REVIEW ARTICLE

Addressing Breast Cancer Disparities in Brazil: A Roadmap for Innovative Strategies

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ABSTRACT

Breast cancer (BC) is the most common malignant disease among women worldwide, with a rising incidence. It poses a significant burden in Latin America, where mortality rates have remained consistently high over recent decades, in contrast to some high-income countries (HICs), where these rates have decreased. The increase in survival rates has been driven by expanded screening coverage and advancements in the treatment of stage II, III, and metastatic breast cancer. Achieving similar improvements in low- and middleincome countries (LMICs) requires the incorporation of these strategies, which has been particularly challenging in resource-limited settings. In this narrative review, we have analyzed laws and ordinances launched by Brazilian government since the creation of its public health system in 1990. Alongside analysis of these governmental landmarks, we have pointed out the main published results regarding breast cancer staging distribution at diagnosis, strategies for timely diagnosis, screening coverage and barriers to treatment access in the last decades, aiming to understand the achievements by implemented public politics. Once, we have described the public health scenario in breast cancer, we have identified factors that represent bottlenecks to improve outcomes in breast cancer in Brazil and have proposed potential actions that might change this landscape. These actions could be centered on timely diagnosis and treatment beginning, attempt to widen access to new medicines, widen telehealth utilization since breast cancer detected abnormalities up to treatment and follow up after treatment conclusion. The authors have discussed how these actions could be implemented in Brazilian public health system, aiming to drive better outcomes.

Keywords: breast cancer, cancer-care, access, Brazilian public health system, timely diagnosis, timely treatment initiation, supportive care, telehealth.

Introduction

Breast cancer (BC) is the most common cancer globally, representing a challenging health care matter worldwide, being expected by 2040 more than 3 million of new cases a year¹. It is a major burden for America Latina where the incidence rates have increased most rapidly with mortality rates steadily high in the last decades². In Brazil, it has been expected 73.600 new cases a year in the triennial period from 2023 to 20253, accounting the most common neoplasm in women⁴. Although mortality rates have recently decreased in high-income countries (HICs), driven by the organized mammography screening, introduction of new medications, advances in tumor biology, and the application of this knowledge to specific molecular subtypes⁵, these improvements have yet to be reflected in better outcomes also for women in low- and middle-income countries (LMICs)6. Regardless of the incidence rates are lower in LIMCs, than HICs (incidence rate is 66.5 in 100.000 in Brazil, 95.9 in USA and 94.0 in UK), the mortality rates are close (13.9 per 100.000 in Brazil v 18.7 in US v 14.0 in UK).

In Brazil, only about one-quarter of the population can afford private health insurance7, highlighting the government's significant responsibility to provide access to cancer care. Good quality cancer care in the public health system will minimize disparities and utmost it will bring improvements in overall survival mitigating differences between private and public systems. Despite the fact, the Brazil has made progresses in public health, notably with creation of the public health system with universal coverage (Sistema Único de Saúde, SUS), mainly in notifiable diseases, the cancer care is yet to be upgraded8. "In the past decade, the Brazilian government established the National Cancer Control Policy⁹; however, several areas still require attention. The overwhelming demand on the three levels of care (primary, secondary, and tertiary), due to the high percentage of the population relying exclusively on the SUS, combined with a rapid epidemiological transition that results in a triple disease burden, fragmented care, and chronic underfunding of the SUS over the years, has led to delayed diagnosis and treatment initiation in breast cancer.

Within cancer units, the lack of strict oversight regarding which clinical procedures are actually being offered to patients has led to a scenario where three different levels of hospitals coexist within the SUS. Some hospitals provide only the minimum services required by the government, others offer less than the minimum, and some exceed expectations¹⁰. The scarcity of clinical research protocols, along with the concentration of the few available protocols in capital cities, has also hindered the participation of women with breast cancer in clinical trials. This significantly delays the development of academic research addressing critical local issues, which is essential for improving care.¹¹.

All these gaps have arguably contributed to poor outcomes in breast cancer patients in Brazil, which need for attention of government and other stakeholders. In this narrative review, we analyzed the timeline of main laws and ordinances by Brazilian government to assist breast cancer patients since the SUS creation, parallelly to results that have been gotten regarding screening coverage, staging distribution, framework to new treatments incorporation. Also, we have highlighted key access barriers and have proposed potential actions that could be implemented, which might improve the outcomes of breast cancer.

