International Journal of Technology Assessment in Health Care, **23:2** (2007), 223–231.

DOI: 10.1017.S0266462307070328

Resource use and costs associated with different states of breast cancer

Mathias Lidgren, Nils Wilking
Karolinska Institutet

Bengt Jönsson
Stockholm School of Economics

Clas Rehnberg
Karolinska Institutet

Objectives: This study investigated the direct medical resource use and cost, informal care cost, and indirect cost associated with breast cancer in different states of the disease in normal clinical practice.
Methods: A retrospective database analysis was used to estimate direct medical resource use and cost, and a patient questionnaire was used to evaluate informal care and work capacity in different states of breast cancer.
Results: For patients younger than 65 years of age, the first year after a primary diagnosis total cost amounted to 280,000 SEK ($39,000) and the first year after a local or contralateral recurrence total cost was 351,000 SEK ($48,900). The second and following years after primary breast cancer or recurrence had substantially lower total cost, amounting to 94,000 SEK ($13,000). For patients with metastatic disease, the annual total cost was estimated to 334,000 SEK ($46,500). For patients older than 65 years of age, the total cost for the first year after a primary diagnosis amounted to 80,000 SEK ($11,200) and the total cost for the first year after a local or contralateral recurrence was 92,000 SEK ($12,900). The total cost for the second and following years after primary breast cancer or recurrence was estimated to 18,000 SEK ($2,600), and the total annual cost for patients with metastatic was 122,000 SEK ($17,000).
Conclusions: Both direct medical costs and indirect cost vary substantially between disease states. For patients under 65 year of age, indirect costs accounted for more than 50 percent of the total cost.

Keywords: Resources use, Direct cost, Indirect cost, Informal care cost, Breast cancer

Breast cancer is the most common female cancer in Sweden, with approximately 7,000 newly diagnosed cases and 1,500 deaths from the disease each year (16;17). Breast cancer is a costly disease for the healthcare system, and from a societal perspective, production losses due to the disease represents a substantial economic cost (9). However, comprehensive studies on the resources use and cost associated with breast cancer patients in normal clinical praxis are few. The aim of this study was to investigate the resources use and costs associated with breast cancer in different states of breast cancer disease in normal clinical practice.

A distinction is made between direct medical costs, direct nonmedical costs, and indirect costs. Direct medical costs are defined as the resources used within the healthcare

We thank all the patients who agreed to participate in this study. We also thank the nurses and doctors at Radiumhemmet, Karolinska Sjukhuset, Solna, as well as research assistant Ulrika Larsson for their help and support in administering the questionnaires to the patients. We also thank Susan Bengtsson and Ingrid Bergström for their help with collecting inpatient episode and outpatient visits data from the electronic records. We are also grateful to Johan Almbrandt at Stockholm Oncology Centre for his help in gathering patient-specific disease data needed to stratify patients into different disease states. This study was funded by Astra Zeneca. The funding source played no role in the design, methods, data collection, analysis, or interpretation of the results of the study. Publication of this study was not contingent on the sponsor's approval.

sector. Direct nonmedical costs are recourses used outside the healthcare sector in relation to the treatment or as an effect of the treatment. Indirect costs are defined as resources forgone due to treatment, morbidity, and mortality for those afflicted by the disease.

It has been recommended that economic evaluations of health care should use a societal perspective in their analysis (18). When performing an economic evaluation of a treatment from a societal perspective, not only the direct costs of the treatment should be included, but also the indirect costs associated with this treatment (5). Not including the indirect costs would favor strategies that achieve lower treatment costs at the expense of higher indirect cost. It is thus important to have reliable data on both direct medical costs as well as indirect costs to be able to perform economic evaluations from a societal perspective.

