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ORIGINAL RESEARCH



## Breast Cancer Quality of Life and Health-state Utility at a Brazilian Reference Public Cancer Center

Renata Leborato Guerra<sup>a</sup>, Neilane Bertoni Dos Reis<sup>b</sup>, Flávia De Miranda Corrêa<sup>a</sup>, Myrian Machado Fernandes<sup>a</sup>, Ricardo Ribeiro Alves Fernandes<sup>a</sup>, Marianna De Camargo Cancela<sup>b</sup>, Rodrigo Moura De Araújo<sup>c</sup>, Susanne Crocamo<sup>c</sup>, Marisa Santos<sup>a,d</sup> and Liz Maria De Almeida<sup>b</sup>

<sup>a</sup>Health Technology Assessment Unit (NATS) of the Division of Population Research of the Brazilian National Institute of Cancer (INCA), Rio de Janeiro, RJ, Brazil; <sup>b</sup>Division of Population Research of the Brazilian National Institute of Cancer (INCA), Rio de Janeiro, RJ, Brazil; <sup>c</sup>Breast Cancer Hospital (HCIII) of the Brazilian National Institute of Cancer (INCA), Rio de Janeiro, RJ, Brazil; <sup>d</sup>Health Technology Assessment Unit (NATS) of the Brazilian National Institute of Cardiology (INC), Rio de Janeiro, RJ, Brazil

### ABSTRACT

**Objectives:** To evaluate health-related-quality-of-life and derive health-state-utility (HSU) from breast cancer patients, before and after routine therapy at a Brazilian reference public cancer center.

**Methods:** In a prospective cohort study, a consecutive sample of outpatients newly diagnosed with breast cancer was submitted to two interviews (baseline, 6-month) to complete EQ-5D-3L/VAS and EORTC-QLQ-C30/BR23 questionnaires. Demographic and clinical information was reviewed from medical records.

**Results:** For 196 patients, EQ-5D domains of pain/discomfort and anxiety/depression were mainly affected, but partially improved overtime, while mobility/usual activities/self-care worsened after therapy. EORTC-QLQ-C30/BR23 scales mostly affected were emotional functioning, insomnia, pain, sexual enjoyment and future self-health perspective at baseline, while financial difficulties, insomnia, fatigue and therapy side-effects at follow-up. Overtime mean scores were 71.4 (95%CI 68.5–74.4) and 76.1 (95%CI 73.3–78.8) for EQ-5D-VAS, and 0.712 (95%CI 0.686–0.737) and 0.732 (95%CI 0.707–0.757) for HSU. HSU was 0.689 (95%CI 0.648–0.730) in stages III-IV, and 0.692 (95%CI 0.652–0.731) under two/three chemotherapy regimens.

**Conclusion:** In a context of impairments in emotional functioning, sexual enjoyment, symptoms burden, and poor future self-health perspective, breast cancer produced a mean HSU of 0.712. After routine care, there was a small improvement in quality of life, with lower HSU particularly in advanced disease and multiple chemotherapy regimens.

### ARTICLE HISTORY

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### KEYWORDS

Breast neoplasm; patient reported outcome measures; health-related quality of life; health status; utility

## 1. Introduction

Patient-reported outcome (PRO) measures have been increasingly used to capture patients' perspectives on health outcomes, such as physical, social and psychological functioning, symptom burden, satisfaction, and welfare [1]. Some PRO measures assessing health-related quality of life (HRQOL) can be used to generate utility estimates by converting patients' self-rated health status to a health-state utility (HSU), value that usually ranges on a scale from death (score of 0) to perfect health (score of 1), based on the general population preferences [2]. HSU is used to estimate quality-adjusted life-years (QALYs), the health benefit measure of cost-utility analysis, by multiplying the time spent in a health state by the HSU value for that respective state [2,3]. Therefore, PRO measures can provide information to clinicians and policymakers on both the health status of the patients and the preferences of the community regarding different health states, which may improve the individual quality of care as well as optimize decisions about the allocation of health resources [1]. Health technology assessment (HTA) agencies have pointed out the informative value of the PRO for evaluating the health

benefits of an intervention and its role as supplementary or equally weighed information compared to clinical outcomes in decision-making [4,5].