Methods

The current study is a narrative review, where authors applied descriptive approach analyzing laws and ordinances launched by Brazilian government, since the creation of its public health system, SUS, in 1990, that represent landmarks in the public oncological assistance in the country (Figure 1). Also, published data regarding screening breast cancer coverage, staging distribution at diagnosis and barriers to access to new medicines were analyzed. The authors drew the Brazilian public health system scenario, pointing out the need for timely access to diagnosis and treatment, need for widen access to new medicines, palliative care and telehealth tools. Following these

steps, the authors proposed innovative strategies that could be implemented aiming to improve outcomes during breast cancer patient's journey.

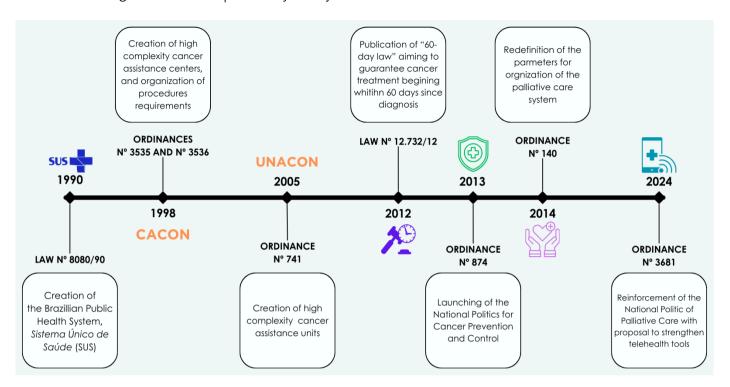


Fig.1 – Landmarks of Brazilian Cancer Care within the Public Health System, Sistema Único de Saúde (SUS). UNACON stands for Unidade de Alta Complexidade em Oncologia (High Complexity Cancer Assistance Unit) and CACON stands for Centro de Alta Complexidade em Oncologia (High Complexity Cancer Assistance Center)

Timely access to cancer diagnosis

In Brazil, there is a high percentage of stage III breast cancer diagnosis, which is an immediate task for stakeholders to change. Advanced stage is correlated with higher risk of disease relapse and worse prognosis than early stages¹². Screening strategies have remained one of the necessary conditions to promote early detection, while most of breast cancers are attributed to non-modifiable risk factor and primary prevention is limited to lifestyle changes including exercise and healthy meals or avoidance of postmenopausal hormone replacement therapy¹³. The rate of breast cancer mortality in US, has decreased in the last four decades. Reasons that have promoted this incremental survival are mammography screening (range 25%), advances in treatment of patient's stage II and III (range 47%) and advances in metastatic disease treatment (range 27%)5.

Mammography screening in Brazil, has been widened, reaching coverage rates range to 65,3% in 20223, although it keeps being opportunistic, and has been documented a major number of screening mammography during Pink October campaigns¹⁴. Also, these policies between 2001 and 2014 do not seem to have had any effect on the stage of breast cancer at diagnosis (figure 2)15. The AMAZONA trial, a big retrospective and multicentric trial that included patients from 2008 and 2009 has shown that 23,2% of these patients were stage III¹⁶, and prospective AMAZONA III, that recruited patients from 2016 to 2017 described 27,0% of patients stage III^{16,17}. On one hand, early detection through screening should be encouraged, as its benefits are well-documented 18-20

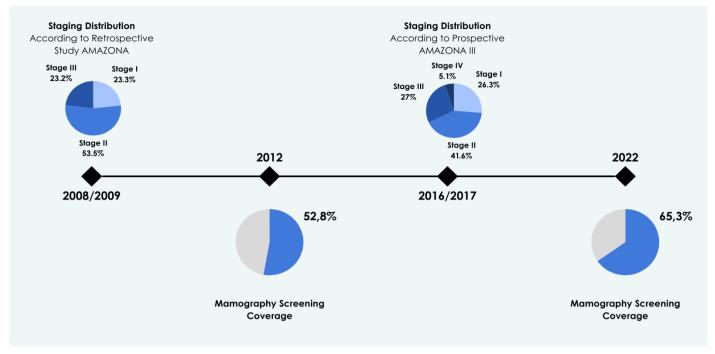


Fig. 2 – Relationship between mammography screening coverage and breast cancer staging.

