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PATIENT NAVIGATION IMPROVED BREAST CANCER OUTCOMES AMONG WOMEN IN THE PUBLIC SYSTEM IN RIO DE JANEIRO, BRAZIL

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Abstract: Purpose: To evaluate whether a Breast Cancer (BC) Patient Navigation Program (PNP) contributes to increasing compliance with the "60-Day Law," which mandates that cancer treatment must start within 60 days of a definitive diagnosis. Consequently, to assess if complying with this Brazilian federal law helps reduce BC mortality in public health system patients.
Patients and Methods: We conducted a longitudinal observational and retrospective study with women over 18 years of age diagnosed with BC. Data were collected from medical records via the PNP. The sample was selected based on an exploratory evaluation of records from the Rio Imagem Diagnostic Center and Heloneida Studart State Hospital in Rio de Janeiro, from 2017 to 2022. Active case follow-up involved cross-referencing medical records and contact via phone or text messages.
Results: Out of 1,022 women diagnosed with BC, 840 were eligible after excluding those lost to follow-up, who refused treatment, died of unrelated causes, or received palliative care. 79 patients died from BC. The 5-year specific survival rate was 92.6%. Survival was higher for patients treated initially with surgery (97.9%, $p < 0.0001$), histological grade 1 (94.5%, $p = 0.002$), Luminal biological profiles (98.4%, $p < 0.0001$), and treatment within 60 days (95.3%, $p = 0.005$). Stratifying 5-year mortality risk by advanced stage revealed higher mortality among women who were not treated within 60 days as per the law (HR=2.00[1.23; 3.24]).
Conclusion: Failure to comply with the "60-Day law" doubled the risk of mortality from BC. Patients starting treatment within 60 days had higher survival rates compared to those who did not. In Brazil, the PNP could be an opportunity to properly implement existing legislation, potentially significantly impacting BC control.
Keywords: breast cancer; patient navigation; survival analysis

CONTEXT

Key Objective: A Breast Cancer Patient Navigation Program can contribute to starting treatment within 60 days and increasing overall survival.

Knowledge Generated: In 2012, the Brazilian government issued Law No. 12.732/12 from the Ministry of Health, the "60-Day Law". This law mandates that cancer treatment for public health system patients must start within 60 days of definitive diagnosis. The average diagnosis time is up to 31 days in private health with 18% of cases diagnosed in stages III and IV, while in the public system, it averages 93 days, sometimes reaching 180 days with 40% of cases in these advanced stages.

Relevance: A Breast Cancer Patient Navigation Program contributes to increased compliance with this federal law by helping to reduce mortality from this disease in public health patients in Brazil.

INTRODUCTION

Despite Brazil's trajectory of breast cancer (BC) prevention and control actions, high incidence, late-stage diagnosis, and mortality remain constant due to barriers to healthcare access[1]. The estimate for 2023-2025 is about 73,610 new cases annually, with an incidence of 66.54 per 100,000 inhabitants[2]. BC deaths lead in the country, accounting for 16.1% of all cancer deaths[3].

Recognizing this situation's negative impact, in 2012, the Brazilian government issued Law No. 12.732/12 from the Ministry of Health, the "60-Day Law". This law mandates that cancer treatment for public health system patients must start within 60 days of definitive diagnosis[4]. The average diagnosis time is up to 31 days in private health with 18% of cases diagnosed in stages III and IV, while in the public system, it averages 93 days, sometimes reaching 180 days with 40% of cases in these advanced stages[5]. Rio de Janeiro has the lowest compliance rate with the "60-Day Law". Ministry of Health data show that in Rio de Janeiro over 90% of women do not start treatment within the mandatory 60-day period[6].