MATERIALS AND METHODS

Study Design

A total of 361 patients were included in a naturalistic cross-sectional observational study. Patients were recruited as they attended a breast cancer outpatient clinic. Female patients with a previous diagnosis of breast cancer were eligible for inclusion. The study protocol was approved by the local ethical committee, and informed consent was obtained from all patients before inclusion. The intention of this study was to estimate the medical resources use and work capacity for patients in various states of breast cancer in normal clinical practice; thus, the study was designed to interfere as little as possible with normal clinical work. The study did not alter or influence the treatment received by the patients in any way, and the choice of treatment method was entirely controlled by the doctor. Patients were only included once in the study, even if they attended the outpatient clinic repeatedly during the recruitment period.

Data Collection

Patients who fulfilled the inclusion criteria were enrolled consecutively, provided that they agreed to participate in the study. The period of recruitment was during April 2005 and May 2005 at a breast cancer outpatient clinic at Karolinska University Hospital, Solna, Sweden (KS). A self-administered questionnaire was distributed to the study sample by a research nurse while patients were waiting to see the doctor/nurse. The questionnaire gathered data on demographic variables, informal care provided by family and friends, and work capacity.

Disease State. The breast cancer disease state was determined based on epidemiological data from the Stockholm Oncology Centre (OC). The data included the date of diagnosis and ICD-10 codes for all primary breast cancer, occurrence of contralateral breast cancer, locoregional recurrence, and distant recurrence for patients in the OC database. These dates where used to determine the disease state at the point in time when the questionnaire was answered.

Of the 361 patients in the study population, 345 were found in the OC database. Patients not included in the OC database were generally patients with their primary diagnosis having been made outside of Stockholm, thus lacking basic epidemiological data in the OC database. Due to the lack of data on these patients, we decided to exclude them from the analysis. Subsequently, the study sample was reduced to 345 patients.

Patients were divided into mutually exclusive groups (states) based on their breast cancer disease. The states were defined to be relevant and useful both in clinical practice and economic modeling. It was thus expected that the states would differ in resource use and cost.

The defined breast cancer states were "first year after primary breast cancer" (state P), "first year after recurrence" (state R), "second and following years after primary breast cancer or recurrence" (state S), and "metastatic disease" (state M).

Patients in state P had a primary diagnosis breast of cancer within 1 year or less before answering the questionnaire, and no metastatic disease. Patients in state R had at least one recurrence within 1 year or less before answering the questionnaire, and no metastatic disease. The state S group consisted of patients whom had not been diagnosed with a primary breast cancer or a recurrence within 1 year before answering the questionnaire. The state M group consisted of patients with at least one distant recurrence.

Medical Resources Use. Medical resources use and costs were collected retrospectively for each patient included in the study from electronic records available through KS. The electronic record contained all inpatient episodes and outpatient visits to all hospitals in Stockholm County. The cost incurred by the hospitals for each inpatient episode and outpatient visit was also available in the electronic record. The cost for an inpatient episode included the cost for staff, equipment, overhead, and drugs for inpatient use.

The cost for an outpatient visit included the cost for staff, equipment, and overhead, but not the cost for outpatient drugs given to the patient. To calculate the resource use and costs associated with current breast cancer treatment strategies, only visits that occurred starting from 2004 were included in the analysis.

Outpatient Drugs. Reliable data on the type and quantity of drugs used in the outpatient setting by the study sample was not available through retrospective analysis of the electronic records gathered through KS. We instead used expert opinion to estimate the type and quantity of outpatient drugs used in the various disease states. Unit costs were derived from the Swedish pharmaceutical reference book (www.fass.se).

Informal Care. The questionnaire asked patients to state the number of hours of informal care (care that is given

https://doi.org/10.1017/S0266462307070328 Published online by Cambridge University Press

free of cost by family and friends) per week that they were receiving because of their breast cancer. The data gathered was used to assess the quantity of informal care received by breast cancer patients in different diseases states.

Production Loss. The questionnaire also asked patients to state if they were in retirement/early retirement as well as the reason for the retirement/early retirement (age, breast cancer, other disease, or other reason).

