



Complementary medicine use and costs in patients with breast cancer who experienced treatment-related side effects: A cross-sectional survey in Korea



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ABSTRACT

Objectives: Population-based information on the costs of complementary medicine for treatment-related side effects in patients with breast cancer is scarce. We aimed to investigate the prevalence and expenditure on complementary medicine in patients with breast cancer who experienced treatment-related side effects.

Design and setting: Two datasets were analyzed: 1) a 2017 survey on direct and indirect costs for treatment-related side effects, which was completed by 100 patients with stage 0-IV breast cancer, and 2) a Korean representative cross-sectional survey (Patient Survey 2014) that examined the prevalence of integrative medicine in 41 patients with breast cancer.

Main outcome measures: The direct and indirect costs for treatment-related side effects.

Results: In the first dataset, the mean total direct medical cost for complementary medicine was US\$1,584 and the mean indirect cost was US\$6,988 per patient per year. Some patients (6%) visited non-medical institutions to utilize complementary medicine and additionally spent US\$460 per patient per year. Approximately one-third of participants reported a substantial-to-heavy financial burden for using complementary medicine. However, only 17% of patients got information about complementary medicine through their physician. In the second dataset, 49% of patients with breast cancer who were discharged from Korean Medicine hospitals in Patient Survey 2014 data indicated that integrative medicine had been used.

Conclusions: Despite some complementary medicine could be reimbursed by National Health Insurance in Korea, a considerable number of patients reported an economic burden associated with their use of complementary medicine. Strategies for guiding patients to receive evidence-based and cost-effective complementary medicine are needed.

1. Introduction

Breast cancer is the most common cancer and cause of cancer-related death in women worldwide.¹ In Korea, the incidence of breast cancer has shown an increasing trend in recent years, being higher than that of Japan.² An estimated 33–47% of patients with cancer worldwide use complementary and alternative medicines (CAMs).^{3,4} In Korea, almost 67% of patients with breast cancer have used CAMs.⁵ Patients with cancer use complementary medicine for various reasons, including cancer treatment, prevention of progression, mitigation of symptoms, and enhancement of the immune system.⁵ A Korean study reported that the most common reasons for the use of complementary medicine by

patients with breast cancer was prevention of progression (39.4%), followed by mitigation of symptoms (32.1%).⁵ Thus, the symptom burden in patients with breast cancer is considerable.

Considering the increasing prevalence of breast cancer and the use of complementary medicine in patients with breast cancer, up-to-date estimates of the expenditure on complementary medicine use in patients with breast cancer are needed. It is well known that breast cancer has a considerable economic burden regarding both direct and indirect costs from hospitalization, pharmaceuticals, and productivity loss.⁶ However, population-based information on the cost of complementary medicine for the treatment-related side effects of breast cancer is scarce. Thus, the primary objective of this study was to investigate the

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economic impacts of the treatment-related side effects, which includes costs of complementary medicine and productivity losses. The secondary objective was to examine the prevalence of integrative medicine, use of complementary medicine in collaboration with conventional oncology treatment, in patients with breast cancer in Korea.

2. Materials and methods

2.1. Survey on the economic burden of complementary medicine for patients with breast cancer

The primary data source used was an online survey that we conducted in February 2017 among patients with breast cancer who experienced treatment-related side effects. The methods and procedures of this survey were reviewed and approved by the Kyung Hee University Institutional Review Board (KHSIRB-16-078(NA)). Letters of informed consent were acquired prior to enrollment, and patients participated in the survey voluntarily. All survey data were stored in a secure server after deidentification. Potential participants in 10 societies of patients with breast cancer in Korea were e-mailed invitations with a Web link, which directed them to a computer-aided Web interview. Of the 121 patients who were invited to participate, 21 did not complete the survey and were excluded.

The 58-item survey was developed to assess complementary medicine use and the costs associated with breast cancer. The questionnaires were developed from a literature review and were revised after discussion with Korean Medicine Doctors at a tertiary hospital in Korea. After distribution to a pilot group of 5 patients, the survey was further revised. In this study, we focused on the costs related to supportive care for treatment-related side effects in patients with breast cancer. We ignored the costs related to screening and active treatments (i.e., chemotherapy, endocrine therapy, or radiation) for breast cancer. Thus, the survey items mainly included followings: (1) sociodemographic data (i.e., age, sex, education, income level) and clinical characteristics (i.e., year of diagnosis, stage of breast cancer, types of treatment-related side effects); (2) types and costs of the complementary medicine, including Korean medicine, over-the-counter (OTC) medications, dietary supplements, and folk remedies; (3) costs of transportation, time, and nursing care; (4) productivity loss at work; and (5) information sources about complementary medicine, financial burden, and effect of complementary medicine overall on symptom.