The World Health Organization (WHO) has outlined two distinct strategies for promoting early breast cancer detection: screening (for asymptomatic patients) and early diagnosis (recognition of symptomatic cancer at an early stage)¹⁵. Additionally, the WHO recommends that countries with limited resources prioritize early diagnosis in symptomatic patients over mammographic screening for asymptomatic patients^{21,22}. For instance, in Brazil, data from a nationwide hospital-based cancer registry estimated that 2,500 breast cancer deaths could have been prevented through effective mammography screening for women aged 50-69. If as many as 80%, and as low as 50%, of all women diagnosed with stage III or IV disease in the previous five years had been downstaged to stage II, an additional 8,000 deaths could have been prevented in 2012. This underscores that screening mammography may not be the optimal approach in countries where women are frequently diagnosed at late stages¹⁵.

Brazil struggles to provide timely access for symptomatic patients, with long waiting times reported at various stages of care: a median of 60 days from self-detected breast abnormalities to mammography and ultrasound, 41 days from mammography to biopsy, and 97 days from biopsy to the start of treatment²³. The reasons cited for these

delays include fragmented care²⁴ and a lack of qualified healthcare professionals in primary care units to properly identify and facilitate timely assistance for these women. This chaotic scenario demands a commitment from the government at all three levels (municipal, state, and federal) and from healthcare professionals to integrate services within fewer facilities. It also requires the implementation of training programs for multidisciplinary teams, as well as the possibility of offering initial procedures such as mammography, ultrasound, and biopsy at primary care units. These strategies aim to shorten waiting times, ultimately leading to improved outcomes²⁵.

Timely access to cancer treatment

A significant issue in Brazil and other LMICs is the prolonged waiting time between cancer diagnosis and the start of treatment. The burden of new breast cancer cases, other malignant tumors, and competing diseases represents a triple disease load, reflecting the rapid epidemiological transition Brazil has undergone. This has contributed to the current scenario, where waiting times from diagnosis to treatment exceed acceptable limits. Although global real-world data is scarce, some researchers have published studies highlighting extended waiting times, further underscoring the heterogeneity of

outcomes. A subgroup analysis of AMAZONA III prospective study, described median of 56 days since diagnosis to treatment beginning in a public cohort²⁶, and Ferreira et al described that 80% of patients in a public health system have started their treatments within 60 days²⁷. However, there is not a systematically documentation of these times, especially regarding each region. Resende et al, for example, described a median of 97 days in a public cohort in Rio de Janeiro state²³. These discrepancies highlighted the heterogeneity of access related to the continental dimensions, and large socio-demographic variations, outstanding the existence of huge disparities within public health system in Brazil.

In 2012, the Brazilian government established the 60-day law (figure 1)²⁸, aimed at ensuring timely initiation of cancer treatment. However, despite this law, delays have continued to be frequently reported. Although the SUS was created in 1988, it has faced chronic underfunding⁸, with a relatively small percentage of the Gross Domestic Product (GDP) allocated to the public health system²⁹. To provide timely treatment, it is necessary to strengthen the National Cancer Control Policy, which would undoubtedly require increased investment.

Access to new medicines

Significant progress has transformed the field of BC, leading to higher rates of early diagnosis, increased detection of curable cases, and longer overall survival in metastatic breast cancer (mBC)³⁰. However, these advancements have also been accompanied by rising healthcare costs, largely driven by (but not limited to) the high price of new medications³¹. This presents a challenge for both high-income countries (HICs) and low- and middle-income countries (LMICs), which are struggling to manage these escalating expenses³². It is actually a challenge for both, HICs and LMICs, which have struggled to incorporate these medications and maintain the sustainability of the systems. It was with perplexity that the world received in July 2024 the news regarding Trastuzumab deruxtecan (Enhertu®) not be incorporated in HER2 low mBC treatment by NICE (National Institute for

Health and Care Excellence) due to high costs. The clinical data clearly demonstrate the benefits of the medication³³; however, in a public healthcare system with broad access, the cost becomes prohibitive. As a result, NICE deemed that pharmaceutical companies were unwilling to offer fair pricing for the medication and announced that it is not recommended in this context³⁴. As the costs have alarmingly increased in oncological care, a broader assessment is essential, considering value proposition. Some strategies have been considered to guide the new incorporations around the world. Ethereal and vague value definition can become obscure the theme and avoid a clear debate, so postponing solutions. Value based cancer care is defined by Leonard Saltz as a ratio of clinical benefit to toxicity including financial toxicity³⁵. Deeping this concept, value proposition can be generated based on how the product will modify the system, how much benefit it will bring which ultimately depends on the treatment options already available³⁶). For example, in adjuvant Receptor hormonal positive, Her 2 negative, breast cancer scenario, where endocrine therapy is the essential strategy³⁷⁻³⁹ to add cyclin inhibitor for high risk patients has improved overall survival⁴⁰⁻⁴³. Now we have two cyclin inhibitors available to apply in this scenario, Abemaciclib and Ribociclib. However, there is a difference between their costs, considering current prices in Brazil⁴⁴, and the length of treatment, 2 years for Abemaciclib with Number Needed to Treat (NNT) of 13, and 3 years for Ribociclib with NNT of $30^{45,46}$. This difference is favorable to abemaciclib. So, this kind of analysis need to be done to help us to choose the best and cost-effective medication.