Patients who were working were asked if they had been absent from work due to breast cancer during the past 3 months. If the patient had been absent from work during the past 3 months, the patient was asked to specify the number of working days that they had been absent and the normal number of hours per day that they worked. Some patients stated the actual number of working days absent, whereas some patients stated the number of months absent. In the case when patients stated the number of months that they had been absent, each month was assumed to correspond to 20 working days. If patients had stated that they had been absent more than 60 days during the past 3 months, this figure was reduced to 60 days.

The number of days absent was multiplied by the number of hours that the patient normally worked per day to calculate the number of working hours lost due to absences from work caused by breast cancer.

Patients stating that they had been absent from work due to breast cancer, but that had missing values on the number of working days absent and/or the normal number of hours worked per day, had the missing values replaced with the average value for the corresponding disease group.

Cost Estimation

Data on resource use and costs for each patient in our study sample were extracted from the electronic record at KS. For each inpatient episode and outpatient visit in the electronic record, a specific unit cost was stated. These data were used to estimate the direct medical resources use and cost in the different disease states.

The cost of informal care was calculated by multiplying the number of hours of informal care per week by the cost per hour of leisure time lost. The valuation of leisure time is not straightforward, and different methods have been proposed (8). In this study, we have chosen to use 35 percent of the gross wage rate as a proxy for the cost of leisure time lost. Because we did not have data on age and sex of the caregiver, we used the average gross wage rate for both men and women of all ages (11).

The indirect costs were based on the human capital theory (7). According to the human capital theory, the value of the production loss is the value produced on the margin by the individual.

The valuation of lost production due to absence from work was based on the hourly pretax salary (11), adjusted to 2005 years level (14), including social insurance contributions paid by the employer (12). The indirect cost of absences from work was estimated by multiplying the number of hours absent from work due to breast cancer by the indirect cost per working hour lost for individuals younger than 65 years of age.

The annual income from employment and business (15), including social insurance contributions (12), was used to estimate the value of the production foregone due to early retirement from breast cancer. The underlying assumption was that, if the patient had not had breast cancer, early retirement due to breast cancer would not arise, and thus, the patient would have an annual income comparable with the national average for the same sex and age group. All costs are given in Swedish kronor (SEK) using 2005 years price levels ($\$1 = 7.18$ SEK, $€1 = 9.20$).

Statistical Analysis

A two-sample Wilcoxon rank sum (Mann–Whitney) test was used to test for differences in resource use and costs, between two disease states. The Wilcoxon rank sum test is a nonparametric alternative to the two-sample t-test, and it is based on the order in which the observations from the two samples fall. The comparator in the tests was the state S. The p value of the test represents the probability that the two states have the same distribution.

A Kruskal–Wallis test is a nonparametric rank analogue of one-way analysis of variance. This test was used to determine for difference in cost between the different disease states. The p value represents the probability that all of the states come from the same distribution.

All resource use and costs were annualized to 1 year. All confidence intervals of the mean have been estimated nonparametric using bias-corrected and accelerated bootstrapping with replacement. All calculations were made using Stata 8.0 for Windows.

RESULTS

Patient Characteristics

Patient age ranged from 28 to 93 years, and the mean age was 57 years when included in the study. The year of primary diagnosis ranged from 1966 to 2005, with a majority of the patients having been diagnosed with primary breast cancer 2001 or later. Of the patients responding to the questionnaire, 21 percent were in their first year after primary breast cancer, 6 percent were in their first year after a recurrence, 54 percent had not had a primary breast cancer or recurrence for at least 1 year, and 19 percent had metastatic disease.

Unit Costs

The mean cost per inpatient episode was approximately 43,000 SEK (95 percent confidence interval [CI], 36,700–50,600). The unit costs for inpatient episodes in our sample were positively skewed, causing the mean to be

https://doi.org/10.1017/S0266462307070328 Published online by Cambridge University Press

substantially higher than the median. The median cost per inpatient episode was approximately 29,000 SEK. The mean cost per outpatient visit was approximately 1,580 SEK (CI, 1,530–1,640).

