



A Cost-of-illness Study on The Economic Burden of Breast Cancer in Türkiye: A Delphi Panel-based Analysis of Direct and Indirect Costs

Simten MALHAN,¹ Muhammed Bülent AKINCI,² Nalan AKYÜREK,³ Ahmet BİLİCİ,⁴
 Umut DEMİRCİ,⁵ Çağlayan GEREDELİ,⁶ Bülent KARABULUT,⁷ Nuri KARADURMUŞ,⁸
 Berna ÖKSÜZOĞLU,⁹ Mehmet Ali ŞENDUR,¹⁰ Çiğdem ŞAR,¹¹ Özge ERGİN¹¹

¹Department of Healthcare Management, Baskent University, Ankara-Türkiye

²Department of Medical Oncology, Ankara Bilkent City Hospital, Ankara-Türkiye

³Department of Medical Pathology, Gazi University, Ankara-Türkiye

⁴Department of Medical Oncology, Medipol HealthCare Group, İstanbul-Türkiye

⁵Department of Medical Oncology, Memorial HealthCare Group, Ankara-Türkiye

⁶Department of Medical Oncology, Medical Park HealthCare Group, İstanbul-Türkiye

⁷Department of Medical Oncology, Acıbadem Healthcare Group, İzmir-Türkiye

⁸Department of Medical Oncology, University of Health Sciences, Gülhane Training and Research Hospital, Ankara-Türkiye

⁹Department of Medical Oncology, Etlık City Hospital, Ankara-Türkiye

¹⁰Department of Medical Oncology, Bilkent City Hospital, Ankara-Türkiye

¹¹Daiichi Sankyo Pharmaceutical Trading Limited Company, İstanbul-Türkiye

OBJECTIVE

To determine the economic burden of breast cancer in Türkiye.

METHODS

In this cost-of-illness study, per-patient annual direct and indirect medical costs for the management of breast cancer (in newly diagnosed and former patients and in metastatic and non-metastatic disease) were determined based on epidemiological, clinical, and lost productivity inputs provided by a Delphi panel consisting of oncology, general surgery, and pathology experts.

RESULTS

The mean annual cost per patient for newly diagnosed breast cancer was \$21,595.62 for metastatic patients and \$4,490.76 for non-metastatic patients. The total annual direct cost of new and former patients was \$222,514,612.10. Non-medical costs included transportation, caregiving, and the need for palliative care. The non-medical direct cost for new patients and follow-up patients was \$18,917,841.62 and \$2,195,169.61, respectively. The total non-medical direct cost of newly and previously diagnosed patients with breast cancer was \$21,113,011.23. While the indirect costs for the newly diagnosed patients amounted to \$815,199,359.02, the indirect cost for the previously diagnosed breast cancer patients was \$169,767,030.43. The total indirect cost was \$982,867,753.58. The economic burden of breast cancer was \$1,230,416,060.71 in Türkiye.

CONCLUSION

This cost-of-illness study indicates that breast cancer poses a significant economic burden for Türkiye. A large share of indirect costs in total costs can provide important guidance to decision-makers in the health-care system to better allocate limited resources to breast cancer prevention and early detection strategies.

Keywords: Breast cancer; direct cost; economic burden; indirect cost.

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Dr. Simten MALHAN

Başkent Üniversitesi,

Sağlık Yönetimi Bölümü,

Ankara-Türkiye

E-mail: simtenmalhan1@gmail.com



INTRODUCTION

Breast cancer is the most common malignancy in women under 60 years of age worldwide and is one of the major causes of morbidity and mortality. One out of every eight women is likely to develop breast cancer at some point in her life. In 2012, one out of every eight cancer cases diagnosed was breast cancer. In 2015, 15% of cancer-related deaths occurred due to breast cancer.[1] According to data from the Ministry of Health (MoH), the incidence of breast cancer in Türkiye in 2017 was 47.7 per 100,000 women, which makes it the most common cancer in women. Mortality due to breast cancer is projected to decrease with the increase in new drugs and targeted therapies over the last 20 years.[2,3]

The incidence of breast cancer in the world has increased in the last 25 years. Certain factors are considered to play a role in this rising incidence, such as developments in technologies that provide high-quality screening and diagnosis of breast cancer, lifestyle characteristics (i.e., alcohol consumption, obesity, lack of physical activity), prolonged hormone replacement therapies (HRT), prolonged life expectancy, and thus prolonged menopause periods.[4–6] Improvements in diagnostic methods, individualized treatment approaches with molecular subgroup classification, and improved treatment response rates have prolonged the life expectancy of patients. With all these characteristics, breast cancer has become a disease that causes significant costs in the utilization of health resources.

