meier.

### RESULTS

We estimate that 44,642 women currently live with MBC in Brazil. This accounts for one in every 2,409 Brazilian women or approximately 41 women per 100,000. Of these patients, 17,544 (39.3%) were initially diagnosed with de novo stage IV disease. This group includes patients diagnosed in 2018 and those surviving after an initial diagnosis of de novo stage IV disease in previous years. Furthermore, our estimations indicate that 27,098 women (60.7%) with MBC were initially diagnosed with stage I-III disease and relapsed. Figure 1 describes the prevalence and incidence of MBC in Brazil, as well as time trends. It is estimated that in 2023, a total of 53,543 will be living with MBC, an increase of 19.9% in 6 years (2018-2023). HR+/HER2- was the most frequent breast cancer subtype, accounting for 25,881 patients (58%), followed by HER2+ and TNBC, as described in Fig 2.

Figure 3 illustrates the proportion of patients living with MBC according to time from diagnosis. The majority of patients with MBC (59%) were diagnosed within the last

2 years, and approximately 9% were diagnosed > 5 years previously. According to the methodology used in this analysis, the median OS of Brazilian women after diagnosis of MBC is 26.2 months (Fig 4).

In our analysis, there were minimal differences in the median OS among different age groups, as illustrated in Fig 5. Median OS rates showed significant differences among breast cancer subtypes (Fig 6). As expected, HR+/HER2- tumors had a better prognosis, with a median OS of 36 months and a 5-year OS of 20.1%. TNBC was associated with the worst prognosis, with a median OS of 16 months and a 5-year OS of only 5.5%. We performed a linear regression analysis for the 3 different breast cancer subtypes and demonstrated that the different results obtained among them are statistically significant ( $P < .0001$ ).

### DISCUSSION

Our study shows that 44,642 Brazilian women live with MBC and that this number will increase by approximately 19% by 2023. Our data are similar to other publications addressing estimations of MBC prevalence. Mariotto et al<sup>3</sup> estimated that in 2017 there were approximately 155,000 women living with MBC in the United States, 75% of whom were initially diagnosed with early-stage disease and later progressed to MBC. Their report also demonstrated an increasing number of patients in the United States living with MBC, likely the result of improvements in treatment and the aging of the population. Although the MBC prevalence rate in 100,000 women in Brazil is 41.5, in the United States it is 82.4. The difference is probably the result of a higher incidence of the disease and the longer lifespan of patients with MBC in the United States in comparison with patients in Brazil. Data from a RWD French observational cohort study