In 2017, in collaboration with the Global Cancer Institute, the State Health Department of Rio de Janeiro (SES RJ), and the National Cancer Institute (INCA), a BC PNP was developed and implemented[7]. It aimed to help women diagnosed with BC in the public system to start treatment at a specialized center within 60 days of diagnosis. As part of the BC PNP program, a trained social worker facilitated patients' navigation through the health care system by providing services such as diagnostic consultation scheduling, follow-up assistance, referral facilitation, and coordinating communication between patients and healthcare professionals[6,8].

The central pillar is recognizing the importance of understanding the patient's experience to advance towards patient-centered care[8]. The problem of accessing healthcare services requires better solutions and for populations in areas where healthcare access is fragmented, and healthcare systems can be fragile and underfunded[8].

Recent initiatives in Rio de Janeiro showed the effectiveness of BC patient navigation in the public health system at two diagnostic centers of SES RJ: Rio Imagem[6] and Heloneida Studart State Hospital[8]. The compliance rate with the "60-Day Law" increased from 10% to 52% in 2017 and from 22% to 86% in 2020, respectively.

This study aims to assess the contribution of a BC PNP to increasing compliance with the "60-Day Law" at both SES RJ diagnostic centers and, consequently, whether complying with this federal law helps reduce mortality from this disease in public health system patients.

MATERIAL AND METHODS

STUDY DESIGN

We conducted a longitudinal observational and retrospective study with women over 18 years of age diagnosed with BC according to the International Classification of Diseases and Health-Related Problems 10th Revision (ICD-10: C50.0 to C50.9), assisted in the state and capital of Rio de Janeiro.

Data for the study were collected from medical records via the PNP. The sample was selected based on exploratory evaluation of BC diagnosis records from the Rio Imagem Diagnostic Center and Heloneida Studart State Hospital in Rio de Janeiro.

STUDY POPULATION

Between August 2017 and December 2022, 1,022 women were diagnosed with BC. Patients were followed up until 20/07/2023 or the final date of follow-up. Active case follow-up involved cross-referencing medical records and contact via phone or text messages.

Exclusion criteria included women who: refused treatment; died from another disease; or received palliative care. Thus, for this study, after exclusion, the sample size of all patients enrolled in the PNP was 840 (n=840).

DATA COLLECTION

The independent study variables were: age at diagnosis - calculated from the birth and diagnosis dates available in the medical record (≤50 years; >50 years); Health Region - Metropolitan 1 – capital, Metropolitan 1 - Baixada Fluminense, and other municipalities; Type of treatment - surgery; hormone therapy; chemotherapy; radiotherapy; no information; Anatomical staging (TNM classification[9]) – 0 to IV (variables related to TNM were dichotomized[10] into early (0 to IIA) and advanced (IIB to IV) staging; Histological type - infiltrating ductal carcinoma (IDC), infiltrating lobular carcinoma (ILC), ductal carcinoma in situ (DCIS), sarcoma; no information); Histological grade (1-3; no information); Biological profile (luminal, HER2 positive, triple negative, no information); Compliance with the "60-Day Law" (Yes; No).

The dependent variable of interest was BC patient survival. For survival estimation, we considered the time from diagnosis to death from breast cancer (failure) or to the last recorded contact (censorship). Cases censored were those with incomplete observational follow-up, including patients who abandoned or refused treatment or died from a cause unrelated to BC.

STATISTICAL ANALYSIS

To estimate the probability of 5-year specific survival, we used the Kaplan-Meier estimator, a non-parametric method that allows comparison between different categories of a variable during the survival period for breast cancer, and the log-rank test, in the form of a Chi-squared test, to statistically evaluate the heterogeneity of the curves to verify if there are statistical differences in life span by groups.

And using Cox Regression, the crude and adjusted Hazard Ratios and the respective 95% confidence intervals (95% CI) were estimated. The survival curves generated were visually inspected, and the models tested according to the risk proportionality test. As the hypothesis of proportional distribution of mortality risks was rejected for the staging variable ($p < 0.05$), the regression analyzes were stratified for each tumor staging variable[11] The Schoenfeld residuals test, with a statistical significance level of 0.05, verified the failure rates' proportionality[12-13]. The final model included only statistically significant variables at $\alpha=0.05$. Statistical analyses were performed with R software version 4.3.1[14].