With the introduction of innovative cancer drugs to patients in Türkiye, it is observed that life expectancy is prolonged and quality of life is improved. However, the cost of breast cancer is not within our knowledge. Therefore, this study aimed to determine the economic burden of breast cancer.

MATERIALS AND METHODS

In this cost-of-illness study, per-patient annual direct (medical and non-medical) and indirect medical costs for the management of breast cancer were determined based on the epidemiological, clinical, lost productivity, and cost inputs, and the consensus achieved through the Delphi panel consisting of oncology, general surgery, and pathology specialists. Each of them represents a different tertiary care health facility and also a different geography of Türkiye. Eight panellists completed three rotations on the questions until they agreed. Average per-patient direct medical costs were calculated

based on cost items including outpatient visits, imaging and laboratory tests, hospitalizations/interventions, and treatment from a payer perspective (Social Security Institution [SSI]) in Türkiye, using the cost-of-illness method. The types of all services/materials in the medical process of the disease and the number of services/materials used in one year were obtained from the Delphi panel, and unit costs were obtained from the list of service prices published by the SSI, which is called Healthcare Implementation Communique (HIC-2022). [7,8] Non-medical costs included transportation, caregiving, and the need for palliative care. Indirect cost according to the social perspective was calculated based on lost productivity and losses due to early retirement and death using the “Human Capital Approach” method, considering the minimum income in the country. The method aims to measure the losses due to the illness of individuals based on the income of the person and necessitates knowing the income earned by sick people. However, since there is no data on the income of each patient, the minimum monthly income in the country is accepted. The minimum income was obtained from the Ministry of Labor and Social Security.[9] Pension and disability pensions were obtained from the official websites of the Social Security Institution.[10]

The total economic burden of breast cancer was calculated based on per-patient costs. The data were analyzed in Microsoft Excel® 2020. Intangible costs were excluded from the study.

The method developed on behalf of the World Bank (WB) and World Health Organization (WHO) was used for direct disease costs calculations.[11] In the method, the clinical pathway is followed, and the number of uses of each expenditure item is multiplied by the percentage of cases using it and unit costs to reach the main total expenditure. The formulation used is as follows:

- Unit cost of health services required to deliver the intervention (C)
- Quantity of each type of service required for the intervention (V)
- Number of people applying to the health institution for that service (n)

$$M_j = \sum_{i=1}^s C_{ij} V_{ij} n_{ij}$$

In the above equation, “i” denotes the service levels, and “j” denotes the services needed for the intervention. The equation assumes that there are s types of appropriate services. If some of the services are not needed in the production of intervention j, the values of V will be zero.

Table 1 Distribution of outpatient clinic visits of breast cancer patients

Outpatient clinics	Metastatic (Stage III-C-IV) disease		Non-metastatic disease	
	%	Times/year	%	Times/year
General surgery	70	1	100	4
Radiology	100	12	100	6
Genetics	40	1	30	1
Medical oncology	100	20	100	10
Radiation oncology	100	3	80	2
Nuclear medicine	100	2	100	1
Physical therapy and rehabilitation	15	1	25	1
Plastic surgery			13	2
Psychiatry	10	4	10	4
Counselling (psychologist)	30	4	15	4
Cardiology	100	2	100	2
Endocrinology	10	1	10	1
Emergency medicine	90	4	35	1
Family Medicine	70	3	70	2
Orthopedics and traumatology	35	1		
Algology	15	1		
Gynecology and obstetrics	55	1	55	1
Nutrition and dietetics	100	1	100	1
Neurology	10	4	10	4

