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COST-EFFECTIVENESS OF BREAST CANCER INTERVENTIONS IN PANAMA

COSTO-EFECTIVIDAD DE LAS INTERVENCIONES CONTRA EL CÁNCER DE MAMA EN PANAMÁ

CUSTO-EFETIVIDADE DAS INTERVENÇÕES DO CÂNCER DE MAMA NO PANAMÁ

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Abstract

Objectives: This study explored the cost-effectiveness of interventions performed to detect breast cancer in women aged under 40 years in Panama and applied utility metrics, such as the EQoL5D3L and Health Utility Index. These measures provided utility scores that were used as weights to compute the quality-adjusted life years.
Methods: The economic cost was determined by measuring the index of health services, QALYs and incremental cost-effectiveness index. The evaluation of the quality of life of the 125 women aged under 40 years participating in this research was carried out using the Euro Quality of Life and Health Utility Index Mark 2 and Mark 3 metrics. The following interventions were compared: (a) mammography, (b) clinical breast examination, (c) ultrasound, (d) breast self-examination and (e) biopsy.
Results: Approximately 50.4% of the study group used breast self-examination as a diagnostic method. The conclusions of this single study provide information to guide public health policy regarding essential education about the risk factors of breast cancer. Most women (73%) presented with the disease at Stages 3-4. Many participants (32%) had triple-negative tumours, and 24.05% of the participants were ER+PR+HER 2-. This study revealed aspects, such as pain, that affect the quality of life and result in a decreased ability to perform everyday tasks. In total, 74% of the participants reported physical pain, 58% of the participants had cognitive impairment and 62% of the participants had emotional impacts.
Keywords: breast self-examination, mammogram, HUI, EQoL-5D-3L, quality of life, QALY, ER RP HER 2

Resumen

El artículo presenta algunos resultados de Costo-Efectividad de las intervenciones realizadas a las mujeres jóvenes con cáncer de mama en Panamá para el diagnóstico de su patología.
Objetivos: Presentar los resultados del estudio costo-efectividad de las intervenciones realizadas para detectar el cáncer de mama en mujeres menores de 40 años en Panamá.

Presentar los resultados de la aplicación de los instrumentos que miden el índice de utilidad, como el europeo índice de calidad de vida 5D 3L (Euro QoL5D3L) y el instrumento de índice de utilidad de salud (HUI). Estas medidas proporcionaron puntuaciones de utilidad que se utilizaron como ponderaciones para calcular los años de vida ajustados por calidad.
Métodos: El costo económico se determinó midiendo el índice de servicios de salud, AVAC y el índice de costo-efectividad incremental. La evaluación de la calidad de vida de las 125 mujeres menores de 40 años que participaron en esta investigación se llevó a cabo utilizando las métricas Euro Quality of Life and Health Utility Index Mark 2 y Mark 3. Se compararon las siguientes intervenciones: (a) mamografía, (b) examen clínico de mama, (c) ecografía, (d) autoexamen de mama y (e) biopsia.
Resultados: Aproximadamente el 50,4% del grupo de estudio utilizó el autoexamen de mama como método de diagnóstico. Las conclusiones de este único estudio proporcionan información para orientar la política de salud pública con respecto a la educación esencial sobre los factores de riesgo del cáncer de mama. La mayoría de las mujeres (73%) presentaron la enfermedad en las etapas 3-4 (apa avanzada de la enfermedd). Muchos participantes (32%) tenían tumores triple negativos, y el 24,05% de los participantes eran ER + PR + HER 2-. Este estudio reveló aspectos, como el dolor, que afectan la calidad de vida y resultan en una disminución de la capacidad para realizar las tareas cotidianas. En total, el 74% de los participantes informó dolor físico, el 58% de los participantes tenía deterioro cognitivo y el 62% de los participantes tuvo impactos emocionales.
Palabras clave: autoexamen de mama, mamografía, HUI, EQoL-5D-3L, calidad de vida, AVAC, receptores hormonales.

Resumo:
Objetivos: Este estudo explorou o custo-efetividade das intervenções realizadas para detectar o câncer de mama em mulheres com menos de 40 anos no Panamá e métricas de utilidade aplicada, como o EQoL5D3L e o Health Utility Index. Essas medidas forneceram escores de utilidades que foram utilizados como pesos para calcular os anos de vida ajustados pela qualidade.
Métodos: O custo econômico foi determinado pela medição do índice de serviços de saúde, QALYs e índice incremental de custo-efetividade. A avaliação da qualidade de vida das **125** mulheres com menos de 40 anos participantes desta pesquisa foi realizada utilizando-se as métricas Euro Quality of Life and Health Utility Index Mark 2 e Mark 3. Foram comparadas as seguintes intervenções: (a) mamografia, (b) exame clínico da mama, (c) ultrassom, (d) autoexame mamário e (e) biópsia.
Resultados: Aproximadamente 50,4% do grupo de estudo utilizou o autoexame das mamas como método diagnóstico. As conclusões deste único estudo fornecem informações para orientar a política de saúde pública sobre a educação essencial sobre os fatores de risco do câncer de mama. A maioria das mulheres (73%) apresentado com a doença nos Estágios 3-4. Muitos participantes (32%) apresentaram tumores triplos negativos, e 24,05% dos participantes apresentaram ER+PR+HER 2-. Este estudo revelou aspectos, como a dor, que afetam a qualidade de vida e resultam em uma diminuição da capacidade de realizar tarefas cotidianas. No total, 74% dos participantes relataram dor física, 58% dos participantes apresentaram comprometimento cognitivo e 62% dos participantes tiveram impactos emocionais.
Palavras-chave: autoexame da mama, mamografia, HUI, EQoL-5D-3L, qualidade de vida, QALY, ER RP HER 2

Introduction

Globally, cancer has been linked to 8.2 million deaths, and 50% of these cases (4.3 million) were premature deaths (aged younger than 70 years) (Alwan, 2011). According to the global report on non-communicable diseases, more than two-thirds of all cancer deaths occur in low- and middle-income countries, and between 10 and 11 million new cancer patients will be diagnosed in 2030 in low- and lower-middle-income countries (Alwan, 2011). In Panama, cancer is a significant public health problem and represents the second most common cause of death, accounting for 16.3% of all deaths (Kwong e al, 2008). According to calculations from the Registro Nacional de Cancer (RNCP), 5,929 new cases of cancer occurred in 2017 (Registro Nacional del Cáncer de Panamá, 2017). The projections for 2020 suggest that 7,195 new cancer cases will occur in Panama, representing an increase of 23% in new cases, with the respective incremental economic cost (INEC, 2017).