A PRO measure may be generic or disease-specific. Generic instruments are designed to assess HRQOL in any disease population, facilitating comparisons between the interventions and across different conditions [1]. The EuroQol 5-dimension (EQ-5D) is a standardized and validated generic instrument intended to assess the HRQOL impairment in a patient population, derive HSU of multiattribute health states, and directly measure patient preferences towards their own health based on a visual analog scale (VAS) [3]. EQ-5D is especially recommended for HTA appraisals of interventions directed to chronic diseases as it shows a reasonable degree of reliability, content validity, construct validity and responsiveness [6,7]. On the other hand, HRQOL aspects that are relevant for a particular patient population are more properly addressed by disease-specific instruments [1,4]. The European Organization for Research and Treatment of Cancer Quality-of-Life Questionnaire (EORTC-QLQ) is a well-known validated instrument for cancer patients with supplementary modules to capture decline in domains of different cancer sites [8].

### Article Highlights

- Breast cancer is the most prevalent and lethal malignant tumor in women worldwide, and patients experience impairments in physical, social and psychological functioning, and overwhelming symptoms.
- In the context of an oncology decision-making process, the appraisal of interventions exclusively based on clinical outcomes may neglect the substantial impact on HRQOL produced by the disease itself and the therapy-related toxicity.
- Generic and disease-specific PRO measures, such as EQ-5D and EORTC-QLQ, are used to capture patients' perspectives on different domains of health outcomes. The EQ-5D may also derive HSU based on the general population preferences, which is used to estimate QALYs, the health benefit measure of cost-utility analysis.
- In our study, breast cancer patients HRQOL was mainly affected by impairments in mental functioning, sexual enjoyment, symptoms of pain, fatigue, and insomnia, and poor future self-health perspective. After a period of routine care, there was a small improvement in quality of life, however financial difficulties and therapy side-effects emerged as impacted domains.

Given the growing importance of HTA in the decision-making process of the Brazilian public health sector, especially in the context of a costly oncology scenario in which the appraisal of oncology therapies exclusively based on clinical outcomes may neglect the substantial HRQOL impairment produced by the disease and the therapy-related toxicity, there is a need to increase the knowledge of cancer patients HRQOL and to quantify the utility assigned to their specific health status by both patients and community. Breast cancer is the most prevalent and lethal malignant tumor in women worldwide, with the number of incident cases and deaths estimated in 2018 to be approximately 2.1 million and 627,000, respectively [9]. In Brazil, breast cancer is the leading cancer among women with 59,700 new cases estimated annually [10]. Previous studies have reported that breast cancer patients often experience impaired or limited function; therefore, the burden of the disease is relevant in terms of disability [11–14]. Nevertheless, national studies prospectively evaluating HRQOL are scarce, and HSU scores have not been reported.

The aim of this study was to evaluate the HRQOL and to derive, for the first time, HSU values of women with breast cancer before and after routine therapy initiation at a Brazilian reference and comprehensive public cancer center.

## 2. Methods

### 2.1. Patients and study procedures

A prospective cohort study was conducted at the Brazilian National Institute of Cancer (INCA) with a consecutive sample of women who were newly diagnosed with breast cancer and treatment naive. Outpatients were recruited from March to May 2017, and those eligible who had given written informed consent underwent a face-to-face interview at baseline (before initiating routine therapy) and at a 6-month follow-up. General health and cancer-specific measures of quality of life were obtained through the following standardized instruments: EQ-5D-3L and EORTC-QLQ Core-30/Breast-23 (C30/BR23). Sociodemographic, work history and health behavior data

were also collected during the interview, and medical records were reviewed to assess clinical and therapy information. This study was approved by the Research Ethics Committee of the INCA.