The cost per hour of leisure time lost used in this study to calculate the cost of informal care was 53 SEK. The cost per working year lost used to calculate the indirect cost of early retirement due to breast cancer ranged from 134,400 to 322,600 SEK. The cost per working hour lost used to calculate the indirect cost of absence from work due to breast cancer ranged from 156 to 202 SEK.

Quantity of Inpatient Episodes and Outpatient Visits

The average annualized number of inpatient episodes was 1.51 for state R, followed by state P and state M with .85 and .72, respectively. State S had the lowest number of inpatient episodes, with .16 per year.

The average annualized number of outpatient visits was substantially higher for each disease state compared with the number of inpatient episodes. State P had the highest number of outpatient visits, with 33.7, whereas state R and state M had 29.9 and 29.4 outpatient visits, respectively. State S had the lowest number of outpatient visits, with 8.0 per year.

Inpatient Episode and Outpatient Visit Costs

All of the disease states had higher outpatient visit costs than inpatient episodes costs, except state R. The average annualized cost for state R was estimated to approximately 95,200 SEK, followed by state M and state P with an average annualized cost of 88,800 SEK and 73,700 SEK, respectively. State S had the lowest average annualized cost, with 21,300 SEK. This value was substantially lower than the other disease states, and the difference was statistically significant ($p < .001$). Results are shown in Table 1.

Outpatient Drugs

In state P, 40 percent of the patients were assumed to receive six cycles of the adjuvant chemotherapy FEC, consisting of fluorouracil (L01BC02), epirubicin (L01DB03), and cyclophosphamide (L01AA01). Sixty-five percent of the patients in state P were also assumed to be receptor positive and, thus, starting adjuvant hormone therapy using tamoxifen (L02BA01). These assumptions resulted in an estimated annualized cost per patient of 5,700 SEK.

In state R, 20 percent of the patients were assumed to receive six cycles of adjuvant FEC, and 20 percent of the patients were assumed to receive six cycles of adjuvant treatment with the taxane docetaxel (L01CD02). As for state P, 65 percent of the patients were assumed to be receptor positive and, thus, receiving hormone therapy using tamoxifen. The use of taxanes to treat this patient group resulted in a higher annualized cost for state R compared with state P, with the annualized cost per patient being estimated to 17,800 SEK.

For state S, hormone receptor-positive patients were assumed to stay on hormone therapy using tamoxifen for 5 years after primary diagnosis or recurrence. This assumption resulted in an estimated annualized cost per patient of 600 SEK.

The outpatient drugs used for patients in state M are less standardized than for the other disease states. The drugs used are dependent on hormone receptor and HER2 expression of the patient, as well as previous treatment history, patient survival time, and the presences of bone metastases. Patients in state M who had not previously been treated with chemotherapy were assumed to sequentially receive FEC, docetaxel, and capecitabin (L01BC06). Patients who had previously received adjuvant chemotherapy were assumed to sequentially receive docetaxel, capecitabin, and vinorelbine (L01CA04).

Receptor-positive patients were assumed to sequentially receive treatment with tamoxifen and anastrozole (L02BG03) in addition to the treatments mention above. Patients overexpressing HER2 were assumed to receive

Table 1. Annual Direct Medical Costs (SEK 2005)

	Mean inpatient episode costs (95% CI)	Mean outpatient visit costs (95% CI)	Mean total inpatient episode and outpatient visit costs (95% CI)	Outpatient drug costs	Total inpatient episode and outpatient visit costs (p value[a])
State					
First year after primary breast cancer	27,088 (20,491–36,773)	46,601 (40,492–52,916)	73,689 (63,008–89,511)	5,700	<.001
First year after recurrence	48,983 (34,220–67,274)	46,279 (35,983–59,051)	95,263 (77,104–120,539)	17,800	<.001
Second and following years after primary breast cancer/recurrence	9,281 (5,283–16,431)	12,015 (9,867–14,548)	21,296 (16,257–29,702)	600	—
Metastatic disease	34,938 (22,314–54,768)	53,825 (48,713–59,012)	88,763 (74,817–108,881)	54,000	<.001