Guidelines as ESMO has proposed a scale to evaluate the real magnitude of benefit provided by a new treatment to prioritizing funding particularly in countries with scarce resources⁴⁷. Although it is not perfect, it a framework that help us in the decision-making process. Other issues are being considered for inclusion of new drugs that bring benefit for a large proportion of the population, as cost-effectiveness alone, budget impact, or both. In countries with limited resources, budget impact

remains as a priority. So, what would be a worthy strategy for Brazilian government to stablish a guideline for new medicines incorporations? A panel of experts has recommended strengthening of national pricing strategies as well the price negotiation between government and pharmaceutical companies, as crucial points to broaden affordability of new drugs⁶. Of note, these strategies will bring unique difficulties in each scenario considering the number of negotiations, discounts and price volume, which makes the transparency across all these processes essential⁴⁸. Aligned to these strategies, the judgment of cost effectiveness as offered by current guidelines will be useful for government to establish fair rules of new medicines incorporation.

Widen access to supportive teams in breast cancer journey

Recent information from the World Health Organization (WHO) indicates that although 70% of countries have established cancer guidelines and 62% report screening programs, at the same time, 40% report important management and treatment access restrictions and less than half have palliative care plans⁴⁹. In Brazil, the public control cancer politics have begun in 1990 with the law 8080 which stablishes public health system, SUS⁵⁰, whiting its principles, health is a citizen's high and one state's obligation. In the following years, several ordinances directed to the cancer care have been published, which have become possible, organizing the public cancer care in public and private hospitals accredited by government to offer such assistance, the units (UNACONs) or centers (CACONs) of high complexity in oncology (figure 1)^{51,52}. However, these hospitals have as main goal the offering cancer treatment, which is reinforced by remuneration model, paying for treatment procedures as chemo, endocrine therapy, radiotherapy and surgery⁵¹. Arguably, this model, where hospitals and health professionals already have been overwhelmed with the burden of new oncological cases, has resulted in a lack of integral assistance. Brazilian government has published other ordinances aiming to complete these gaps, being considered a landmark the ordinance 874 in May 2013, which stablishes the National Politic of Prevention and Cancer Control⁹. Complementing it, two other ordinances came into country, in 2014 and 2024 both reinforcing the obligation of provider services in oncology, to offer palliative care⁵³. According to the palliative care Atlas, in 2020, Brazil is a country with actions in the area, multiple sources of funding and able to provide opioids access and few educational initiatives⁵⁴. Actually, educational actions by government, have been occasional, being most of the courses offered by private sector^{55,56}.

Despite these ordinances and governmental actions, only 66% of Brazilian oncologists that have assisted breast cancer patients, answered they have palliative team in their hospitals⁵⁷, which is in line with WHO date. The scarcity of supportive teams, including palliative care is critical issue in oncology, but specially in breast cancer, due to increasing incidence and prevalence. Many countries do not know number of patients living with metastatic disease, because their registries do not record relapses, however governments are expected to provide access to treatments and supportive strategies that alleviate suffering for all, ensuring that no one is forgotten or left behind⁵⁸.

To offer integral assistance is particularly challenging in models where there is no specific remuneration for supportive procedures and teams. These difficulties are gotten worse due to a scarcity of qualified human resources. To mitigating the lack of palliative assistance in UNACONS and CACONS, it would be worthy to offer continuously training programs funding by government, which certainly would broaden availability of this service. Currently, these programs have been offered predominantly by private institutions, which brings a need for health professionals paying for the training, hindering the palliative care team's formation in the public system. Also to adopt a framework to deliver telehealth palliative care might will optimizing resources and to provide access for a major number of patients⁵⁹.