The statistical data from the RNCP show a sustained increase in the diagnosis and mortality of breast cancer (BC) since 2000. A significant percentage of cases are in an advanced stage of the disease at the time of diagnosis. BC is the leading cause of death among women in Panama (Registro Nacional del Cáncer de Panamá, 2017). In general, initiatives, such as mass mammography campaigns among the female population, have not been shown to be effective in reducing the mortality associated with breast cancer in Panama.

BC is a sporadic disease in the young population; therefore, the risk of developing of BC is low (Kwong A. C., 2008). In developed countries, BC in young women (aged under 40 years) accounts for 2%–4% of breast cancer cases (Yankaskas, 2006) (Kwong A. P., 2008). In Panama, 8-10% of deaths from BC occur in women under 40 years of age

(Registro Nacional del Cáncer de Panamá, 2017). The data from the 2013 National Oncology Institute (NOI) cancer register show that 70 of 558 new cases occurred in women aged under 40 years, representing 11.9% of the total number of cases (Pinzón, July 2014). This issue is important since 60-80% of patients with BC receive treatment at the NOI. In 2013, sixty-four of 70 (91.4%) women aged under 40 years were diagnosed with invasive carcinoma, accounting for 10.9% of all BC cases (Pinzón, July 2014). Research involving this age group is scarce, especially research assessing the economic cost, cost of years of life lost (YLL), and social and economic effects of years lived with disability (Murray, 1999). Different protocols are used at the global level (Aronson, 2009) to calculate or estimate the impact of an event or disease situation on the health of a population, such as the number of deaths, the mortality rate (raw or standardized), and the years of life lost due to sickness (Aronson, 2009). The mortality rate does not distinguish between death at an early age and death at old age. When measurements, such as years of life lost, are considered, premature deaths have a greater weight (Gardner, 1990) (Organization, The global burden of disease: 2004 update, 2008). Researchers have conducted many studies investigating the barriers to performing BC early detection in developed countries. However, scientific evidence concerning the lack of breast screening among Latin American and Caribbean (LAC) women, specifically Panamanian women, is scarce.

Many studies have focused on social approaches rather than economic approaches (Freimuth, 1990). The impact of receiving a diagnosis of BC before the age of 40 years has socioeconomic implications for the family and society (Kwong A. C., 2008). In this study, the economic cost was measured by calculating the health utility index (HUI), QALYs, and incremental cost-effectiveness (ICER). The quality of life was assessed by applying the metrics EQOL-5D-3L, HUI2, and HUI3.

One way to measure the economic impacts of BC at a young age is to estimate the cost-effectiveness (CE) of BC detection interventions and compare the CE with the associated QoL outcomes, as measured by the cost per QALY. The costs acquired within the healthcare system (i.e., mammogram, biopsy, surgery, clinician visit, chemotherapy, and palliative care) and outside the healthcare system (family out-of-pocket, including transportation, special food, and over-the-counter drugs) (Barr, 2004) were considered in this study.

The compared interventions included (a) mammography, (b) clinical breast examination (CBE), (c) mammography and ultrasound, (d) breast self-examination (BSE), and (e) biopsy.

The goal of the research was to identify the effectiveness of interventions to detect BC in young women and the CE of these interventions in the Republic of Panama. This study also aimed to contribute to the growing body of knowledge regarding BC using available data and the CE, QALYs, and ICER of BC detection interventions and treatments.

The study refers to findings, such as the cost of years lived with disability and the QoL with disability, based on the collateral effects of treatment. The results describe the factors interfering with the QoL, such as pain, and visual and auditory limitations that diminish the QoL of the participants since they are not able to perform their daily life activities. This article addresses the topic of BC in women aged under 40 years and the societal, economic and QoL impacts of this disease in relation to scientific evidence showing the aggressiveness of the disease at younger ages (Horvath 2012; Kwong 2008; Yetkin et al. 2021).

Methods

The results were obtained by comparing the cost of early detection intervention with the effect of the intervention, resulting in a cost per effect or cost per year of life gained across interventions. The cost-effectiveness analysis (CEA) considered the ratio of the measured gains in health using the QALYs to the cost of the intervention undertaken to determine the gain in health. A CEA is most appropriate for comparing at least two interventions (Bell, 2006; Cookson, 2021). In this study, the interventions compared were the methods used to detect BC in Panama. The calculations considered the dollars per year of life gained. The dependent variable was the outcome of the interventions, which was measured as the cost per QALY. The CE calculations produced the ICER (Bell, 2006; Cookson, 2021); the ICER indicated the effectiveness of the interventions in increasing early detection of breast cancer among young women in Panama.

A CEA is more appropriate for measuring the denominator of the ratio as a gain in health based on a metric and the numerator as the cost required to produce the benefit in health (Bleichrodt, 1999). The CEA compared the cost of the BC detection interventions with the associated QoL outcomes, as measured by the cost per QALY. Knowledge of the economic value of BC is vital for the development of public health policies, awareness programs, and education directed towards the community.