The EQ5D-3L comprises five dimensions (mobility, self-care, usual activities, pain/discomfort, and anxiety/depression), and each has three levels of response (no problems, some problems, extreme problems). The EQ5D also has a vertical visual analog scale (EQ-VAS) to record the respondent's self-rated health on a scale ranging from zero (worst imaginable health state) to 100 (best imaginable health state) [15]. The EORTC-QLQ-C30 includes five functional scales (physical, role, cognitive, emotional, social), three symptom scales (fatigue, pain, nausea/vomiting), six single items (constipation, diarrhea, sleep, dyspnea, appetite, financial problems), and two items of a general health scale (GHS). Most items use a scale ranging from 1 ('not at all') to 4 ('very much'), except for the global quality of life, which was rated from 1 ('very poor') to 7 ('excellent'). The QLQ-BR23 module, which is used to complement the core questionnaire with questions for breast cancer patients, comprises five domains (body image, sexuality, arm symptoms, breast symptoms, and systemic therapy side effects) in which the items use a scale ranging from 1 ('not at all') to 4 ('very much') [16]. The Portuguese versions of both questionnaires were used after copyright permission.

### 2.2. Statistical analysis

Descriptive analysis of the sample characteristics was performed using mean and standard deviation (SD) for continuous variables, and frequency and percentages for categorical variables. Quality of life data were analyzed according to the respective measures manuals [15,16]. The proportion of problem levels reported for each dimension of the EQ5D was estimated for the sample, while the individual health states were converted to an HSU score based on the valuation of the Brazilian population [17]. The two-proportions z-test, with the significance level alpha as 5%, was used to test problems proportion differences within EQ-5D domains. The sample HSU and the overall self-rated health (EQ-VAS, EORTC-GHS) were calculated by measuring the mean and respective 95% confidence intervals (95% CI). Cases of death and withdrawal before the second interview were considered missing data in the analysis. The EORTC raw scores of each scale were transformed to a score ranging from 0 to 100, with higher scores representing either better functioning/HRQL or increased symptom/item burden according to the evaluated scale in the sample. All analyses were performed using the software R version 3.5.1.

## 3. Results

A total of 196 breast cancer patients were included in the study, and 183 were submitted to the second interview (three cases of withdrawal and 10 deaths). The characteristics of the study sample are described in Table 1. Most patients were between 50 and 69 years old with basic education level, and about one half of them were nonwhite and married. Approximately one-third had a remunerated job, and 80% had a monthly household

**Table 1.** Description of the study sample.

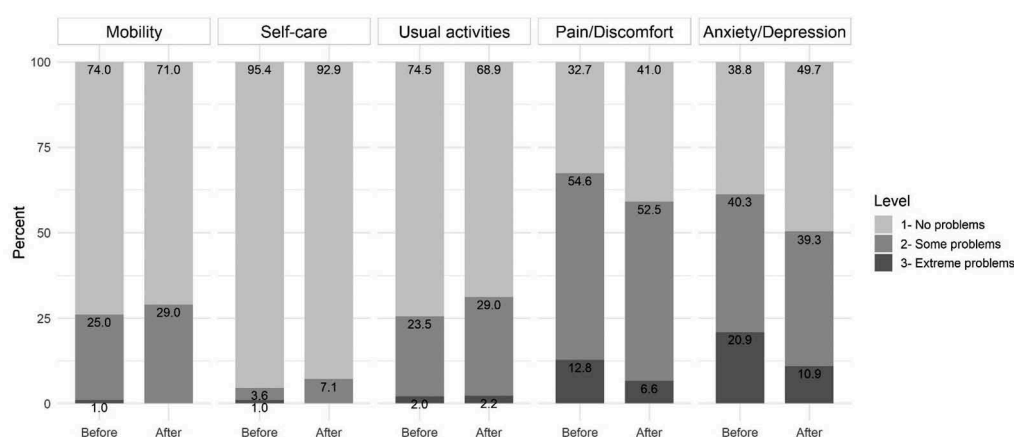
Characteristic	n	%
<b>Age (years)</b>		
< 40	12	6.1
40–49	38	19.4
50–59	58	29.6
60–69	53	27.0
> 69	35	17.9
<b>Race</b>		
White	92	46.9
Nonwhite	104	53.1
<b>Marital status</b>		
Single	29	14.8
Married	105	53.6
Divorced	31	15.8
Widowed	31	15.8
<b>Education level</b>		
Not literate	5	2.6
Literate	74	37.8
Fundamental	93	47.5
High school	16	8.2
College	8	4.1
<b>Paid work activity</b>		
Yes	70	35.7
<b>Household monthly income (US\$)*</b>		
Mean (SD)	536.32	(473.68)
<b>Smoking</b>		
Never	122	62.2
<b>Alcohol intake</b>		
Never	118	60.2
<b>Comorbidity</b>		
Yes	130	66.3
<b>Type of comorbidity</b>		
Cardiovascular	111	56.6
Diabetes	40	20.4
Thyroid disorder	11	5.6
Others	51	26.1
<b>Cancer stage at diagnosis</b>		
0	4	2.0
I	37	18.9
II	63	32.2
III	79	40.3
IV	11	5.6
Not known	2	1.0
<b>Therapy since diagnosis</b>		
Surgery	82	41.8
Radiotherapy	11	5.6
Endocrine therapy	31	15.8
Chemotherapy	135	68.9
<b>Number of chemotherapy regimens (n=135)</b>		
One	53	39.3
Two	77	57.0
Three	5	3.7