RESULTS

For this study, the sample size included all patients enrolled in the PNP, amounting to 840 patients diagnosed with BC (Figure 1).

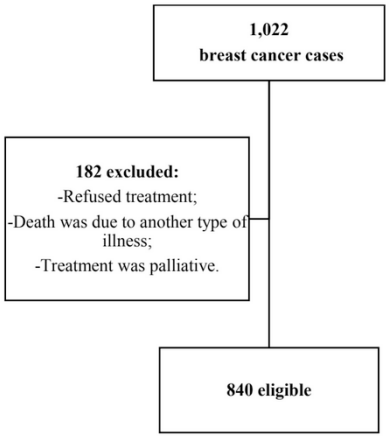


Figure 1. Flowchart of breast cancer cases from some reference centers for treatment in the State of Rio de Janeiro, 2017-2022.

A total of 840 women with BC were studied, and 79 died from this disease. It was found that the highest proportions were in women: over 50 years old (71.3%), where the Health Region for treatment reference was in the Capital (60.5%), who received chemotherapy treatment (54.0%), with histological type - IDC (Invasive Ductal Carcinoma) (86.2%), Histological grade 2 (67.4%), with the biological profile of Luminal diseases (63.3%), and who did not comply with the "60-Day Law" (60.4%) (Table 1).

The overall specific survival at 5 years was 92.6% for breast cancer. When stratified by disease staging, survival is higher in the early stages, and the highest survival was in: women over 50 years old (97.9%), where the Health Region was in the Capital (97.4%), underwent treatment through surgery (97.9%), with histological type - IDC (97.5%), Histological grade 1 (97.5%), with Luminal biological profile (98.4%), and where treatment complied with the "60-Day Law" (97.8%) (Table 1).

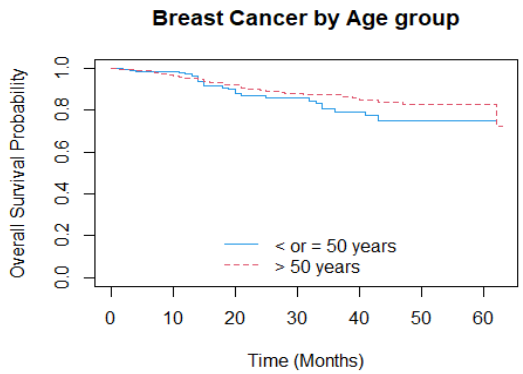
Significant differences were observed between the specific survival curves in the independent variables (Table 1): type of treatment, grade, biological profile, and compliance with the "60-Day Law".

The results of the Cox regression analysis are presented in Table 2, with both adjusted and unadjusted analyses for variables by disease staging.

When stratifying the 5-year mortality risk (hazard ratio) according to stage 0-IIA, it was observed that the risk of mortality is higher among women who underwent hormone therapy and had a HER2 positive biological profile. It was found that the variables 'grade' and compliance with the '60-Day Law' showed no associations.

When stratifying the 5-year mortality risk according to stage IIB-IV, it was observed that the highest risk of mortality was among women who underwent treatments of hormone therapy (HR=5.54[1.39; 22.17]) and chemotherapy (HR=5.46[1.71; 17.39]), with triple-negative biological profile (HR=3.45[2.02; 5.91]) and in cases where the treatment did not comply with the '60-Day Law' (HR=2.00[1.23; 3.24]). It was found that the variable 'grade' showed no association.

After adjusted analysis, it was observed that the risk of mortality in 5 years remained associated with the same variables for both stages (Table 2).