RESULTS

Epidemiological Inputs

According to the Turkish Cancer Statistics 2020, breast cancer is the most common cancer with an incidence of 47.7/100,000 people.[2] Globocan 2020 data on breast cancer statistics in Türkiye revealed that the number of new cases was 24,175, and the number of prevalent cases (5-year) was 83,973, along with 7,161 deaths.[12] Overall, 44.5% of the patients were aged 50–69 years, and 40.4% were aged 25–49 years. When the stages of breast cancer were analyzed, 11.1% of the invasive cases in the database were at the distant stage. On the other hand, 47.9% were localized, and 41.2% were regional.[2] Breast cancer is seen in 11,250 premenopausal women and 12,925 postmenopausal women.[12] In a study conducted by Özmen et al. on 20,000 patients, the rate of diagnosis in premenopausal status was 45%, while the molecular subtyping revealed HER2 in 12% of cases, Luminal A in 50%, Luminal B in 30%, and TNBC in 8%.[13] The 5-year OS was 90%, and the 10-year OS was 80%. Stage I+II was 75%, and Stage III+IV was 25% at the time of diagnosis. Histological grade type 1 was found to be 15%, type 2 60%, and type 3 20%.[13] In the study, Stage I was accepted as Stage

1A (T1N0), 1B (T1N1mik), 2A (TXN1; T1N1, T2N0), and Stage 2 as Stage 2B (T2N1; T3N0).

Direct Medical Cost

Outpatient Follow-up Cost Item

Outpatient clinic visits were considered to vary according to metastasis status, and the patients with metastatic disease were estimated to be more likely to receive outpatient services. The distribution of outpatient clinic visits is presented in Table 1. Based on unit costs, the total per-patient annual cost related to outpatient follow-up was calculated to be \$145.96 for non-metastatic patients and \$220.35 for metastatic patients.

Laboratory/Imaging Tests Cost Item

Laboratory tests/imaging tests included biopsy, and rates were considered to differ in metastatic and non-metastatic patients (Table 2). While the average cost per metastatic patient is \$143.50, the average annual cost per non-metastatic patient is \$82.12. The average annual imaging costs are \$260.56 in metastatic patients and \$228.01 in non-metastatic patients. Biopsies were distributed in accordance with SUT. Different types of biopsies are performed in metastatic and non-metastatic patients. For metastatic patients, 10% breast biopsy and 30% sharp/thick needle biopsy are

Table 2 Distribution of laboratory and imaging tests requirements of breast cancer patients

	Metastatic disease		Non-metastatic disease	
	%	Times/year	%	Times/year
Laboratory tests				
CA 15-3 and CEA, CA 27.29	100	4	100	2
Biochemistry	100	12	100	2
Hormones	90	2	100	1
Bleeding tests	90	2	100	1
Blood count	100	12	100	4
Calcium-Vitamin D	75	2	75	2
PTEN PKB1	30	1		
BRCA1 gene, 17q 12, q21	25	1	40	1
BRCA2 gene, 13q 12-q13, p53	25	1	40	1
Estrogen and progesterone receptor (ER-PR)	100	1	100	1
Androgen receptor (AR)	100	1	100	1
Imaging tests				
Mammography	50	1	100	1
PET-CT or thorax CT	65	2	60	1
Abdominal CT	100	2	60	1
Bone Scintigraphy	35	1	40	1
Brain MRI/CT	80	1	15	1

CA: Carcinoma antigen15-3; CEA: Carcino embryonic antigen; PTEN: Phosphatase and tensin homolog; PKB: Protein kinaz B ; PET-CT: Positron emission tomography; MRI: Magnetic resonance imaging

needed, while 100% of non-metastatic patients need breast biopsy, 70% sharps/thick needle biopsy, 10% incisional biopsy, 5% stereotactic core biopsy, 10% ROLL (Radioguided Occult Lesion Localization-Radioguided by Radionuclide), and 5% USG-guided core biopsy and MR-guided core biopsy.

Hospitalization/Intervention Cost Item

In the Delphi panel, two approaches for tumour surgery were foreseen. Lumpectomy for 65% of Stage 1 patients and 40% of Stage 2 patients, mastectomy and reconstruction surgery for 35% of Stage 1 patients and 35% of Stage 2 patients. Non-metastatic patients are considered to be hospitalized for 3 days in general surgery, 1 day in the general surgery intensive care unit, and then 3 days in the ward. Breast reconstruction is delayed in 10% of patients, sentinel lymph node removal is performed in 100% of patients, biopsy in 75%, and lymph dissection in 20% of patients. In locally advanced breast cancer patients, breast-conserving surgery is performed in 10%, radical mastectomy in 90%, and breast reconstruction in 40%. In metastatic breast cancer patients (55% postmenopausal and 45% premenopausal), the interven-

tions included radical mastectomy (15%), sentinel lymph node biopsy (5%), axillary dissection (15%), and hospitalization. In light of this information, the average annual hospitalization/intervention cost was estimated to be \$1,285.42 in non-metastatic patients and \$1,112.25 in metastatic patients.