\*Converted from Brazilian reais (mean R\$2,038; standard deviation R\$1,400; 1R\$ = 3.8US\$ in October 2018).

income of less than US\$600. About 40% had current or previous history of alcohol consumption and smoking, and 66% had comorbid conditions such as cardiovascular disease and diabetes. Disease stages 0–II were presented in approximately 53% of the cases, while stage III and metastatic disease comprised 40% and 5.6%, respectively. Almost 70% of the patients had undergone chemotherapy within six months after baseline, 60% of whom received more than one regimen.

The EQ-5D domains mainly affected were pain/discomfort and anxiety/depression with some and extreme problems reported by, respectively, 67.4% and 61.2% of the breast cancer patients at baseline. In contrast, these values were 26% for mobility, 4.6% for self-care and 25.5% for usual activities. After six months, the proportion of patients with pain/discomfort and anxiety/depression problems dropped to 59.1% and 50.2%, respectively, notably because extreme problems in these two domains were halved from 12.8% to 6.6% ( $p = 0.06$ ) and from 20.9% to 10.9% ( $p = 0.01$ ), respectively. On the other hand, problems related to mobility, usual activities and self-care increased to 29%, 7.1%, and 31.2%, respectively (Figure 1).

The mean scores of the EORTC questionnaire scales are presented in Table 2. Among the core functional scales, emotional functioning was the most affected scale, with a score of 62.2 (SD 30.7) at baseline. After therapy initiation, the score increased to 69.1 (SD 29.8;  $p = 0.03$ ), however it remained the most affected functioning scale at follow up. Physical functioning, on the other hand, was less affected at baseline, but its score decreased after therapy initiation from 81.7 (SD 20.6) to 77.1 (SD 21.3;  $p = 0.03$ ). Among the core symptom scales/single items, insomnia and pain accounted for greater burden at baseline with scores of 33.5 (SD 38.1) and 29.8 (SD 28.8), respectively. After therapy initiation, the pain score significantly decreased to 21 (SD 27.9;  $p = 0.01$ ), while financial difficulties became the most impactful item with an increase in its score from 22.1 (SD 33.4) to 31.7 (SD 40.8;  $p = 0.01$ ), followed by insomnia (30.6, SD 39.7) and fatigue (25.4, SD 26.8). Among the breast functional scales, lower functioning was observed in the scales of sexual enjoyment (35.3, SD 31.3) and future perspective about patient's own health (41.8, SD 39.9). After therapy initiation, there was a significant improvement in the future perspective scale with a score of 56.3 (SD

**Figure 1.** Proportion of problem levels by EQ5D domains before and after therapy initiation.

Pain/discomfort: extreme problems decreased from 12.8% to 6.6% ( $p = 0.06$ ). Anxiety/depression: extreme problems decreased from 20.9% to 10.9% ( $p = 0.01$ ).