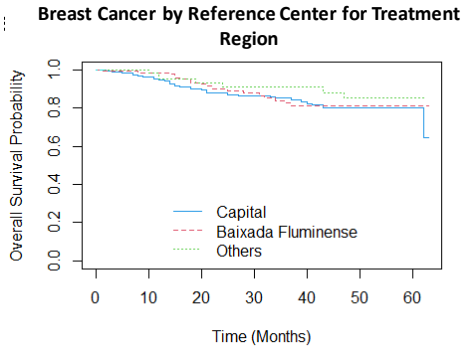


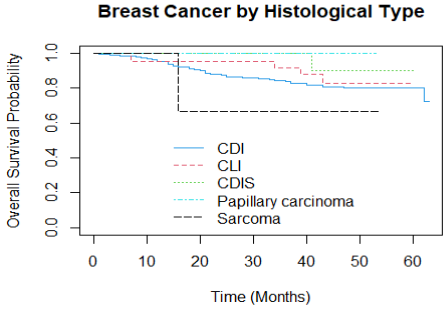
Variables	Stage		Total (n)	%	Deaths		5-year survival (%)			Log-rank test (p)
	0-IIA	IIB-IV								
	n	n			n	(%)	0-IIA	IIB-IV	Total	
General	**337**	**503**	**840**		**79**	**100**	**97.5**	**89.2**	**92.6**	-
Age										
≤ 50 years	80	161	241	28.7	26	32.9	93.7	88.7	91.2	0.20
>50 years	257	342	599	71.3	53	67.1	97.9	89.4	92.9	
Health region for treatment										
Capital	210	298	508	60.5	52	65.8	97.4	87.2	91.5	
Baixada Fluminense	88	161	249	29.6	20	25.3	96.5	90.3	92.9	0.70
Other municipalities	39	43	82	9.8	7	8.9	93.3	88.8	93.2	
No information	0	1	1	0.1	-	-	-	-	-	
Type of initial treatment										
Surgery	252	75	327	38.9	7	8.9	97.9	95.7	97.7	
Hormone therapy	18	36	54	6.4	8	10.1	81.3	85.3	87.9	<0.0001
Chemotherapy	64	390	454	54.0	64	81.0	95.2	87.6	88.7	
Radiotherapy	0	2	2	0.2	-	-	-	-	-	
No information	3	0	3	0.4	-	-	-	-	-	
Histological type										
IDC	276	448	724	86.2	72	91.1	97.5	88.5	92.4	
ILC	16	43	59	7.0	5	6.3	-	91.9	91.9	0.40
DCIS	38	7	45	5.4	1	1.3	90.0	-	90.0	
Sarcoma	5	2	7	0.8	-	-	-	-	-	
No information	2	3	5	0.6	1	1.3	-	-	-	
Histological grade										
1	75	53	128	15.2	7	8.9	95.7	90.4	94.5	
2	220	346	566	67.4	46	58.2	97.0	90.2	93.5	0.002
3	37	99	136	16.2	25	31.6	95.8	83.0	86.5	
No information	5	5	10	1.2	1	1.3	-	-	-	
Biological Profile										
Luminals	244	288	532	63.3	34	43.0	98.4	91.8	95.3	
HER2 positive	30	84	114	13.6	13	16.5	76.9	87.1	88.3	<0.0001
Triple negative	45	100	145	17.3	26	32.9	91.3	79.7	85.6	
No information	18	31	49	5.8	6	7.6	-	-	-	
Treatment within 60 days										
Yes	90	243	333	39.6	49	62.0	97.8	92.4	95.3	0.005
No	247	260	507	60.4	30	38.0	94.8	87.9	88.0	