Treatment Cost Item

Neoadjuvant chemotherapy is given to 35% of non-metastatic patients. All brands under the active ingredients of the relevant chemotherapies were calculated appropriately according to their posology and included in the publicly paid costs. The side effects of each active substance were calculated based on the cost-of-illness methodology. Accordingly, 80% Adriamycin, 80% Paclitaxel, 20% Pertuzumab, and 80% Trastuzumab, 13% Carboplatin, 80% Cyclophosphamide, 30% Docetaxel, and 8% Doxorubicin and Cyclophosphamide are included in the treatment of patients over four cycles. Adjuvant trastuzumab treatment in non-metastatic breast cancer and neoadjuvant trastuzumab treatment and related side effects are included (Table 3).

Details of drug treatments in locally advanced and metastatic patients are presented in Table 4. In

Table 3 Neoadjuvant and adjuvant trastuzumab therapy

Neoadjuvant therapy			
Adjuvant trastuzumab therapy	Cyclophosphamide-adriamycin/doxo-FU	%	Cure
HER2			
Total 17 doses of trastuzumab	Docetaxel+T	5	4
	Cyclophosphamide-Adriamycin Paclitaxel+T	60	4
	Cyclophosphamide-Adriamycin Docetaxel+T	5	4
	FEC+Paclitaxel+T	20	4
TNG 15%			
25% Chemotherapy	TC (Docetaxel+Cyclophosphamide)	60	4
	AC (Doxorubicin+Cyclophosphamide)	40	4
Adjuvant therapy			
Adjuvant trastuzumab	95% below 0.5 cm		
HER2			
HER2+ (90%–95%)	Cyclophosphamide-Adriamycin/doxo-FU	95	6–8
	Docetaxel+T and Herceptin		
Neoadjuvant	In combination with Neo adjuvant	5	17
Trastuzumab	FEC+Paclitaxel+T	60	4
	Endocrine Therapy+T	40	4

HER2: Human epidermal growth factor receptor2; FEC: 5-fluorouracil, epirubicin, and cyclophosphamide; TNG: Triple negative gene; TC: Docetaxel+Cyclophosphamide; AC: Doxorubicin+cyclophosphamide

metastatic breast cancer patients, first-line treatment of TNBC patients (60%) was AC, Carboplatin, Gemcitabine+Paclitaxel, Cisplatin+Gemcitabine, Paclitaxel+Docetaxel+Cyclophosphamide for 3 months, second-line Capecitabine for 3 months and Capecitabine and Eribulin for 1 month. Patients with metastatic breast cancer also receive additional endocrine therapy. Five percent of patients receive Tamoxifen, and 95% Aromatase inhibitors (AI). CDK 4/6 inhibitors as systemic therapy; 50% Palbociclib and 50% Ribociclib were included in the calculations.

Accordingly, the total drug/side effects cost was determined to be \$2,687.84 per patient per year for non-metastatic breast cancer patients and \$17,067.32 per patient per year for metastatic breast cancer patients (Table 5).

Non-Drug Treatments

Patients with locally advanced breast cancer may need radiotherapy after chemotherapy. Adjuvant radiotherapy (RT) after mastectomy is between 45 and 50 Gray. One percent of patients have to undergo lymphoedema treatment and lymphatic bypass, 1% vascularized lymph node transfer, 1% flap surgery, 1% lymph suction, and 1% excisional surgery. Flap necrosis is treated in 5%, infection in 5%, and seroma in 4% of breast reconstruction patients. Treatment of brain metastasis in 15% of

patients, lung/liver metastasis in 25%, and bone metastasis in 70% of patients are included in the calculations. In patients with bone metastasis, 75% were treated for clinically severe pain, 10% for pathological fracture, 2% for spinal cord compression, 3% for bone marrow failure, and 5% for severe hypercalcemia. In addition, 14.3% of the patients relapsed and received breast-conserving surgery and radiotherapy, 24% received breast-conserving surgery and tamoxifen, and 9.7% received breast-conserving surgery, tamoxifen, and radiotherapy.