**Table 2.** EORTC core/breast cancer mean scores before and after therapy initiation.

	Before	After	Mean difference	p value
Mean (SD)	Mean (SD)			
<b>EORTC QLQ-C30 (core)</b>				
<b>Functional scales</b>				
Emotional functioning	62.2 (30.7)	69.1 (29.8)	6.9	0.03
Cognitive functioning	78.3 (26.1)	78.7 (27.3)	0.4	0.89
Physical functioning	81.7 (20.6)	77.1 (21.3)	-4.6	0.03
Role functioning	83.8 (25.0)	80.2 (28.2)	-3.6	0.19
Social functioning	90.0 (21.4)	88.4 (23.4)	-1.6	0.51
<b>Symptom scales/items</b>				
Insomnia	33.5 (38.1)	30.6 (39.7)	-2.9	0.47
Pain	29.8 (28.8)	21.0 (27.9)	-8.8	< 0.01
Fatigue	22.4 (26.2)	25.4 (26.8)	3.0	0.26
Financial difficulties	22.1 (33.4)	31.7 (40.8)	9.6	0.01
Constipation	20.2 (35.5)	21.7 (36.1)	1.5	0.70
Dyspnea	15.8 (27.7)	14.8 (27.4)	-1.0	0.71
Appetite loss	13.8 (27.2)	13.8 (30.7)	0	0.98
Nausea and vomiting	7.7 (16.6)	7.7 (17.7)	0	0.96
Diarrhea	4.1 (12.4)	7.8 (21.7)	3.7	0.04
<b>EORTC QLQ-BR23 (breast)</b>				
<b>Functional scales</b>				
Sexual enjoyment	35.3 (31.3)	31.2 (35.7)	-4.1	0.53
Future perspective	41.8 (39.9)	56.3 (39.5)	14.5	<0.01
Sexual functioning	80.3 (27.8)	85.4 (23.4)	5.1	0.05
Body image	87.1 (17.5)	85.7 (23.6)	-1.4	0.51
<b>Symptom scales/items</b>				
Upset by hair loss	31.9 (40.2)	17.8 (31.2)	-14.1	0.09
Breast symptoms	29.8 (28.2)	14.3 (19.2)	-15.5	<0.01
Arm symptoms	21.6 (25.4)	15.8 (20.3)	-5.8	0.02
Systemic therapy side effects	17.7 (16.2)	26.9 (21.8)	9.2	<0.01

SD: standard deviation.

Scales are listed in decrescent order from the most to the least affected at baseline (before therapy initiation).

For functional scales, a maximum score of 100 indicates high/healthy level of functioning, and a minimum score of 0 indicates low functioning. Therefore, a score increase at follow-up reflects functioning improvement.

For symptom scales, a minimum score of 0 indicates no symptom burden, and a maximum score of 100 indicates high level of symptomatology. Therefore, a score decrease at follow-up reflects symptoms improvement.

39.5;  $p = 0.01$ ), while sexual enjoyment remained as the most impaired functioning. Among the breast symptom scales/single items, concern about hair loss (31.9, SD 40.2) and breast symptoms (29.8, SD 28.2) were the most affected scales at baseline. However, the respective scores were reduced to 17.8 (SD 31.2;  $p = 0.09$ ) and 14.3 (SD 19.2;  $p < 0.01$ ) after therapy initiation, while the score of systemic therapy side-effects increased from 17.7 (SD 16.2) to 26.9 (SD 21.8;  $p < 0.01$ ).