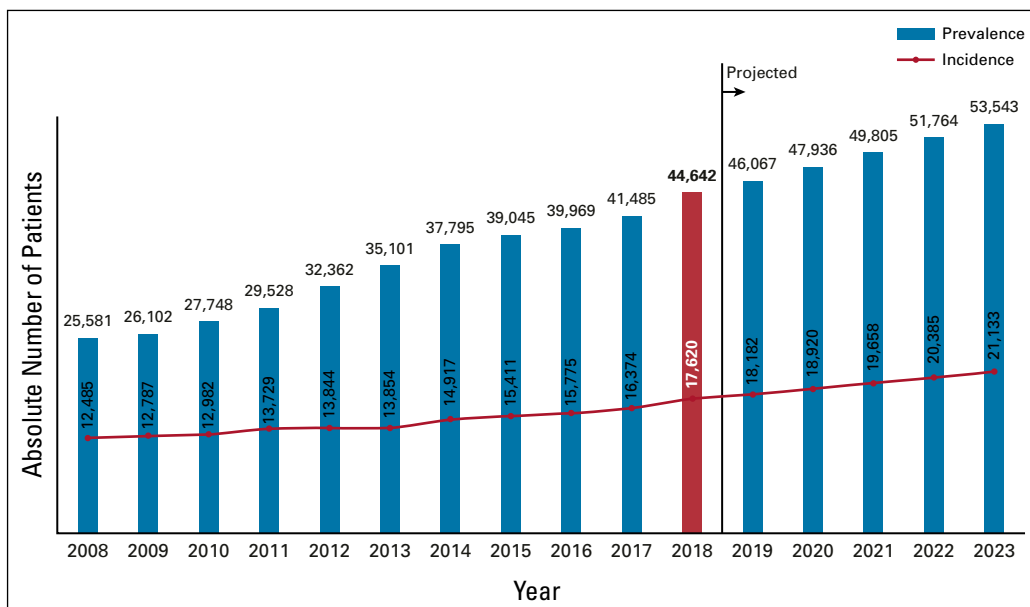
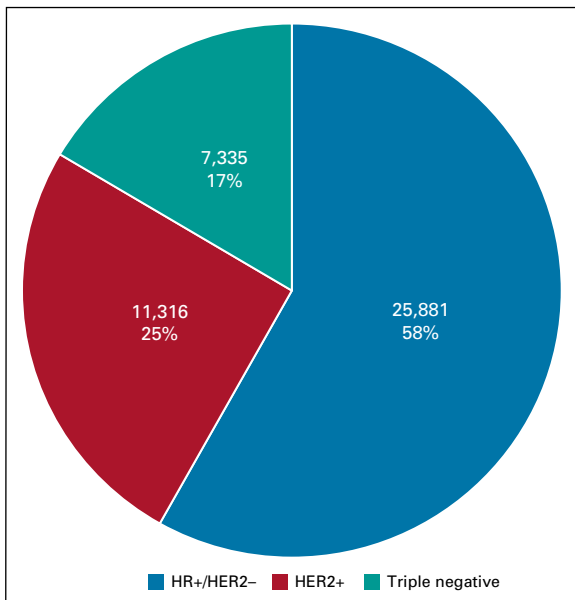
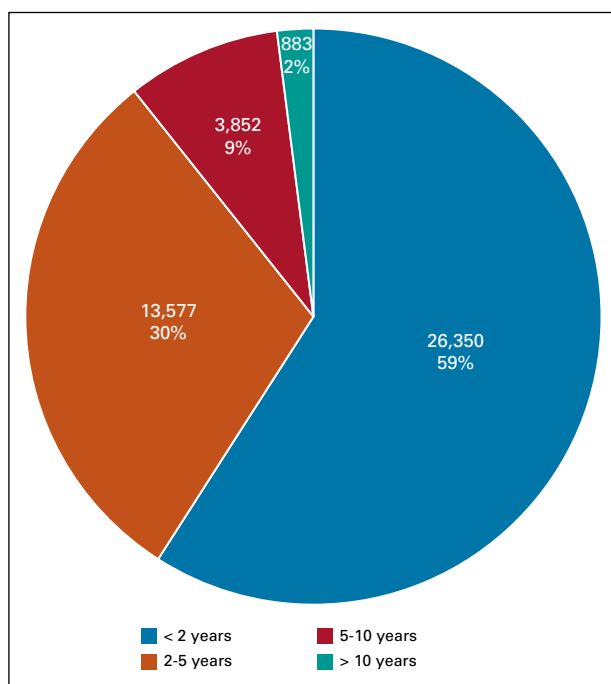


FIG 1. Prevalence and incidence of metastatic breast cancer in Brazil, actual and projected (2008-2023).

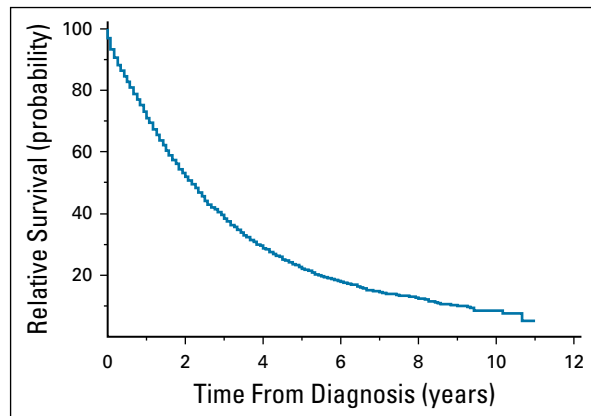


**FIG 2.** Women with metastatic breast cancer in Brazil by subtype. HER2, human epidermal growth factor receptor 2; HR, hormone receptor.