According to these data, the total intervention cost for metastatic locally advanced-stage patients is \$1,112.24, the metastasis cost is \$2,006.83, the recurrent patient cost is \$116.30, and the complication cost is \$162. The best supportive treatment cost (BSC) of the patients for the last month is \$567.88.

Monitoring Costs

Stage I-IIA patients who have been diagnosed with breast cancer but have been on follow-up for the last 5 years are expected to have received medical oncology outpatient clinic visits four times a year, routine laboratory tests four times a year, breast USG two times a year, and mammography once a year, while the average annual cost per patient is \$25.45. Stage IIA-IIIB-IIIC patients need oncology visits four times a year, routine laboratory tests four times a year, 20% CT, 10% bone

Table 4 Drug therapy in locally advanced breast cancer and metastatic (Stage IIIC-IV; 55% postmenopausal) breast cancer

Locally advanced breast cancer			%	Cure
HR+	Adjuvant	Cyclophosphamide Docetaxel	30	4
HER2-		Cyclophosphamide-Adriamycin Paclitaxel	70	4
	Neo-Adjuvant	Cyclophosphamide-Adriamycin Paclitaxel	100	4
Metastatic breast cancer (Stage IIIC-IV)			%	Cure
HR+(%80)	Endocrine %80	Fulvestrant (55%)	20	6–8
		CDK 4–6 inhibitors and palbociclib	50	6–8
		CDK 4–6 inhibitors and ribociclib	50	6–8
	At each step	LHRH	8	6–8
		CDK	90	4–6
	Target chemotherapy (20%)	Everolimus+exemestane	20	4
		Adriamycin+capecitabine	20	4
		Carboplatin+paclitaxel	20	4
		Gemcitabine+paclitaxel	20	4
		Capecitabine+paclitaxel	20	4

HR: Hormone receptor; HER2: Human epidermal growth factor receptor 2; CDK: Cyclin-dependent kinase inhibitors; LHRH: Luteinizing hormone releasing hormone

Table 5 Per patient total annual direct medical cost in metastatic and non-metastatic setting

	Metastatic patient	Non-metastatic patient
Cost items		
Total outpatient clinic cost	220.36	145.96
Total laboratory tests cost	82.12	143.50
Total cost of imaging	260.56	228.02
Total hospitalization /intervention cost	1,112.25	1,285.42
Total drug - side effect cost	17,067.32	2,687.84
Best supportive treatment cost (BSC)	567.88	
Total per patient cost (\$)	21,595.62	

scintigraphy, 20% thorax CT, 10% systemic CT, 10% mammography, and the average annual cost per patient is \$30.06. For Stage IIIC-IV patients, the average annual cost per patient is \$17.99 with the need for four visits to medical oncology and one systemic CT per year. In the study, follow-up patients were accepted as prevalence patients and were determined as 83,973 people.

Total Direct Cost

The metastatic breast cancer patient rate of 25% and the non-metastatic patient rate of 75% were taken from the Ministry of Health Cancer Diagnosis, Prevention, Screening, and Treatment Guidelines. The average annual cost per new metastatic breast cancer patient diagnosed in the last year was \$21,595.62, and the average annual cost per non-metastatic patient was \$4,490.76 (Table 5). The incidence is 25,381 patients.

For metastatic and non-metastatic weighted direct cost calculations, the total direct breast cancer disease cost is \$22,251,461.20, taking into account the number of new/incidental patients and the number of previously diagnosed prevalent patients. The total direct disease cost of the new patient is \$1,822,047.94.

Direct Non-Medical Costs

Direct non-medical costs were identified by the Delphi panel as transport, home care, and palliative care. The rate of those in need of professional care and palliative care was accepted as 25% and 10%, respectively. According to the Healthcare Implementation Communique (HIC), the daily palliative care fee is \$5.58, and the home care fee is \$227.49 per month. The daily wage for labor loss was taken over the 2023 minimum wage (\$446.32) and calculated as \$9.88 per day. Forty percent of patients

Table 6 Direct non-medical cost for newly diagnosed and formerly diagnosed breast cancer patients annually