The mean scores of HSU based on the Brazilian social tariff and of the overall self-rated health measured by the EQ-VAS and the EORTC-GHS are demonstrated in Table 3. The HSU was 0.712 (SD 18.2; 95% CI: 0.686–0.737) at baseline and 0.732 (SD 17.8; 95% CI: 0.706–0.757) at follow-up. The EQ-VAS and the EORTC-GHS scores were, respectively, 71.4 (SD 21.1; 95% CI:

68.5–74.4) and 69.5 (SD 24.3; 95% CI: 66.1–72.9) at baseline, while 76.1 (SD 19.3; 95% CI: 73.3–78.8) and 73.3 (SD 21.2; 95% CI: 70.2–76.4) at follow-up.

Pretreatment HSU was somewhat higher among patients in disease stages 0-II (0.729; 95% CI: 0.698–0.760) than in patients in stages III-IV (0.689; 95% CI: 0.648–0.730). Among the patients submitted to chemotherapy, the HSU values at follow-up were 0.726 (95% CI: 0.693–0.759) compared to 0.747 (95% CI: 0.707–0.787) among patients not under chemotherapy until the second interview. Specifically, HSU was notably higher among those who received only one therapy regimen (0.781; 95% CI: 0.727–0.836) than those submitted to two or three regimens (0.692; 95% CI: 0.652–0.731). This trend in results was similar for stages 0-II (0.770; 95% CI: 0.688–0.853 and 0.677; 95% CI: 0.614–0.740, respectively) as well for stages III-IV (0.796; 95% CI: 0.731–0.861 and 0.700; 95% CI: 0.650–0.751, respectively), as shown in Table 4.

#### 4. Discussion

Breast cancer plays an important role on patients HRQOL impairment, especially concerning pain/discomfort and mental health, as shown by the high proportion of over 60% of patients reporting some or extreme problems in the EQ-5D respective domains at baseline. Despite the notable improvement achieved in those with greater severity after treatment implementation, impairment remained after six months, with about half of the patients still reporting problems. On the other hand, the domains mainly associated with functional limitations, such as disability or activity limitations, were more severely affected after therapy – about one-third of the patients reported problems with mobility and usual activities.

Although a generic instrument may lack the responsiveness needed to measure alterations associated with a specific feature of the disease, in our study, the impact on domains relevant to cancer patients was indeed captured by the EQ-5D with the results reproduced by the comparable EORTC scales. Accordingly, emotional functioning was by far the most affected core functional scale of the EORTC, showing partial improvement, while physical functioning impairment was accentuated after therapy initiation.

Despite the heterogeneity of previous studies on breast cancer conducted at the national level in terms of the setting, sample size, data collection methods and groups of patients analyzed, our results are generally consistent in demonstrating that patients experience a significant decrease in emotional functioning and overwhelming symptoms of fatigue, insomnia, and pain, some of which may also be attenuated overtime by the therapeutic process [11–14,18,19]. Interestingly, clinical presentation of only one of these symptoms is indeed unusual, as patients often present with clusters of symptoms, which are interrelated and may share a common etiology [20]. Considering that baseline emotional functioning has been described as one of the variables with prognostic value for survival in breast cancer, the identification of patients expressing a cluster of symptoms/impaired functioning may allow targeted monitoring and management, as well as adjustment of the therapeutic process to obtain a better clinical response [21,22]. Similar implications may arise from financial difficulties, a topic that has also emerged as an important

**Table 3.** HSU, EQ-VAS, and EORTC-GHS mean scores before and after therapy initiation.

Before		After	
Mean (SD)	95% CI	Mean (SD)	95% CI
71.2 (18.2)	68.6–73.7	73.2 (17.8)	70.7–75.7
71.4 (21.1)	68.5–74.4	76.1 (19.3)	73.3–78.8
69.5 (24.3)	66.1–72.9	73.3 (21.2)	70.3–76.3

HSU: health state utility; EQ-VAS: visual analog scale of the EQ5D questionnaire;

EORTC-GHS: general health scale of the EORTC questionnaire.

HSU values were multiplied by 100 for comparison.