[a] The comparator is "Second and following years after primary breast cancer/recurrence." Total cost Kruskal–Wallis, p value = .0001.
SEK, Swedish kronor; CI, confidence interval.

https://doi.org/10.1017/S0266462307070328 Published online by Cambridge University Press

Table 2. Annual Cost of Informal Care (SEK 2005)

	N	Mean no. of hours of informal care per week	Annual cost of informal care	(95% CI)	*p* value[a]
State					
First year after primary breast cancer	72	3.8	10,392	(5,742–19,273)	<.001
First year after recurrence	21	.8	2,100	(525–7,874)	.360
Second and following years after primary breast cancer/recurrence	185	.8	2,205	(1,125–5,192)	—
Metastatic disease	67	3.0	8,350	(3,887–15,610)	.019
Total	345				

[a] The comparator is "Second and following years after primary breast cancer/recurrence." Kruskal–Wallis, p value = .0001.
SEK, Swedish kronor; CI, confidence interval.

trastuzumab (L01XC03) in addition to docetaxel. For patients with bone metastases, it was assumed that pamidronic acid (M05BA03) was administered. Using these assumptions, we estimated the annualized cost per patient in state M to 54,400 SEK. The results of outpatient drug costs in the different disease states are summarized in Table 1.

Informal Care

The average annualized cost of informal care due to breast cancer was estimated to 10,400 SEK for state P and to 8,300 SEK for state M. The average annualized cost of informal care was substantially lower for state R and state S, with 2,100 SEK and 2,200 SEK, respectively. The difference in cost of informal care for state P and state M compared with state S was statistically significant ($p < .02$) (Table 2).

Absence from Work

The indirect cost of absence from work was substantial in all of the disease states and age groups. For age group <50, state P had the highest average annualized indirect cost, amounting to 226,500 SEK. For age group 50–64, state R had the highest indirect cost with 294,500 SEK. State S had the lowest indirect costs in both age groups, and the difference compared with state P, state R, and state M was statistically significant ($p < .01$) (Table 3).

Early Retirement

The share of patients who were in early retirement due to breast cancer was higher in all of the different disease states for the age group 50–64 compared with the age group < 50. No patients in state P were in early retirement due to breast cancer, which seems logical due to the short time span since these patients received their initial breast cancer diagnosis. State M had the highest indirect cost of early retirement in both age group < 50 and age group 50–64, with 55,000 SEK and 121,900 SEK, respectively (Table 4).

Indirect Cost

We also estimated the total annualized indirect cost for patients in the different states, combing the indirect cost of

Table 3. Annual Indirect Cost of Absences from Work (SEK 2005)

	Age < 50				Age 50–64			
	N	Working hours lost during 3 months	Annual indirect cost of absence from work (95% CI)	*p* value[a]	*N*	Working hours lost during 3 months	Annual indirect cost of absence from work (95% CI)	*p* value[a]
State								
First year after primary breast cancer	22	284	226,537 (164,343–286,217)	<.001	28	258	205,967 (156,787–256,936)	<.001
First year after recurrence	5	260	209,463 (93,326–384,685)	.015	6	368	294 520 (155,556–368,722)	<.001
Second and following years after primary breast cancer/ recurrence	40	75	59 820 (32,317–101,086)	—	67	56	44,387 (25,489–75,207)	—
Metastatic disease	17	188	151,397 (93,056–202,046)	.0019	15	157	125,903 (70,287–192,969)	.0023
Total	84				116			

[a] The comparator is "Second and following years after primary breast cancer/recurrence." Kruskal–Wallis test for age group < 50, p value = .0001. Kruskal–Wallis test for age group 50–64, p value = .0001.
SEK, Swedish kronor; CI, confidence interval.

https://doi.org/10.1017/S0266462307070328 Published online by Cambridge University Press

Table 4. Annual Indirect Cost of Early Retirement (SEK 2005)