The CER was calculated using the responses to metrics collected from the study participants and the cost data gathered from the National Plan for Cancer Prevention and Control (Ministerio de Salud, 2019).

The ratio was calculated by dividing the cost of the measured intervention (numerator) by the estimated gain in health (denominator), which was the target dependent variable. Comparing the mean CERs of various intervention types was necessary to identify

the intervention that was most cost effective. This calculation answered the question "To what extent are the interventions used to detect breast cancer in women aged less than 40 years in Panama cost effective?"

Data

The data in this study were obtained based on the costs of treatment, which included hospitalization; several visits to doctors, nurses, physiotherapists, dieticians, and other services; the periodic use of laboratory and follow-up tests; and chemotherapy, surgery, and radiotherapy treatments. The participants provided their cost of out-of-pocket expenses, such as transportation, special foods, and the use of over-the-counter medications. Some data were obtained by reviewing the records of the treated patients participating in the study.

The QoL was the variable of interest. The QoL included behaviours, physical health, and psychological health. The metrics applied were the HUI, which is a questionnaire consisting of 40 items based on the theory of the utility of multiple attributes (Furlong, 2001-2006), and a quality of life questionnaire with five dimensions and three levels, which considers time according to the Time-Trade-Off theory (TTO).

HUI classification system

HUI2 and HUI3 are complementary systems that describe the general state of health and well-being of each participant in addition to measuring the degree of capacity or disability in each attribute. The HUI2 includes seven attributes, each with three to five levels, and describes 24 different health states. The attributes measured by the HUI2 include (a) sensation, (b) mobility, (c) emotion, (d) cognition, (e) personal care, (f) pain, and (g) fertility. The HUI3 classification system comprises eight attributes, each with five to six levels, and differentiates normal capacities from severe degrees of disability. The

HUI3 can represent up to 972,000 different health conditions. The attributes measured by the HUI3 include (a) vision, (b) hearing, (c) speech, (d) ambulation, (e) dexterity, (f) emotion, (g) cognition (including memory and thinking), and (h) pain (Horsman, 2003, p. 3).

The health utility indexes HUI2 and HUI3 have attributes with the same name, but their meanings differ, providing the researcher an opportunity to delve into the underlying constructs (Horsman, 2003). The single attribute morbidity score scale varies from the worst level at a score of -0.36 (worse than being dead) to 0.00 (has died) to 1.00 (perfect health) (Furlong, 2006).

EQoL-5D-3L descriptive system

This system comprises five dimensions, each with three levels. The dimensions allow for the determination of the presence of problems and identification of the present problems, allowing for the determination of whether there are extreme health situations in one or several of the dimensions. Each level was categorized with numbers ranging from 1 to 3 that have no arithmetic value (Rabin, 2011). The dimensions included in the questionnaire are "(a) mobility, (b) self-care, (c) usual activities, (d) pain/discomfort, and (e) anxiety/depression" (Rabin 2011, p. 7). The patient or individual can perform a self-assessment of their health status using a visual analogue scale (EQ-VAS). The EQoL-5D-3L describes 243 different health states, each of which has an assigned utility score function derived from the general population in the United Kingdom using the time-sharing method (TTO)(Rabin, 2011) If a participant responds to a domain that his/her condition is excellent without problems, the participant is categorized as 1; therefore, a person with a perfect health status has a score of 1-1-1-1-1. Health conditions considered worse than death range from 0 to -0.39 (Wee, 2007).

The data analysis performed in this research consisted of summary statistics and CER. The analyses included calculating the cost of the treatment offered to the 125 participants in the study according to protocols established for each stage of the disease, the effectiveness of the treatments, the incremental cost, the incremental effectiveness and the ICER.

A Kruskal-Wallis test was performed to determine the importance of the averages of the cost-effectiveness ratio per intervention. The objective of the test was to determine whether the scores of more than two independent groups significantly differed.

The independent variables in the Kruskal-Wallis test were the different interventions used for the diagnosis of BC in women aged under 40 years. The dependent variable was the CER of each intervention. After determining whether there were significant differences, the statistical tests determined the best intervention by comparing the difference in the means of the CER.

No further statistical analysis was necessary to calculate the CER. A ratio greater than one indicated that the cost of early breast cancer detection was higher than the savings in terms of the QALYs.

The survey questions collected data necessary for generating useful scores, and the health status of the subjects was classified to determine the health-related quality of life (HRQoL). The HRQoL is the value assigned to "the duration of life as modified by impairments, functional states, perceptions and social opportunities influenced by illness, injury, treatment or policy" (Patrick, 1993, p. 22).

The analysis addressing RQ2 was performed by calculating the average ICER, and the QALY calculation determined the CE of each detection intervention. The QALY was based on the number of years of life added by the intervention. The ICER calculation was

based on the relationship between the cost of treatment and the QALYs in each participant in the study.

Results

The economic cost analysis was completed by measuring the HUI, QALY and ICE in 125 Panamanian women younger than 40 years of age who were diagnosed with BC. The data used for the analysis were obtained using the metrics of Euro EQoL-5D-3L and HUI. The economic effect of BC in different stages of the disease was determined by calculating the HUI, time trade-off (TTO) values, QALYs, and ICER. The study included a comparison of the CE of different interventions to promote the detection of BC. The CEA compared the cost of the BC detection interventions with the associated QoL outcomes as measured by the HUI2, HUI3, and EQoL-5D-3L. The interventions compared included (a) breast self-examination, (b) physician physical examination, (c) mammogram, (d) mammography and ultrasound, and € biopsy. The participants in the study were women aged under 40 years with a BC diagnosis.