evaluating 16,072 consecutive patients with MBC reported superior survival outcomes in comparison with our data.<sup>7</sup> In the French study, the median OS of the whole cohort was 37.2 months and the median OS of the HR+/HER2-, HER2+, and TNBC subcohorts were, respectively, 42.1, 44.9, and 14.5 months. These figures clearly indicate that Brazilian patients with HR+



**FIG 3.** Women with metastatic breast cancer in Brazil by time since diagnosis.

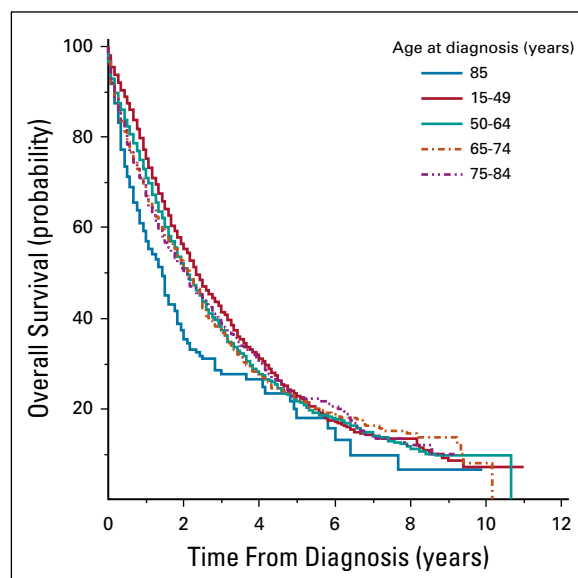


**FIG 4.** Relative survival by time since diagnosis for women diagnosed with de novo stage IV breast cancer between 2008 and 2019 at ages 18-84 years.

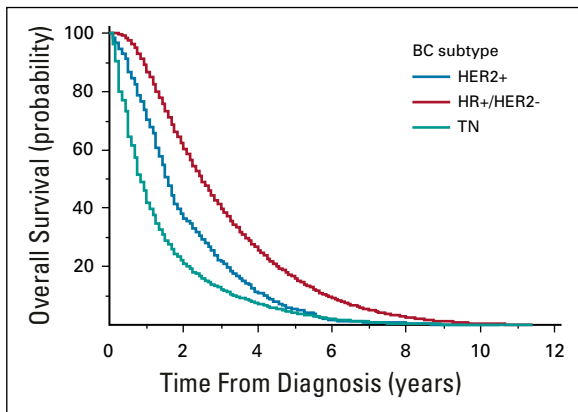
HER2+ MBC have inferior survival in comparison with patients from HIC.

We found a median OS of 26 months in the entire study population with differences according to breast cancer subtypes. A prior retrospective observational study (LACOG 0312) reported a median OS of 34 months in patients diagnosed with MBC in 2012.<sup>8</sup> Furthermore, the median OS of the different subtypes of breast cancer resulted in comparable figures.

The reasons for this critical discrepancy are likely multifactorial and probably reflect what may be happening in other developing countries like Brazil. Among the different factors that may have an impact on the outcomes of patients with breast cancer we can cite hardships while accessing the health care system, lack of patient education, ineffective screening programs, delayed diagnosis with a higher proportion of patients in more advanced stages,



**FIG 5.** Overall survival estimates among different age groups.



**FIG 6.** Overall survival estimates among breast cancer subtypes. BC, breast cancer; HER2, human epidermal growth factor receptor 2; HR, hormone receptor; TN, triple negative.

and lack of access to staging tests and therapeutic procedures considered standard of care, such as anti-HER2 drugs and new generation endocrine agents.

Concerning the access problem, our group has published data indicating that approximately 5,000 patients with HER2+ breast cancer died in Brazil between 2006 and 2013 while there was no access to adjuvant trastuzumab in the public health care system.<sup>9</sup> Furthermore, we presented an analysis estimating that every year there are 768 premature deaths among patients with HER+ MBC because of a lack of access to trastuzumab and pertuzumab in the public setting.<sup>10</sup> A growing number of innovative systemic therapies for MBC (such as newer anti-HER2 agents, CDK4/6 inhibitors, PI3KCA inhibitors, immune therapies, among others) will denote additional challenges for the public (as well as for the private) health sectors and will probably lead to even larger disparities, further declining outcomes.