	Age < 50				Age 50–64			
	N	Patients in early retirement due to breast cancer	Annual indirect cost of early retirement (95% CI)	*p* value[a]	*N*	Patients in early retirement due to o breast cancer	Annual indirect cost of early retirement (95% CI)	*p* value[a]
State								
First year after primary breast cancer	22	0%	0 (−)	.4639	35	0%	0 (−)	.0262
First year after recurrence	6	0%	0 (−)	.7021	9	22%	67,480 (33,740–202,440)	.4467
Second and following years after primary breast cancer/ recurrence	41	2%	7,212 (0–43,275)	—	101	13%	39,272 (24,052–69,525)	—
Metastatic disease	22	18%	54,987 (26,883–135,636)	.0278	33	39%	121 919 (74,762–179,424)	.0005
Total	91				178			

[a] The comparator is "Second and following years after primary breast cancer/recurrence." Kruskal–Wallis test for age group < 50, *p* value = .0274. Kruskal–Wallis test for age group 50–64, *p* value = .0001.
SEK, Swedish kronor; CI, confidence interval.

absences from work and early retirement. For patients younger than 50 years of age, the total annual indirect cost was estimated to 226,537 SEK (CI, 162,270–282,986) for state P, 174,553 SEK (CI, 59,744–320,485) for state R, 65,574 SEK (CI, 34,729–105,360) for state S, and 171,976 SEK (CI, 119,801–221,925) for state M. For patients between 50 and 64 years of age, the total annual indirect cost was estimated to 164,773 SEK (CI, 117,154–216,767) for state P, 263,826 SEK (CI, 119,691–335,307) for state R, 68,717 SEK (CI, 45,280–96,551) for state S, and 179,147 SEK (CI, 124,970–225,499) for state M.

Total Cost

The total cost was estimated for all the different disease states and for several different age groups. The total cost was substantially higher for the patients groups that were younger than 65 years of age, due to the high indirect costs caused by absence from work and early retirement incurred by these patients. In all age groups, state S had considerably lower costs than the other states (Table 5).

DISCUSSION

This study used retrospective database analysis to estimate direct medical resources use and costs and a patient questionnaire to evaluate informal care and work capacity of breast cancer patients in different states of their disease. Direct medical costs were substantially higher for state P, state R, and state M compared with state S. This finding seems logical because curative treatment for breast cancer normally is concentrated within the year following a primary diagnosis or a recurrence and that palliative treatment is given to patients with metastatic breast cancer. However, patients in state S still had substantial direct medical costs. The direct medical

Table 5. Annual Total Cost of Breast Cancer in Different Disease States and Age Groups

	Age < 50		Age 50–64		Age < 65		Age 65+		All patients	
State	*N*	Total cost	*N*	Total cost	*N*	Total cost	*N*	Total cost	*N*	Total cost
First year after primary breast cancer	22	343,759 SEK ($47,877)	35	239,356 SEK ($33,337)	57	280,360 SEK ($39,047)	15	80,431 SEK ($11,202)	72	239,100 SEK ($33,301)
First year after recurrence	6	301,821 SEK ($42,036)	9	384,648 SEK ($53,572)	15	350,906 SEK ($48,873)	6	92,369 SEK ($12,865)	21	278,119 SEK ($38,735)
Second and following years after primary breast cancer/recurrence	41	94,876 SEK ($13,214)	101	92,933 SEK ($12,943)	142	93,621 SEK ($13,039)	43	18,374 SEK ($2,559)	185	76,183 SEK ($10,610)
Metastatic disease	22	312,796 SEK ($43,565)	33	345,850 SEK ($48,169)	55	333,663 SEK ($46,471)	12	122,284 SEK ($17,031)	67	296,222 SEK ($41,257)
Total	91		178		269		76		345	

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https://doi.org/10.1017/S0266462307070328 Published online by Cambridge University Press

cost of patients in state S was considerably higher compared with the year before their primary breast cancer diagnosis, suggesting that, even if the patients remains recurrence free, breast cancer increases the direct medical costs.