The question "To what extent are the interventions used to detect BC in women younger than 40 years of age in Panama cost effective?" was answered by calculating the HUI and TTO value before calculating the QALYs. The average ICER was computed to calculate the CE of each detection strategy. The basis of the QALY was the number of years of life added after receiving treatment following diagnosis. The utility measure of QALY combines the time lived with the disease and the QoL in a single index (Wee, 2007).

The HUI system has four components as follows: "A health status classification system, a preference-based scoring function, data collection questionnaires, and coding algorithms for deriving HUI variables from responses to the questionnaires" (Horsman, 2003, p. 3).

Table 1. General demographic characteristics of the 125 young women participating in the research. Republic of Panama, 2014

	Frequency	Percentage
Age		
15-20	1	0.8
21-30	13	10.4
31-35	44	35.2
36-40	67	53.6
Race		
White	22	17.6
Hispanic	56	44.8
Afro	30	24
Indigenous	3	2.4
Other	9	7.2
Chinese	1	0.8
Missing	4	3.2
Education		
None	1	0.8
Primary School	14	11.2
High School	60	48
University	50	40
Occupation		
Professional	40	32
White Collar	8	6.4
Blue Collar	36	28.8
Homemaker	39	31.2
Student	1	0.8
Other	1	0.8
Income (US Dollars $)		
0-250	33	26.4

251-500	36	28.8
500-750	22	17.6
751-1500	19	15.2
1501-3000	3	2.4
3001-5000	9	7.2
5001 and Above	1	0.8
Missing	2	1.6
Insurance		
Social Security	63	50.4
Private Insurance	1	0.8
None	54	43.2
SS & PI	5	4
Missing	2	1.6
Type of Surgery		
Biopsy	10	8.2
Quadrantectomy	19	15.6
Mastectomy	91	74.6
Tumourectomy	2	1.6

Findings: Descriptive Statistics

This study involved 125 women aged between 17 and 40 years, and most participants were patients who visited the National Cancer Institute. The general demographic data are shown in Table 1. The age of 54.4% of the participants ranged from 36-40 years. The age range with the highest incidence of BC recorded in this study was 36-40 years. According to the results described in the literature, BC is most frequent in older women. This finding presents a relationship between age and BC; the older the women, the greater the chance of developing the disease, even in groups younger than 40 years.

Regarding ethnicity and racial groups, the largest group was Hispanic (n = 52, 41.6%), followed by afro-descent (n = 30, 24%) and White (n = 22, 17.6%), while 3% of

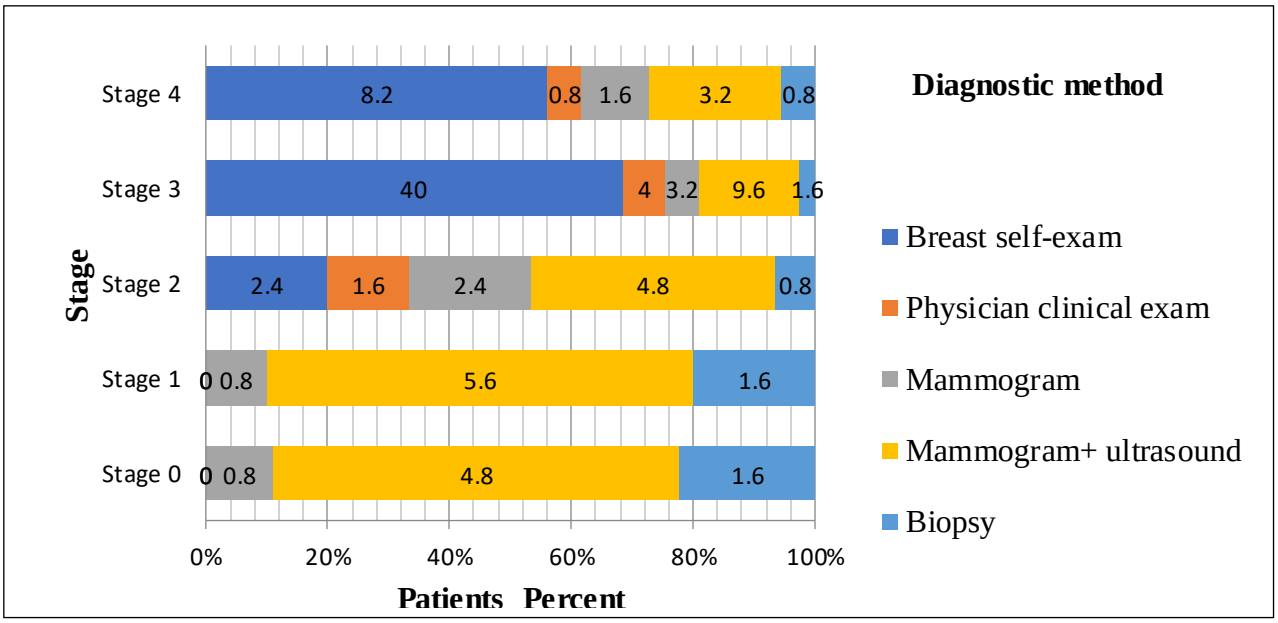
the participants were indigenous or of Chinese descent. Nearly half of the participants had a high school education (48.0%), and 32% of the participants were professionals. There is a relationship between the education level and income, and approximately 34% of the participants earn an average of $1000.00 US monthly, which is 2.5-times the minimum salary, and most participants had social security as insurance (n = 63, 50.4%). Most participants had undergone surgery (n = 115, 92.0%), and the most frequent surgery was mastectomy (n = 91, 74.6%). Chemotherapy was administered to 92% of the participants, and 84% of the participants received the following three modalities of treatment: radiotherapy, chemotherapy, and surgery. In contrast, only 5.6% of the participants received palliative care. In total, 16% of the study sample had received a diagnosis within one year of the study, while 11.2% of the participants had received a diagnosis five years prior to the study. In total, 29% of the participants had received a diagnosis of BC two years prior to the study.