The methodology used in this study was presented in other analyses<sup>11</sup> and was recently validated using data from the AMAZONA-III prospective cohort study, which included > 3,000 patients with breast cancer from all Brazilian regions.<sup>12,13</sup> It offers a new and innovative approach to measuring the prevalence and incidence of cancer in Brazil. When compared with the commonly used estimations from the Brazilian National Cancer Institute, this method presents a more realistic perspective and allows for a much more granular analysis of the information, addressing characteristics such as patient age, tumor subtype, and interval from diagnosis, among other variables. Our final data set included almost 87% of all oncologic patient populations in Brazil with a variety of data types and longitudinal perspectives. Therefore, it allows direct and detailed querying to estimate numbers of patients and to generate important information. Particularly important is that the data sources are updated on a monthly basis, so that the analysis can be updated in an extremely timely fashion.

Our study has some limitations. The final data set was generated over a core database that includes mainly data on public patients, and some differences may be observed and bias may be introduced when we extrapolate to the total population and include privately insured patients. To diminish this effect, we developed the Private Algorithm, increasing confidence in the final data set when extrapolated to the total population (see Data Supplement). Furthermore, the fact that the information is collected from a multitude of institutions raises the important issue of the quality of the input. Although this is a recognized weakness of RWD research, we do not have control over this aspect of the information.

These results have potential implications in a variety of settings. They certainly inform public health policies because they estimate the large dimension of the problem of women with MBC with their multitude of issues. At the same time, the data fuel interest in this group of patients, leading to increased and more focused efforts by society in general and patient advocate organizations. Too often, the emphasis is placed on success stories (patients who survive the disease), neglecting the important and multiple needs of patients living with advanced breast cancer. Recognizing the thousands of patients in this situation will certainly generate initiatives addressing the specific issues of this population.

In addition, the evidence indicating suboptimal survival should generate a collaborative and careful analysis of the potential causes of the poor outcomes. Public educational efforts and the development of strategic solutions to the access problem are needed. In this regard, the numbers also point to a huge opportunity for research initiatives, even though a partial solution, clinical research and access to drug development protocols, represents, in many regions of the world, the only opportunity for access to the standard of care treatments and to innovative therapeutic strategies in development.

At the same time, additional epidemiologic exploration of the problem and much needed translational efforts by academic institutions should be able to inform particular characteristics of these populations of Brazilian patients and contribute with the advancement of scientific knowledge in the area. Collaboration with established academic institutions and big research networks around the world are certainly an important part of these initiatives.

Ultimately, the information we generated here is expected to change the status quo and stimulate all interested players, such as the government, health care providers, patient advocate groups, the pharmaceutical industry, academic institutions, and medical organizations among others, to initiate an active and productive dialogue with the clear goal of improving the observed outcomes.

Breast cancer represents an increasing health care challenge for developing nations such as Brazil. The significant number of patients living with MBC should

inform and raise the interest of the many stakeholders involved. Action calls for the development of a specific strategic plan to address the causes of the suboptimal

outcomes and to propose context-dependent solutions. This collaborative effort is a clear requirement to improve the lives of these patients.

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## AUTHORS' DISCLOSURES OF POTENTIAL CONFLICTS OF INTEREST

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**Consulting or Advisory Role:** Boehringer Ingelheim, Roche/Genentech, Novartis, GlaxoSmithKline, Eisai, Pfizer, AstraZeneca, Libbs, MSD Oncology, United Medical

**Research Funding:** Pfizer, Novartis, Amgen, AstraZeneca, Boehringer Ingelheim, GlaxoSmithKline, Roche/Genentech, Lilly, Sanofi, Taiho Pharmaceutical, Mylan, Merrimack, Merck, AbbVie, Astellas Pharma, Biomarin, Bristol-Myers Squibb, Daiichi Sankyo, Abraxis BioScience, AB Science, Asana Biosciences, Medivation, Exelixis, ImClone Systems, LEO Pharma, Millennium, Janssen, Atlantis Clinica, INC Research, Halozyme, Covance, Celgene, inVentiv Health

**Travel, Accommodations, Expenses:** Roche/Genentech, Novartis, Pfizer, BMS Brazil, AstraZeneca, MSD Oncology

No other potential conflicts of interest were reported.

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