Direct non-medical costs	Year/ day	Number of patients	Unit cost	Total cost
Newly diagnosed patients				
Need for a carer	12	3,173	227.49	8,660,966.63
Person in need of palliative care	30	179	1,078.51	5,792,407.58
Metastatic-non metastatic patient transport cost				995,971.13
Total (\$)				18,917,841.62
Formerly diagnosed follow up patients				
Metastatic-non metastatic patient transport cost				
Total (\$)				2,195,169.61

receive treatment from outside the city, and 60% from within the city. It was estimated by the Delphi panel that 32% of the patients traveled by taxi, 32% by private car, and 36% by public transport. For public transport, the Istanbul Municipality bus ticket fare was accepted as \$1 for a round trip and \$22.03 for out of Istanbul. For private vehicles, the calculation was made based on the fuel consumption per 100 km as well as the weight of the best-selling cars in Türkiye in 2016. The fuel consumption types of the vehicles were weighted, and the average fuel prices for Istanbul were taken. The average distance to the centre of Istanbul is calculated as 8.1 km, and the average distance of the closest cities to Istanbul is calculated as 141.8 km. Transport by private car and taxi was calculated separately for the number of patients traveling to and from the hospital, as well as for the number of incidental and prevalent patients, based on these distances and fuel costs. The direct non-medical cost for the new patient is \$18,917,841.62, and the direct non-medical cost for the follow-up patient is \$2,195,169.61 (Table 6). The total direct non-medical cost of new and existing diagnosed breast cancer patients is \$21,113,008.62.

Indirect Costs

Indirect costs represent the costs of loss of labor force, early retirement, and early death. The average age of patients is 53 years, and the retirement age is 54 years in Türkiye. As a result of the Delphi panel, it was determined that 30% of the patients were active employees, and non-metastatic patients were on sick leave for approximately 6 months and metastatic patients for 1 year. Premature mortality was 10%, and the years of life lost calculated according to the life expectancy were found to be 23 years. The daily wage of labor loss calculated based on the 2023 minimum wage (\$446.32) was \$9.88 per day. The average disability pension is \$367.26 and is considered 5 years. The labor loss for the days spent in the hospital and for the days of sick leave was calculated over the daily amount of the

minimum wage. Indirect costs are calculated separately for new and follow-up patients, and it is seen that new patients face a higher cost due to their first diagnosis and treatment in the hospital. Accordingly, while the indirect costs for new patients were \$815,199,359.02, they were \$169,767,030.43 for follow-up patients (Table 7). The total indirect cost is \$982,867,753.58.

Total Burden Of Disease

The 5-year prevalence of breast cancer patients in Türkiye according to GLOBOCAN data (2020) is 83,973. The number of new patients is 25,381, and the number of deaths is 7,161. The premenopausal patient rate is 45%, and the postmenopausal patient rate is 55%. According to molecular subtypes, HER2 is 12%, Luminal A 50%, Luminal B 30%, and TNBC 8%. In the direct cost calculations made in light of all these data, the new patient annual direct cost was calculated as \$222,514,612.06, and indirect cost as \$834,117,200.66, amounting to a total of \$1,056,631,812.73. The total annual direct cost for the formerly diagnosed patients was \$1,822,047.94, and indirect costs were \$171,962,200, amounting to a total of \$173,784,247.98 annually. The total direct and indirect cost of new and formerly diagnosed patients is \$1,230,416,060.71 (1\$ = 19.03 TL—Turkish Liras) (Table 8).

DISCUSSION

Breast cancer is an important disease burden for Türkiye, as it is for the world. In a study conducted in 27 European Union countries, the burden of breast cancer in 2019 was determined as €126 billion, and medical costs amounted to €51 billion (40% of the total burden), while the indirect costs comprised 60% of the total.[14] In a cost study conducted on 2,923 newly diagnosed patients in Spain, only medical costs totalled €469,920,731.[15] In a cost calculation based on na-

Table 7 Indirect Costs - New and former patients annually

Indirect costs	Year/ day	Number of patients	Cost	Total cost
Newly diagnosed patients (incidence)				
Loss of labor force due to days spent in hospital (metastatic)	83	6,395	9.62	5,065,768.84
Loss of workforce due to days spent in hospital (non-metastatic)	56	196	9.62	10,253,604.41
Loss of labor force arising from disability retirement	20	286	4,407.14	25,167,938.09
Loss of labor force arising from reported days (non-metastatic)	180	19,035	9.62	32,958,014.17
Number of reported days (metastatic)	365	6,345	9.62	22,277,176.24
Loss of labor force due to early retirement	5	1,142	4,407.14	25,167,938.09
Loss of labor force due to premature death	28	7,161	3462.75	694,308,919.20
Total (\$)				815,199,359.02
Formerly diagnosed patients (prevalence)				
Loss of labor force due to days spent in hospital (met)	4	20,993	9.62	807,715.11
Loss of workforce due to days spent in hospital (non-met)	4	62,980	9.62	2,423,145.33
Loss of labor force arising from disability retirement	20	945	4,407.14	83,268,084.99
Loss of labor force due to early retirement	5	3,779	4,407.14	8,326,8084.99
Total (\$)				169,767,030.43