A relationship was observed between the diagnostic method and BC stage at the time of diagnosis. In total, 50.4% of the patients in this study were diagnosed by a breast self-examination; of these patients, 2.4% were in Stage 2, 40% were in Stage 3, and 8.2% were in Stage 4. According to the literature, cancer diagnosed by BSE is always in an advanced stage of the disease.

In the study, 58.4% of the participants were in Stage 3, and 14.6% of the participants were in Stage 4. Only 6.4% of patients reported having obtained a diagnosis after a clinical examination by a physician, which draws attention to the statistic that only 15.4% of the study participants were in Stages 0 or 1 of the disease at the time of diagnosis, and these patients were diagnosed by mammogram, mammogram and ultrasound, and

biopsy. Only 1.6% of the diagnoses were made by mammogram, suggesting that mammograms are not an effective diagnostic method in women younger than 40 years **(Figure 1).**

Distribution of young women with breast cancer by disease stage and diagnostic method, Panama, (N = 125).



Methodological considerations

The HUI metrics measure the attributes of HUI2 and HUI3, which, despite having the same names, weigh different emotional and cognitive spheres, allowing for a broader analysis of the impact of BC on the quality of life of the young women who participated in the study. The emotion construct measured by HUI2 refers to anguish and anxiety, while the emotion construct in HUI3 focuses on the state of happiness versus the state of depression. The cognitive construct in HUI2 measures the learning capacity, while the cognitive construct in HUI3 focuses on the ability of the participants to solve problems in

daily life. Regarding pain, HUI3 considers the intensity of pain, while in HUI2, the frequency of pain and the type of control are included (Horsman et al, p. 7). The results indicated that 76.0% of the study group presented some level of pain from Level 2 to Level 4; 60% of the participants showed some degree of cognitive impairment; 63.2% of the participants experienced emotional effects; and 36.8% of the participants reported an alteration in dexterity. Pain and emotion were the health states with the highest attribute level (> 1), which may be indicative of an adverse effect on the QoL. The impact in these domains is related to HUI and the quality of life (Table 2).

Table 2.

Breast cancer patients by HUI3 attribute levels

	Level											
Attribute	1		2		3		4		5		6	
	F	%	*f*	%	*f*	%	*f*	%	*f*	%	*F*	%
Vision	88	70.4	21	16.8	2	1.6	11	8.8	0	0.0	3	2.4
Hearing	117	93.6	0	0.0	0	0.0	7	5.6	0	0.0	1	0.8
Speech	110	88.0	6	4.8	2	1.6	7	5.6	0	0.0	n/a	n/a
Ambulation	94	75.2	24	19.2	2	1.6	0	0.0	4	3.2	1	0.8
Dexterity	83	66.4	5	4.0	0	0.0	28	22.4	8	6.4	1	0.8
Emotion	46	36.8	41	32.8	20	16.0	16	12.8	2	1.6	n/a	n/a
Cognition	50	40.0	12	9.6	19	15.2	29	23.2	14	11.2	1	0.8
Pain[1]	30	24.0	20	16.0	50	40.0	25	20.0	0.0	0.0	n/a	n/a

[1] $p < 0.05$

Utilities representing the HRQoL were used to calculate the QALYs in combination with the amount of time that had elapsed for each participant after receiving the diagnosis of breast cancer.

A patient presenting a HUI of 1 in all attributes measured (vision, hearing, speaking ability, verbal communication, walking, daily manual skills, emotional and cognitive aspects, and the frequency and intensity of pain) had an HRQoL equal to 1.0. If the same patient had been living with the disease for three years, the QALY value is calculated by multiplying the HUI score by the time with the disease. In this case, the QALY value is three.

The cost calculations used prices from the year 2014 based on the estimated expenses from the public system, which differ from expenses in the private sector. If the cost of one year living with a disability significantly increases the prices in the public health system, the cost for one year living with a disability would be even more expensive in private facilities.

In addition to the average ICER, computing the QALYs was necessary to determine the cost-effectiveness of each detection intervention. The QALY was the product of years of life after the participants received their diagnoses and the HUI presented by each patient at the time of answering the questionnaire.

The breast self-examination detection intervention yielded more additional years of life at an average of 3.29 as measured by HUI2, HUI3, and EQoL-5D-3L. Mammography produced an average of 2.66 QALYs. Mammography and ultrasound yielded a QALY average of 2.50. The lowest QALY was achieved with biopsy at an average QALY of 1.12 (Table 3).

Table 3.

QALYs by detection intervention based on HUI2, HUI3, and EQoL-5D-3L in young women with breast cancer, Panama.

	HUI2_index			HUI3_index			EQoL-5D-3L			QALYs
Diagnostic Method	*F*	*M*	*SD*	*F*	*M*	*SD*	*f*	*M*	*SD*	*M*
Breast Self-examination	63	3.29	1.83	63	2.69	2.35	63	3.71	1.74	3.23
Physician Clinical Examination	8	2.57	1.07	8	1.52	1.58	8	3.26	1.10	2.45
Mammogram	11	3.12	2.01	11	2.09	2.26	11	2.79	2.00	2.66
Mammogram & Ultrasound	35	2.56	2.23	35	2.05	2.61	35	2.91	2.30	2.50
Biopsy	8	2.25	1.41	8	1.01	1.91	8	2.35	1.20	1.12

Table 4.