Informal care were not a large part of the total cost of breast cancer. However, because informal care can be considered a nonmarket commodity, it is difficult to assign a value, because there is no market price available. We used 35 percent of the gross wage rate as a proxy for the cost of leisure time lost (8). Had we instead assumed that caregivers do in fact reduce their employment level to provide informal care, we would instead have used the human capital theory to estimate the value of the resulting production loss. This strategy would have lead to an estimated cost per hour of informal care of 213 SEK instead of the 53 SEK we used in this study, thus substantially increasing our estimated cost of informal care.

Indirect costs constitute a substantial share of the total cost for breast cancer patients younger than 65 years of age. This finding is consistent with previous studies where it was estimated that the cost for hospitalization and ambulatory care in Sweden was lower than the indirect cost of absence from work and early retirement (9). The mean number of working hours lost from absences due to breast cancer was generally higher for the age group younger than 50 years of age compared with the age group 50–64. This finding seems reasonable because an increasing age is associated with a decrease in labor force participation (13). Our study also indicates that the year following initial breast cancer diagnosis or breast cancer recurrence is associated with a high degree of absences from work, which substantially decreases the following years, if the patients remain recurrence free. It also suggests that advancing to metastatic disease is associated with a substantial decrease in work capacity. This conclusion is consistent with previous studies that have found absence from work is being caused by treatment-related symptoms (3).

Using data on distant recurrences, we also performed subgroup analysis on patients with metastatic disease. Metastatic patients who did not have a new distant recurrence more than 1 month after their first distant recurrence registered in the OC database had a mean annual inpatient episode and outpatient visit cost of 76,335 SEK (CI, 64,124–91,443), a mean annual cost of informal care of 5,684 SEK (CI, 2,165–12,919), a mean annual indirect cost of 173,924 SEK (CI, 119,563–226,768) for patients younger than 50 years of age, and a mean annual indirect cost of 168,141 SEK (CI, 114,645–221,561) for patients between 50 and 64 years of age. Metastatic patients who had at least one new distant recurrence more than 1 month after their first distant recurrence had a mean annual inpatient episode and outpatient visit cost of 155,111 SEK (CI, 103,547–234,870), a mean annual cost of informal care of 21,923 SEK (CI, 5,011–52,615), a mean annual indirect cost of 159,640 SEK (CI, 61,070–295,711) for patients younger than 50 years of age, and a mean annual indirect cost of 240,780 SEK (CI, 60,732–315,020) for patients between 50 and 64 years of age. Only the difference in annual inpatient episode and outpatient visit cost between the two groups was statistically significant at the .05 level.

To our knowledge, there are no recent studies that have investigated the resource use and cost in different states of breast cancer in Sweden, but there are studies from the United States and France. A study by Bercez et al. (1) found that direct medical cost in the year following a locoregional recurrence and distant recurrence was approximately 70,000 FFR and 125,000 FFR, respectively (corresponds to approximately 110,000 and 197,000 SEK, respectively, in year 2005 SEK). The cost for the first year after a locoregional recurrence is consistent with our study, but the cost for the first year after a distant recurrence is higher than our estimates for the annual direct medical cost following metastatic disease.

A study by Rao et al. (10) found that patients with metastatic breast cancer had significantly higher direct medical costs compared with a control group of matching age. Rao et al. reported a mean direct medical cost of $35,164 per metastatic breast cancer patient during an average follow-up of 16.2 months (corresponding to approximately 199,000 per year in year 2005 SEK). This value was higher than our estimate of the annual cost following metastatic disease, which could be explained by the fact that it reflects a cost relevant to the U.S. healthcare system.

In cost-effectiveness analysis of breast cancer treatments, costs have to be assigned for each possible state of breast cancer included in the analysis. A study by Bonneterre et al. (2) estimated the annual direct medical cost of patients receiving adjuvant chemotherapy for their primary breast cancer to range between €9,132 and €11,294 (corresponding to approximately 85,000–106,000 SEK in year 2005 SEK). This finding was consistent with our estimate of the annual direct medical cost in the year following primary breast cancer.