Table 8 Total breast cancer burden of disease

	Newly diagnosed patients	Former patients
Direct cost	222,514,612.06	1,822,047.94
Direct non-medical cost	18,917,841.62	2,195,169.61
Indirect cost	815,199,359.04	169,767,030.43
Total cost of illness	1,056,631,812.73	173,784,247.98
Total breast cancer burden \$		1,230,416,060.71

tional social security data between 2008 and 2016 in Italy, the average inpatient treatment of 75,000 women was found to be €300 million per year.[16] In a study conducted in Korea between 2007 and 2010, it was found that the total socioeconomic cost increased by 40.7% in 3 years, from \$668.49 million to \$940.75 million.[17] Direct costs were 1.4 times higher than in 2007 and increased from \$278.71 million to \$399.22 million. Non-direct medical costs increased from \$50.69 million in 2007 to \$75.83 million in 2010. The total cost of breast cancer was found to be \$339.09 million in 2007 and \$465.70 million in 2010, increasing by 37.3%.[17]

In our study, indirect costs in breast cancer patients were 75% of the total cost. Direct costs in both metastatic and non-metastatic patients are covered from the perspective of reimbursement due to the country's health policies. Another important reason for the high indirect costs is that all patients are assumed to be working. Since it is a disease with very high social costs, especially for female patients, indirect costs were calculated for each patient. Türkiye has a population of approximately 86.5

million people, half of which is female, in a large geographical area. Of course, every woman has different access to health services. As in every country, there are differences in health services between developed regions and rural areas of Türkiye. Differences in culture and awareness among geographies also affect people's demand for health services. There are differences in patients' use of preventive medicine services or awareness of the importance of applying to a health institution. Referral of patients to more developed provinces may sometimes cause delays in diagnosis. All these possibilities are reflected in costs. Economic burden studies to be conducted on a regional basis may reveal these differences. In a breast cancer cost study conducted in Sweden in 2002 with the same methodology, indirect costs accounted for 70% (2.1 billion SEK) and direct costs accounted for 30% (895 million SEK) of the total cost, supporting our results. The total cost was SEK 3 billion, with indirect costs tripling the direct costs due to premature deaths and labor loss. The detection of more cancer cases under the age of 65 due to new technologies, early retire-

ment, days off work due to illness, and premature death all contributed to the cost of lost production.[18] In an economic burden study of 5 years of patient follow-up, production losses were found to account for 89% of the total cost and medical costs 11%.[19] Similarly, a study conducted in Jordan found that treatment costs are the highest cost item among direct costs.[20] In a 2021 study conducted in Saudi Arabia, it was stated that the highest cost item among direct costs was the cost of treatment (67%) and trastuzumab-based regimens.[21]

The most important reason why costs in Türkiye seem lower than in Europe is that a single reimbursement agency undertakes the health expenses of the entire population. In Türkiye, citizens are covered by general health insurance, and the reimbursement agency makes payments to healthcare facilities based on a low-margin price list to ensure smooth public access to healthcare services.

There are many similar studies in the literature worldwide. Breast cancer is the most common cancer in women, and it has become a disease whose direct cost has increased over the years with the results of being in the screening program in many countries and the patient's survival for many years with newly developed drugs. That's why the indirect cost of breast cancer has gradually become smaller. When new drugs enter breast cancer treatment algorithms, the overall survival of the patient is longer than in previous years, leading to increased costs.

CONCLUSION

In conclusion, this cost-of-illness study confirms the substantial economic burden of breast cancer for Türkiye in terms of both direct and indirect costs. The large share of indirect costs in total costs can provide important guidance to decision-makers in the healthcare system to better allocate limited resources to breast cancer prevention and early detection strategies.

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