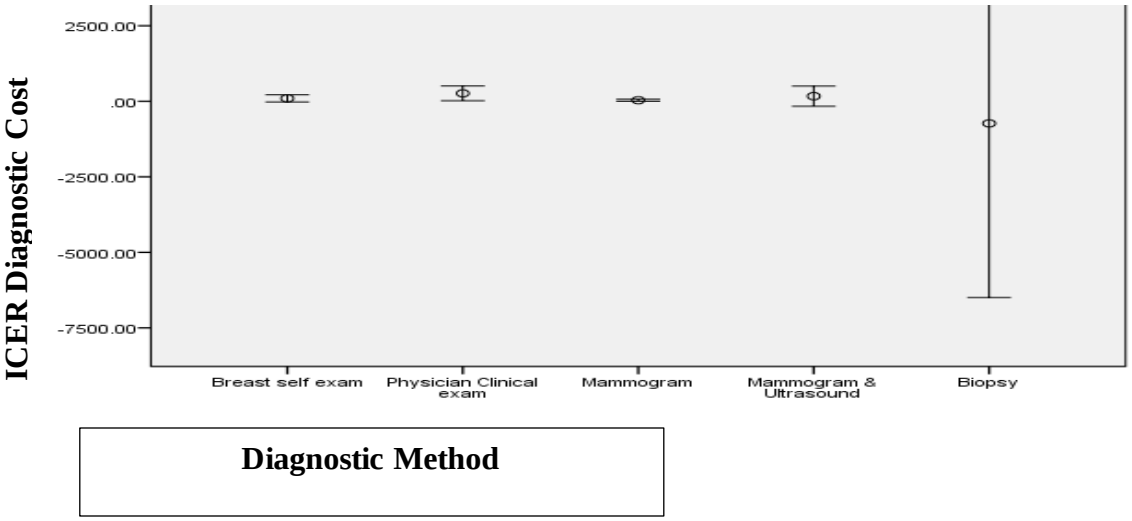
Average ICER of detection interventions in young women with breast cancer, Panama.

	ICER_Dx		
Diagnostic Method	*f*	*M*	*SD*
Breast Self-examination	63	96.62	468.34
Physician Clinical examination	8	263.09	291.01
Mammogram	11	35.18	52.83
Mammogram & Ultrasound	35	170.14	968.42
Biopsy	8	-730.98	6893.56

Table 4 reports the test results of the average ICER of the detection interventions in women aged under 40 years with breast cancer. The highest mean ranked ICER across all detection strategies was the physician clinical examination at 263.09, followed by the combination of mammography and ultrasound at 170.14, breast self-examination at 96.62, mammography at 35.18, and biopsy at -730.98. According to the Kruskal-Wallis test (at the 0.05 level of significance, $X^2 = 23.21$, $df = 4.0$, Asymp. $p = 0.0001$), there was sufficient evidence to conclude that significant differences existed among the five detection interventions based on the ICER values. The highest variability in ICER was observed in the biopsy intervention at a negative value of -730.98. In contrast, the lowest ICER variability was observed in the mammogram intervention at a value of 35.18. Regarding the cost-effectiveness, the biopsy appeared to be more useful for early detection but had the highest cost. The biopsy intervention had the highest average ICER, and the mammogram had the lowest average ICER. The average incremental cost of performing one detection intervention compared to another significantly differed. Regarding the economic cost, the biopsy strategy, which had a negative value of -730.98, was the most effective. However, regarding the quality of life, the patients with the biopsy diagnostic method exhibited the worst quality of life and had negative HUI and TTO values considered worse than death.

Figure 3.

Average ICER of detection interventions in young women with breast cancer, Panama, N(125)



The treatment of breast cancer is expensive and includes hospitalizations, periodic visits to specialists and other professional services, and periodic laboratory tests for the clinical monitoring of treatments, such as chemotherapy and radiotherapy. Additionally, the out-of-pocket expenses associated with over-the-counter medicines, transportation, food and special care must be considered. The costs of treating BC place a heavy financial burden on the health systems and families of the affected women. Of course, the costs are not only monetary. The treatment often results in a considerable impact on the quality of life. The incremental cost-effectiveness was calculated by dividing the expenses related to

the treatment by the QALYs. Before calculating the ICER, in the current study, the QALY was calculated by assigning numerical scores to health states using the HUI2, HUI3, and EQoL-5D-3L rating scales.

Breast cancer: younger versus older women

Limiting epidemiological studies to women aged under 40 years results in an accurate representation of BC only in young women since the incidence in young women differs from that in older women (Yankaskas, 2006). In total, 53.6% of the participants in the current study were aged between 36-40 years. Using population-based data, researchers have determined that breast cancer in young women accounts for 1% to 11.5% of all cancers. The Danish BC Cooperative Group (2008) independently conducted a study compared the risk of dying from breast cancer in 10 years between women younger than 35 years and women aged 45-49 years. The investigation concluded that the 10-year hazard ratio of all women younger than 45 years to that of older women was 2.2. Comparing 35– to 39-year-old women to women aged 45–49 years, the ratio was 1.4. The data from the NOI register indicate that 125 of new cases were women younger than 40 years (Pinzón, July 2014). According to research involving young women with BC, this population presents at a more advanced disease at the time of diagnosis and more aggressive tumour characteristics (Kwong A. P., 2008).

The increased numbers of new cases and increase in mortality rates in lower and middle-income countries are expected to result in a disproportionate increase in healthcare expenses between developed and developing countries in Latin America and the Caribbean by 2025. The paradox is that developed countries spend nearly 10% of their gross domestic product on healthcare, whereas poorer countries spend only 5% of their GDP, and resources attributed to screening programmes are insufficient.