**Table 4.** HSU mean scores after therapy initiation, stratified by disease stage and number of chemotherapy regimens.

	Number of chemotherapy regimens			
	None	Any	One	Two/Three
	HSU (95% CI)	HSU (95% CI)	HSU (95% CI)	HSU (95% CI)
All stages	0.747 (0.707–0.787)	0.726 (0.693–0.759)	0.781 (0.727–0.836)	0.692 (0.652–0.731)
Stages 0–II	0.748 (0.704–0.793)	0.723 (0.670–0.775)	0.770 (0.688–0.853)	0.677 (0.614–0.740)
Stages III–IV	0.740 (0.638–0.842)	0.729 (0.687–0.770)	0.796 (0.731–0.861)	0.700 (0.650–0.751)

The 10 cases of death and the 3 cases of withdrawal were not included in the follow-up analysis:

- None regimen: 5 cases of death (stages III–IV) and 1 withdrawal;
- One regimen: 4 cases of death (stages III–IV);
- Two/three regimens: 1 cases of death (stages III–IV) and 2 withdrawal.

problem for patients attending our cancer center, even though the Brazilian Unified Health System provides universal coverage for cancer care in the public health sector. In fact, financial stress has been associated with cancer, which may be due to a reduction in income or an increase in out-of-pocket expenditures related to the disease [23]. In a study conducted in Canada, where healthcare is also publicly funded, early breast cancer patients were shown to have lost, on average, 27% of their projected usual annual wages over the first 12 months after diagnosis [24].

HTA authorities recommend the use of preference-based PROs measures to capture HSU data to support pricing and coverage decisions, based on whether the cost of a new intervention is justified by its added health benefits [1,6]. Market regulatory agencies, on the other hand, emphasize that PROs should target the specific patient population of interest, since trials are primarily designed to evaluate efficacy and safety to support labeling claims [7]. Although it has been increasingly common for trials to collect PRO measures, only a few have set HRQOL as a primary endpoint, and even fewer have used a preference-based PROs measure to derive HSU scores. The EORTC Quality of Life Group has evaluated published trials of locally advanced and metastatic breast cancer and has shown that the number of studies in which HRQOL was the primary outcome has decreased by 11% and that the frequency of use of exclusively disease-specific measures has increased by 44% over the last decades [25]. Therefore, although clinical trials play an important role in producing utility estimates, HSU data obtained from routine clinical practice are most needed and may produce more representative data for guiding decision-making [4].

In our study, the breast cancer patients who were under routine healthcare presented a mean HSU of 0.712, with advanced and metastatic disease, as expected, representing lower values than early-stage disease (0.689 vs. 0.729). These results were similar to previously reported estimates, yet at the lower range boundary. In a systematic review reporting EQ-5D utility scores in patients with breast cancer, values ranged from 0.55 to 0.75 for metastatic disease while from 0.74 to 0.88 for non-metastatic disease [26]. Exposure to chemotherapy has also been associated with decreases in utility followed by rapid and sustained recovery after 12 months [27]. Our data did not capture the decline at 6-month follow-up, however HSU was slightly lower in patients undergoing chemotherapy than patients who have received other cancer treatment. Among those submitted to chemotherapy, patients beyond

first chemotherapy regimen presented an HSU value even lower than patients who had received only one regimen, irrespective of disease stage. This finding may be explained by an overload of distressing symptoms secondary to sequential chemotherapies or may even be considered roughly related to disease progression in those with advanced disease.