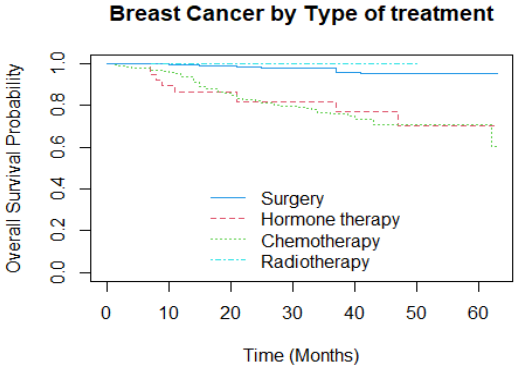
Table 1. Distribution of sociodemographic, clinical, and treatment-related variables, deaths, and 5-year survival in women with breast cancer. State of Rio de Janeiro, 2017-2022

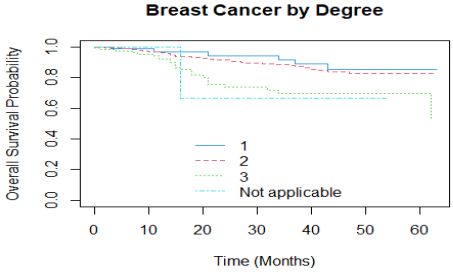
Variables	Stage 0-IIA		Stage IIB-IV	
	Hazard ratio	Hazard ratio adjusted	Hazard ratio	Hazard ratio adjusted
	HR (CI 95%)	HR (CI 95%)	HR (CI 95%)	HR (CI 95%)
Type of initial treatment				
Surgery	1	1	1	1
Hormone therapy	7.61 (1.39; 41.60)	1.99 (1.46; 272.51)	5.54 (1.39; 22.17)	6.33 (1.55; 25.87)
Chemotherapy	1.04 (0.12; 9.29)	0.36 (0.05; 3.62)	5.46 (1.71; 17.39)	3.90 (1.20; 12.67)
Radiotherapy	-	-	-	-
Histological grade				
1	1		1	1
2	1,33 (0,16; 11,41)	1,10 (0,12; 10,26)	1,07 (0,46; 2,53)	0,81 (0,34; 1,95)
3	2,10 (0,13; 33,65)	0,86 (0,04; 17,80)	2,09 (0,85; 5,14)	1,06 (0,41; 2,76)
Biological Profile				
Luminals	1	1	1	1
HER2 positive	15.33 (2.43; 96.53)	57.00(4.42; 735.55)	1.51 (0.78; 3.00)	1.51 (0.74; 3.09)
Triple negative	3.82 (0.64; 22.88)	13.13 (1.09; 157.90)	3.45 (2.02; 5.91)	3.89 (1.46; 10.34)
Treatment within 60 days				
Yes	1	1	1	1
No	2.97 (0.66; 13.39)	1.68 (0.29; 9.81)	2.00 (1.23; 3.24)	1.75 (1.06; 2.87)

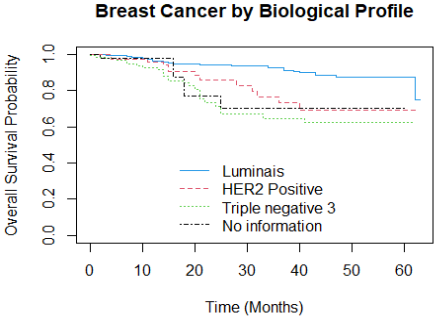
Table 2. Cox regression model for survival analysis of women with breast cancer according to variables by staging, State of Rio de Janeiro, 2017-2022.











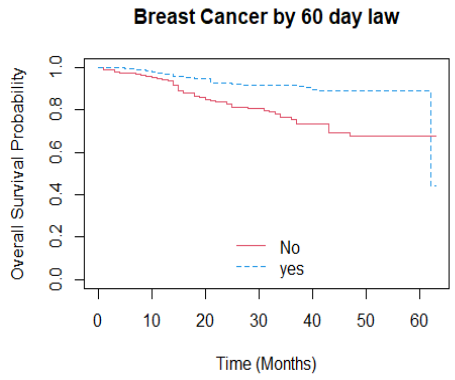


Figure 2. Estimated specific survival curve by Kaplan-Meier for general breast cancer with a 95% confidence interval and according to sociodemographic, clinical, and treatment variables.