Breast cancer characteristics in Panama and the social and economic context

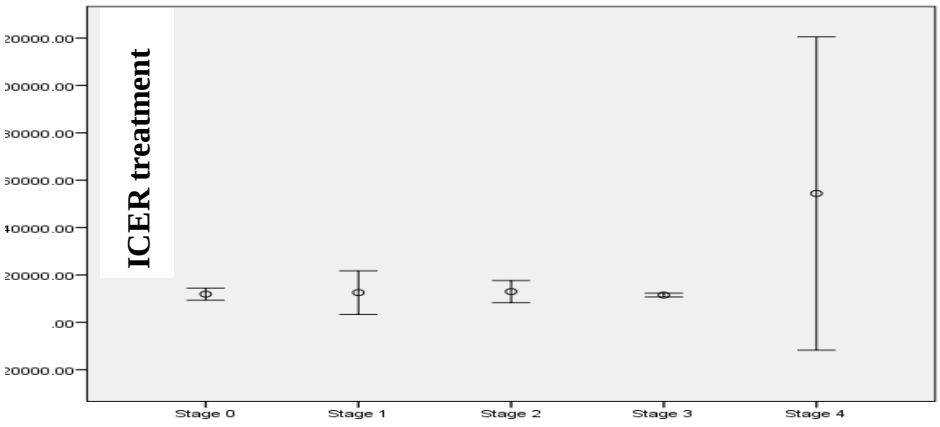
In Panama, BC is the primary cause of mortality in women, surpassing cervical cancer. According to the data from the NOI cancer registry in 2013, 585 new BC cases were diagnosed, and 543 of these newly diagnosed cases were invasive carcinomas (92.8%) (Pinzón, July 2014). The increase in BC mortality in Panama has been progressive and sustained.

Comparing the five disease stages (0-4), the treatment cost was the highest in Stage 4.

Stage 0 showed the lowest mean cost. An ANOVA was performed to determine whether significant differences existed among the average treatment costs. At the 0.05 level of significance (X^2 =, df = 4.0, p = 0.038), the Stage 4 treatment cost significantly differed among the five stages at the time of diagnosis. The highest significant difference among the treatment costs was observed in Stage 4 of the disease, and the lower the disease stage at the time of diagnostic, the lower the cost of treating the disease (Figure 4). Additionally, 24.05% of the participants were ER+PR+HER 2-negative, and 32% of the study participants had triple negative tumours (TNT), which are more aggressive tumours that can be large in the advanced stages, with metastases at the time of diagnosis (Aliasghar 2017; Yetkin et al 2021). TNT has a poorer prognosis than other breast cancer tumours with an augmented risk of distant relapse and death, particularly during the first five years after appearance (Horvath, 2012; Yetkin,et al 2021).

Figure 4.

Treatment cost according to the disease stage at the time of diagnosis in young women with breast cancer, Panama.



Discussion

Our findings provide quantitative evidence of the health-related and economic impacts of breast cancer in women before the age of 40 years. Economically and socially, BC represents an emotional and social loss and a loss for the Panamanian economy. The impact is higher if the disease occurs in young women. This impact highlights the importance of health authorities and policymakers investing in the development of useful actions that allow for early BC detection in women in this age group and the identification of the risk factors in this age group.

Developing guidelines for women aged under 40 years is very important since screening programmes are not available for these women. The development of a comprehensive training programme for primary care physicians, nurses, social workers, and other healthcare professionals and the development of a network to help increase women's

access to early diagnostics within the healthcare system would be helpful (Orlewska, 2018). The study findings show that the participants presented many side effects, such as pain, cognitive impairments, and emotional distress, that affected their quality of life, with poorer breast cancer survival outcomes.

Among younger women, the risk factors for BC in women that are in an older age range increase the risk of developing BC (Rosenberg, 2005). In the risk literature reviewed for the study, the emphasis was on studies involving women younger than 40 years highlighting the differences between young women and older women. Some consistent findings emerged across the literature regardless of the study population, method used, or definition of young age, i.e., the breast cancer incidence rises with age in younger women and older women (Althuis, 2003; Brennan, 2000; Tai, 2005; Brenner, 2016). Using population-based data, researchers have determined that breast cancers in young women account for 1% to 11.5% of all cancers. The variation in the incidence rates in young women depended on the ages and data sources applied (Basro, 2010; Kwong, 2008). In this study, 50.4% of the participants were in Stage 3, and 12% of the participants were in Stage 4; thus, 61.6% of the participants were in advanced stages of the disease.

The increase in new cases and mortality rates in lower and middle-income countries is expected to result in a disproportionate increase in healthcare expenses between developed and developing countries in Latin America and the Caribbean by 2025. The paradox is that developed countries spend nearly 10% of their gross domestic product on healthcare, whereas poorer countries spend only 5% of their GDP, and resources for screening programmes are insufficient.

Our study revealed a significant difference among the five detection strategies based on the ICER values, and the intervention with the lowest incremental cost was

mammogram. A significant difference was observed among the five detection strategies based on the QALY values measured by the HUI2, HUI3, and EQoL-5D-3L, and the procedure with the highest number of years of life gained was mammography. The use of mammography and the combination of mammography and ultrasound added an average of 3.29 years of life.

The highest significant difference among the treatment costs was observed in Stage 4 of the disease.

The biopsy strategy was the most cost-effective intervention for breast cancer detection from an economic point of view; however, the effectiveness of biopsy could not be measured in terms of the QoL. The study calculations suggested that one quality-adjusted life year had a cost of $19,660.16 (in U.S. 2014 dollars) for the Panamanian women who participated in the study. Sufficient evidence emerged to suggest that a positive correlation exists between treatment cost and QALYs ($p < 0.01$), which can be expressed by the following equation:

Y = Tx Cost Model = Treatment cost - $ = $B_{0+}B_1$HUI2QALY + B_2HUI3 QALY + B_3EQoL-5D-3L QALY

Tx Cost-$ = $B_0 + B_1$HUI3 QALY

Y = Tx Cost Model = 43932.19-28380.59X + 4647.56X2, where X is the QALY

Implications for health policy

Breast cancer is a public health problem in Panama. BC is the primary cause of death in Panamanian women and has far-reaching consequences at all levels of society. From a social perspective, the present study reflects that the impact of BC at an early age has implications for families, especially for young women at the reproductive age. A diagnosis of BC at a young age carries a severe cost of human capital for society. The age

range of 17-40 years included in this study represents an age group with significant potential working and reproductive years. The findings of this research highlight the need to implement or strengthen early detection strategies for this group because of the disadvantage of being at an advanced stage at the time of diagnosis. The currently applied interventions, such as screening mammography for early detection in older women, do not work effectively in women younger than 40 years due to the density of the breast tissue. According to the RNCP, breast cancer in women aged under 40 years has increased slowly but continuously over the last decade. The calculation of the QALYs in this study provided an approximation of the HRQoL.