The reported HSU, which represent the preferences of the Brazilian population towards the health states of patients in our setting, was in accordance with the respondents' self-rated health scores gathered by the EQ-VAS, especially at baseline. Although not statistically or clinically significant, there was an overall trend of improved HRQOL at follow-up, however the gain in HSU was lower than in VAS score. Interestingly, the descriptive data of the EQ-5D parallely demonstrated an increase in disability/activity limitations, while a decrease in anxiety/depression problems. Although our results are unable to allow such a conclusion, it is interesting to presume that a transition to a state of increased physical problems, despite the reduction of anxiety/depression, may be less hypothetically valued by the healthy community than by the patients themselves. In fact, the domains of mobility/usual activities were associated with higher losses in HSU than anxiety/depression in the Brazilian valuation study [17]. In addition, difference between health state utilities elicited from patients and non-patients has been detected, with higher valuations given by the patients than those from the members of the public in distinct elicitation methods [28]. The difference may be explained by the phenomenon of adaptation whereby patients often adjust to an unfavorable condition, while people without the experience of such health status may fail to anticipate this ability to adapt [29]. The trend in lower community valuation of health states at follow-up may suggest that the difficulty to anticipate adaptation to physical disabilities may be even exacerbated.

Our study has some limitations. Although it was conducted at the major national reference public cancer center, our findings might not be applicable to other settings, since HRQOL is influenced by clinical, psychological and environmental aspects. Accordingly, our main results might not be reproducible for metastatic disease since these patients were poorly represented in our convenience sample. Another limitation is the uncertainty related to the HRQOL changes experienced by the patients over time. Indeed, a major challenge in HRQOL measurement is the interpretation of those differences that should be translated as the smallest change that patients perceive as beneficial or that would result in a change in treatment [30,31]. Since this minimal important difference may vary by population characteristics and

across PRO measures, our conclusions were mainly based on previous reported data from cancer population [32,33].

## 5. Expert opinion

Breast cancer patients experience an important impact in health related quality of life. Patient reported outcome (PRO) measures can provide information about the health status of the patients, by capturing the domains of quality of life affected by the disease, and about the community preferences regarding different health states, by converting patients' self-rated health status to an utility estimate. Utility values of health states related to the natural history of cancer represent important information for cost-effectiveness models. Therefore, PRO measures can generate potential information targeted to improvements in the individual quality of care as well as to optimize decisions about the allocation of health resources.

In this study, the authors prospectively evaluated the quality of life and derived utility values from breast cancer patients at a Brazilian reference public cancer center. Breast cancer patients were especially affected with regard to emotional functioning, burden of symptoms (insomnia, pain, fatigue), sexual enjoyment and future self-health perspective at baseline, while to financial difficulties and therapy side-effects after therapy initiation. Baseline emotional functioning has already been shown as one of the variables with prognostic value for survival, emphasizing the importance of increased knowledge about patient reported outcomes in this population. Therefore, the identification of patients expressing a cluster of symptoms and/or impaired functioning may allow targeted monitoring and early management to obtain a better clinical response, representing a more patient-centered approach in cancer care.

## 6. Conclusion

In a context of HRQOL mainly affected by impairments in mental functioning, sexual enjoyment, symptoms of pain, fatigue and insomnia, and poor future self-health perspective, breast cancer produced a mean HSU of 0.712. After routine care, there was a small improvement in HRQOL, however lower utility estimates were particularly observed in patients with advanced disease and undergoing multiple chemotherapy regimens. Our results provide information for a more comprehensive understanding of the impact of the disease and its treatment, enabling the pursuit of improved clinical management and better health outcomes. In addition, they may be used in future health technology assessments for breast cancer, thus contributing to a more efficient decision-making scenario.

The mean HSU was 0.712 among all patients, 0.689 in those with advanced disease and 0.692 in patients undergoing multiple chemotherapy regimens.

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## Authors contribution statement

RLG, FMC, MMF, RRAF, MCC, RMA, SC, MS and LMA were involved in the conception and design of the study; NBR and RLG were involved in the analysis and interpretation of the data; RLG and NBR drafted the paper; FMC, MMF, RRAF, MCC, RMA, SC, MS, LMA revised it critically for intellectual content; all authors approved the paper final version, and agreed to be accountable for all aspects of the work.

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## Declaration of interest

The authors have no relevant affiliations or financial involvement with any organization or entity with a financial interest in or financial conflict with the subject matter or materials discussed in the manuscript. This includes employment, consultancies, honoraria, stock ownership or options, expert testimony, grants or patents received or pending, or royalties.

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