When analyzing by staging, it is observed that the highest 5-year specific survival for breast cancer was for patients who complied with the '60-Day Law'. For early stage, it was 97.8% and for advanced stage, it was 92.4% (Figure 3).

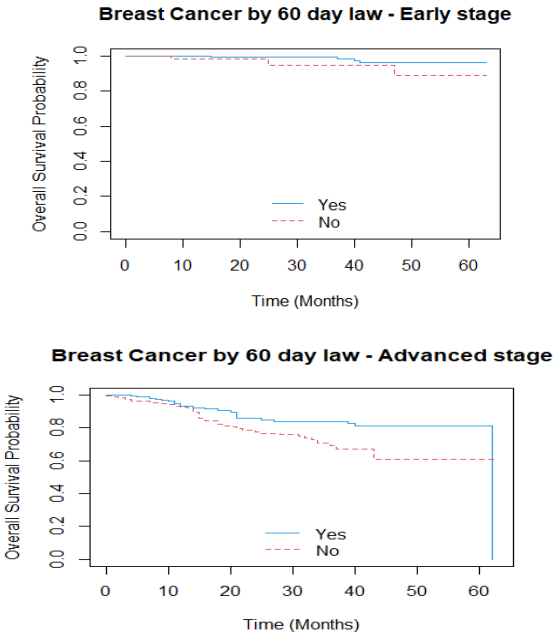


Figure 3. Estimated specific survival curve by Kaplan-Meier for breast cancer by staging according to compliance with the '60-Day Law'.

DISCUSSION

Cancer significantly impacts the lives of both the patient and their loved ones. Routines are disrupted and anxiety, stress and fear can be generated throughout diagnosis and treatment, including from diagnostic tests, obtaining referrals to specialists, multiple visits to care facilities, costs of treatment, maintaining employment, delays in being able to access treatment, uncertainty around treatment response, fear of dying, and, above all, the stigma associated with the diagnosis[15].

Patient-centered care management enhances interprofessional collaboration and the continuum of care in the cancer care network, enabling the provision of comprehensive and effective actions. Oncology patients require support in "a coordinated process of individualized care" that allows "patients to overcome barriers in accessing timely and quality care in complex healthcare systems"[16]. The patient navigator (PN) can alleviate health system barriers, improving outcomes for breast cancer patients[17-18].

PNP utilizes culturally competent and trained individuals to assist cancer patients, along with standard care professionals (doctors, nurses, social workers), to reduce or eliminate health disparities in oncology treatment[16]. The two main goals of patient navigation are to reduce barriers to cancer-related care and ensure adequate timing in the provision of healthcare services[17-18].

PNP facilitates the patient's journey with breast cancer (BC)[6] by:

- Helping patients better understand their diagnosis and the proscribed treatment, addressing clinical and non-clinical issues, identifying, and addressing barriers to care.
- Providing logistical coordination of care for the patient.
- Serving as a link in coordination between patients and their care providers (doctors, oncology reference center, etc.).

- Using local experience to proactively identify and address patient needs and identify barriers and/or improvements in strategic planning processes.
- Providing monthly information on defined metrics and measures, process planning, and offering solutions for improvement.
- Serving as a single point of contact for patients throughout the continuum of care until the start of treatment, meeting all encountered needs.
- Being responsible for establishing and maintaining positive working relationships with patients and other professionals (doctors, clinic managers, nurses, psychologists, nutritionists, etc.).
- Independently using judgment and decision-making to meet the patient's needs throughout their care.