The application of the HUI allowed for a quantitative measurement of the state of health that considered many aspects, such as the ability to perform manual tasks and mobility, while also assessing the emotional state and the presence or absence of pain using a unique numerical value. A score of one on this scale indicates a perfect state of health, 0 indicates death, and negative values indicate a condition that patients value as worse than being dead (Crott & Briggs, 2010). The importance of calculating the severity of a patient's condition increases the utility of this metric since this value provides a closer idea of the particular health condition of a specific individual (Nord & Johansen, 2015). The severity value is inversely related to the HUI values (0 indicates a perfect state of health, and a value close to one or higher indicates a severe state of health) (see Table 6).

Table 5. Health state of the participants by UTILITY and severity

RANGE							
Lower		Upper	Midpoint	Width	*F*	%	Severity
0.89	<	1.00	0.9455	0.1190	32	25.6	0.11
0.77	<	0.89	0.8265	0.1190	19	15.2	0.23
0.65	<	0.77	0.7075	0.1190	27	21.6	0.35
0.53	<	0.65	0.5885	0.1190	7	5.6	0.47
0.41	<	0.53	0.4695	0.1190	9	7.2	0.59
0.29	<	0.41	0.3505	0.1190	21	16.8	0.71
0.17	<	0.29	0.2315	0.1190	6	4.8	0.89
0.05	<	0.17	0.1125	0.1190	3	2.4	0.95
-0.07	<	0.05	-0.0065	0.1190	1	0.8	1.07

Limitations

A limitation of the study was that many intangible costs, such as the reduction in the quality of life due to pain and difficulties performing daily activities, were not considered.

In this study, only Panamanian women aged under 40 years with a diagnosis of BC were included.

Extrapolating the results of this study to other countries is challenging since the social, cultural, and economic characteristics are different. However, this study is important since it quantitatively presents the issues related to the quality of life of women receiving treatment for breast cancer.

Conclusions

Regarding cost-effectiveness, biopsies appear to be the most useful for early detection in women younger than 40 years but have the highest cost. The biopsy intervention had the highest average ICER, and mammograms had the lowest average

ICER. Regarding economic cost, the biopsy strategy, at a negative value of -730.98, was the most effective. Nevertheless, by measuring the quality of life and the physical, economic and social impacts, the patients with the biopsy diagnostic intervention exhibited the worst quality of life, negative HUI values, and TTO values worse than death.

The results of this study involving young women diagnosed with breast cancer showed some anticipated effects, such as a decrease in the quality of life associated with mobility difficulties, changes in emotional and cognitive aspects, limitations in self-care, and the presence of mild to moderate or intense pain.

Given these findings, we reconsidered the economic implications of the disease in this age group since these women are in the productive phase of their lives.

This study highlights the breast self-examination controversy because 54.4% of the participants obtained a breast cancer diagnosis through BSE. Self-examination for the detection of breast cancer in young women cannot be underestimated. In this study, only 6.4% of the diagnoses were performed by BCE, and biopsies diagnosed 3.2% of the participants. In total, 28% of the participants were diagnosed by mammography plus ultrasound. Only 3.2% of the participants were in Stages 0 and 1. Emphasizing the importance of breast clinical examinations in women aged under 40 years is necessary.

The data from the RNCP exhibited a trend suggestive of a sustained increase in the incidence rate of breast cancer among women aged under 40 years in Panama.

This study demonstrates the need to develop protocols in primary care at the level of healthcare facilities informing professionals of the appropriate actions when young women present with a suspicious lesion.

Healthcare personnel in oncology centres must consider the aspects of treatment that affect the quality of life in addition to outcome, and patients must be regularly evaluated to address side effects in a timely manner.

Pain, cognitive decline, emotional strain and other symptoms can be treated as a part of the continuum of care. Developing a team of healthcare professionals for the treatment of symptoms related to treatment could be beneficial.

This study is the first study in Panama to consider the QALYS, ICER, economic implications and QoL of women aged under 40 years with breast cancer. This study showed that there is a continuous increase in BC in young women in Panama. One aspect highlighted here that was also found in the literature is that young women tend to have a more advanced disease and more aggressive tumour characteristics, suggesting the probability of a worse prognosis at the time of diagnosis (Horvath, 2012; Kwong. 2008; Wilke, 2009).

This study is the first to consider the QALYs, ICER, economic implications, and quality of life of Panamanian women breast cancer patients younger than 40 years of age. This study brings attention to the fact that there is a continuous increase in young women presenting with breast cancer in Panama.

In this study, 50.4% of the cases were in Stage 3 at the time of diagnosis, and 11.2% of the cases were in Stage 4 of the disease; therefore, 61.6% of the participants were in an advanced stage of the disease at the time of diagnosis.

Regarding hormonal receptors, 25% of the participants presented TNT, while 20.05% of the participants were ER + PR + HER 2-negative.

This study confirms the relationship between the young age and the risk of higher mortality. Also, the quality of life is an important fact to take into consideration in the discussion of treatment options.

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