Integration with digital tools

Telehealth is a digital tool that has been increasingly integrated to the in-person assistance in medical care⁶⁰. It is a helpful strategy to deal with growing number of new cases of cancer and survivorship⁶¹. Its utilization has permitted to assist major number of patients, improving quality of care. Specially during and after COVID pandemic its use has been adopted by most of medical services providers⁶².

The Brazilian government published in May 2024 an ordinance 3.681 (Programa Nacional de Cuidado Paliativo, PNCP) which reinforces the need for palliative care services with broad coverage and preconizes the telehealth use in the public health system⁶³. The effects of this newest ordinance yet have no measured. Certainly, the implantation of these tools in public health system will bring more equity, by becoming possible the navigation of patients, for instance in the management of scheduling treatments, registration and orientation about acute side effects of the

chemotherapy and follow up of patients after the end of chemotherapy (figure 3). Also, during endocrine therapy phase, aiming to provide support in the chronic side effects. The long length of endocrine therapy in breast cancer, frequently 10 years, has been associated with low rates of adherence, with some records of 60% of patients have discontinued or have adherence below 80%, which is clearly related to the profile of side effects⁶⁴. The success of digital platforms, in this scenario, has been documented around the world⁶⁵. In Brazil, one notably example is THUMMI app, an applicative developed by Brazilian researchers including oncologists that is now operating in few Brazilian hospitals, including two public hospitals⁶⁶. Its utilization up to now, has demonstrated major treatment adherence and better management of side effects. The ideal scenario would be the large utilization of this kind of digital instrument, composition of teams with navigator nurses, as preconized by ordinance, that could broaden access to the health care system for patients in the public system.

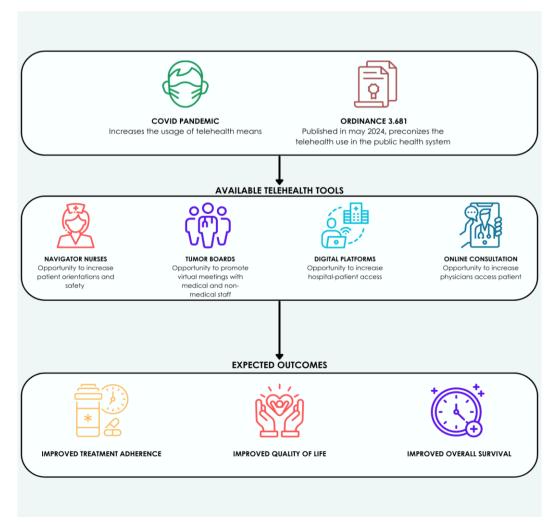


Fig. 3 – Increasing usage of telehealth within the Brazilian Public Healthcare System, Sistema Único de Saúde (SUS).

Another need for broadening high quality assistance access is continuous commitment of the whole team during patient's treatment and making decision. Multidisciplinary teams (MDTs) or tumor boards have been implemented in the medical teams for many years, and numerous studies have demonstrated its contribution in improving patient management⁶⁷. However, MDTs has happened more frequently in academic centers⁶⁸. In Brazil, it has been frequently underutilized and misunderstood, mainly in the public health system⁶⁹. There are several points at the time, responsible for this low reproducibility of MDTs, among those the lack of protocol previously stablished, low representativity of some medical specialties and non-medical staff ⁷⁰. Nowadays one recent difficult is to gather the team at a same hospital at a same time, due to new models of work, where oncologists and other members of multidisciplinary teams have worked in more than one institution. The proposition is the use of digital platforms, provide by institution, which would offer the opportunity to meeting involved physicians despite of they are not in that hospital in that day. It would be a first step toward construct a culture of participation in MDTs. After this first step, it would highlight other challenges and certainly would help to improve institutional process and quality of management care.

Conclusion

Breast cancer care in Brazil has evolved over recent decades, particularly since the creation of the SUS. However, mortality rates have remained consistently high, in contrast to HICs, where rates have declined during the same period. Addressing barriers such as reducing waiting times from self-detected abnormalities to diagnosis, and from diagnosis to treatment initiation, is an urgent priority. A possible strategy would be to centralize care in one or two facilities to reduce bureaucracy. Additionally, providing medical training for primary care physicians and multidisciplinary teams to ensure timely diagnostic steps is essential. Equally important is the development of sustainable models for incorporating new treatments, including medications, within a

value-based care framework, alongside training programs for supportive teams. All of these efforts must be recognized and prioritized by the government, healthcare providers, and medical societies to move forward into a new era of breast cancer care in Brazil.

Conflict of Interest:

None

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None

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