PNP ethically assesses the patients' journey with all its variability, allowing for evidence of relevance from real-world data. The data can be used to: inform decision-making, understand patients and trends, provide smarter services and products, improve internal operations, and optimize the use of financial resources[18]. Patient navigation has often been proposed and implemented to address the challenges of access to oncological care in high-income countries[19]. There are few studies reported on patient navigation interventions in cancer treatment in low- and middle-income countries (LMICs) in Asia, South America, and Africa, but all suggest that the provision of navigation services can improve access to oncological care in these countries[19]. All barriers to accessing health resources are associated with negative impact on health, overall survival, and mortality rates, which is why a PN program is so important.

In 2016, the National Health Agency (ANS) released the report of the Oncorede Project: the (re)organization of the oncological care network[20]. Patient navigation was identified as an important tool to achieve patient-centered care, and "care assistant" roles were created to "navigate" patients through their care journey and assist with difficulties encountered.

In 2019, the ANS released the results of the Oncorede Project pilot project[21]. Participating institutions reported difficulties implementing a PN program including: problems with a professional profile that could work in an integrated manner with other professionals, acting as a care navigator; post-discharge evolutionary tracking of all patients who received BC treatment; establishment of therapeutic outcome indicators relative to the assisted population; access to patients at the time of diagnosis for the implementation of a care line; more effective participation by patients, especially in educational and support groups, taking into consideration their unstable clinical conditions; filling out the patient monitoring spreadsheet, as well as the proper filling out of medical records; and, structuring a health service payment method based on indicators (such as survival, quality of life, progression-free survival, reduction in the number of chemotherapies performed in the last days of life).

Delay in cancer treatment is a problem in health systems worldwide. An eight-week delay in breast cancer surgery increases the risk of death by 17%, and a 12-week delay increases the risk by 26%[22]. In this study, non-compliance with the "60-Day Law" doubled the risk of mortality from BC. The risk of mortality was also high for patients who started systemic treatment as their first treatment, probably because they were patients with more advanced staging. Patients with triple-negative biological profile had more than a threefold increase in the risk of mortality, showing the need for better therapeutic approaches for this subtype of BC, regardless of the initial staging. Patients who

started treatment within the 60-day period had higher survival compared to those who did not comply with the law (95.3% x 88%; p=0.005).

This study demonstrated the positive results of patient navigation in optimizing the start of treatment. In addition, the study achieved an increase in compliance with the "60-Day Law" from 10% to 40%. The initial goal was compliance with the law in at least 70%[6], but chronic structural problems in Rio de Janeiro, such as a deficit of human resources and medical supplies, made it difficult to achieve this goal. Local managers were informed of the structural improvement needs involving partnerships from municipal, state, and federal powers[23-25].

This study has limitations that could possibly change the analyses related to monitoring patients in referral hospitals for treatment. For example, many patients only had staging exams available upon arrival at hospitals, which led this study to stratify the disease into early (O-IIA) and advanced (IIB-IV)[9-10]. The staging of this study was clinical and carried out on the day the histopathological report was delivered to the patient at the diagnostic center. Another limitation refers to data on the quality of treatment offered by public hospitals, as well as the correct sequence of treatment, available medications, or patients' adherence to treatment. These factors affect patient survival. The time factor for starting treatment has been shown to be important, as it prevents the progression of the disease from worsening. Another study carried out in Rio de Janeiro[26] showed a lower risk of death for patients who started treatment earlier (<6 months after diagnosis), which indicates better survival rates associated with early diagnosis and timely adequate treatment.

In conclusion, this study offers those interested in the subject, especially managers and health professionals, encouragement to understand, plan, and evaluate BC control actions along the care continuum in which patient navigation allows the appropriate application of the "60-Day Law". Policies focused on minimizing delays in access to the start of cancer treatment save lives[22]. The implementation of a PNP to optimize the start of treatment contributed to raising the compliance rate with the "60-Day Law". The start of BC treatment within the 60-day period was associated with a lower risk of mortality and a higher 5-year survival rate. In the Brazilian context, PNP programs can represent an opportunity to properly implement existing legislation and, as such, would have great potential to favor BC control in the country.

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