A study by Delea et al. (4) estimated that the direct medical cost in the year following a contralateral and a locoregional recurrence to $24,483 and $19,500, respectively, (corresponds to approximately 182,000 and 143,000 SEK, respectively, in year 2005 SEK), which was higher than our estimates. Delea et al. also estimated that the direct medical cost in the year following a distant recurrence was $42,300, with the cost dropping to $21,900 per year in the following years (corresponds to approximately 311,000 and 161,000 SEK, respectively, in year 2005 SEK), which also was higher than our estimates.

A study by Elkin et al. (6) estimated, based on a previously published article, the direct medical cost of progressive metastatic disease to $390 per week, corresponding to approximately 155,000 SEK per year in year 2005 SEK. This value is consistent with our estimated direct medical cost for metastatic patients who had at least one new

distant recurrence more than 1 month after their first distant recurrence.

In terms of limitations to this study, our selection method of using consecutive patients coming for outpatient visits might cause a selection bias. For nonmetastatic patients, it can be expected that patients with more severe disease symptoms will tend to be overrepresented in the study, because these patients are more likely to visit an outpatient clinic than patients with less severe symptoms. This situation would tend to overestimate the direct medical cost and underestimate the work capacity of these patients. Patients with metastatic breast cancer included in this study could be expected to have better health and mobility than the average metastatic breast cancer patient. The reason for this conclusion is that no breast cancer patients who were admitted to inpatient care or any terminal care facilities were included in our study, thus excluding those metastatic breast cancer patients who could be expected to have the highest direct medical costs and lowest work capacity.

Another limitation was that all the patients included in the study came from the same geographic area: Stockholm County. Demographic factors and socioeconomic factors that influence the direct medical resource use and work capacity could very well be different in Stockholm County compared with the rest of Sweden. Treatment patterns for breast cancer could also be different in Stockholm County compared with the rest of Sweden, influencing the direct medical resources use.

POLICY IMPLICATIONS

When designing policies for the detection, prevention, and treatment of breast cancer, it is important to take into consideration the indirect costs as well as the direct costs of breast cancer, because the indirect costs constitute more than 50 percent of the cost for patients younger than 65 years of age. Although indirect costs do not burden the healthcare budget, they still represent an important economic cost, and ignoring these costs could lead to suboptimal policy decisions from a societal perspective.

CONCLUSIONS

The first year following a primary breast cancer diagnosis or a recurrence is associated with high direct medical costs as well as high indirect costs. For patients who remain recurrence free, the second and following years after primary breast cancer or recurrence have substantially lower direct medical cost and indirect costs, indicating that most of the resource use and negative labor effects due to breast cancer are concentrated in the year following a primary breast cancer or recurrence. However, the direct and indirect costs for recurrence-free patients are not zero, indicating a permanent effect on medical resources use and on labor supply caused by breast cancer. Patients advancing to metastatic breast cancer have a substantial increase in direct medical costs and indirect costs compared with recurrence-free patients in their second or following years after a primary breast cancer or recurrence.

CONTACT INFORMATION

Mathias Lidgren, Bachelor of Science in Business Administration (hemli@hhs.se), PhD student, Medical Management Centre, Karolinska Institutet, Nobels väg 5, SE 171 77 Stockholm, Sweden

Nils Wilking, MD, PhD (nils.wilking@telia.com), Associate Professor, Department of Oncology, Karolinska Institutet, SE 171 76 Stockholm, Sweden

Bengt Jönsson, PhD (Bengt.Jonsson@hhs.se), Professor, Department of Economics, Stockholm School of Economics, Sveavägen 65, SE 113 83 Stockholm, Sweden

Clas Rehnberg, PhD (clas.rehnberg@ki.se), Associate Professor, Medical Management Center, Karolinska Institutet, SE-171 77 Stockholm, Sweden

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https://doi.org/10.1017/S0266462307070328 Published online by Cambridge University Press