To estimate the direct medical costs associated with treatment-related side effects, questionnaires inquired about all complementary medicine used. Each patient was asked about the following: number of outpatient, inpatient, and emergency department visits; types of hospitals visited; types and expenditure on complementary medicine. To estimate direct non-medical costs, including transportation, time, and nursing costs, we asked each patient about the following: types and costs of transportation to the hospital, time required for visiting the hospital; and time spent with a caregiver and type(s) of caregiver(s).

To estimate indirect costs, each patient was asked to complete a modified version of the Work Productivity and Activity Impairment (WPAI) questionnaire v2.0. The WPAI assesses productivity at work during the previous 7 days and has six questions.⁷ Because there is no version of the WPAI related to breast cancer treatment-related side effects, we modified the WPAI and had it reviewed by experts and physicians. Absenteeism was calculated as the hours missed because of breast cancer treatment-related side effects divided by the hours usually worked. Presenteeism was calculated as the percentage of impairment due to breast cancer treatment-related side effects experienced while working. Overall productivity loss was calculated as follows: (percentage of hours missed) + [(percentage of hours actually worked) × (percentage of impairment while working)]. The percentage of each type of productivity loss ranged from 0% to 100%, with higher values indicating a greater degree of impairment. The human capital approach was used to calculate the indirect costs. We calculated the indirect costs

by multiplying the hours lost from work by the average hourly wage in Korea.

To investigate the financial burden to use complementary medicine, we asked survey participants to answer by selecting a number on the following five-point scale: 1 = absolutely no burden; 2 = no burden; 3 = moderate burden; 4 = substantial burden; 5 = heavy burden. Then, we grouped 1 and 2 as 'no burden', 3 as 'moderate burden'; and 4 and 5 as 'substantial-to-heavy burden'. In addition, we further explored the monthly household income distribution by each financial burden.

To investigate the effects of complementary medicine overall on symptom, we asked survey participants to answer by selecting a number on the following five-point scale: 1 = greatly exacerbated; 2 = exacerbated; 3 = same as previous; 4 = relieved; 5 = greatly relieved. Then we grouped 1 and 2 as 'symptom exacerbation', 3 as 'no change in symptom', 4 and 5 as 'symptom relief'.

All costs were adjusted to the 2016 Korean won by using the consumer price index from Statistics Korea and converted from Korean won to US dollars based on the currency rate. Multiple responses were allowed for questions about the types of treatment-related side effects, types of complementary medicine, and hospitals visited. We selected a limited recall period of 1 year.

2.2. Survey on the prevalence of integrative medicine use by patients with breast cancer

The secondary data source was a Korean representative cross-sectional survey (Patient Survey 2014). This survey had several advantages. First, it used a representative sample of Koreans, covering all medical institutions and regions. In addition, the survey was completed by hospital personnel other than patients, so detailed medical resource use information could be obtained. The survey data consisted of outpatient data and discharged patient data, and included the following domains: demographics, diagnosis codes (*International Classification of Diseases, Tenth Revision [ICD-10]*), procedure codes (*International Classification of Diseases, 9th Revision: Clinical Modification*), type of medical institution, results of treatment, status of insurance coverage, activities of daily living score, integrative medicine use, and the purpose of integrative medicine treatment.⁸ Because integrative medicine data was only included in discharged patient data, we identified patients with breast cancer based on the following: (1) patients who were discharged from Korean medicine hospitals and (2) patients who were diagnosed as having breast cancer (*ICD-10* code C50).

2.3. Statistical analysis

All data were entered into Microsoft Excel (Microsoft Corp., Redmond, WA, USA) and analyzed using SPSS version 22.0 (IBM corp., Armonk, NY, USA).

3. Results

3.1. Patient characteristics

A total response rate of 83% was achieved. From February 8 to February 22, 2017, 100 participants completed the survey. The characteristics of the survey participants are shown in Table 1. The mean age was 55 years, with 100% of the participants being female. The proportions of cases of stage 0, I, II, III, and IV breast cancers were 1%, 25%, 34%, 38%, and 2%, respectively. Seventeen respondents were divorced or separated, and 85 respondents had no job. For household income per month, 24% reported < 2 million KRW (< US\$1723), 33% reported 2–4 million KRW (US\$1723–3447), 27% reported 4–6 million KRW (US\$3447–5170), 7% reported 6–8 million KRW (US\$5170–6894), and 9% reported ≥ 8 million KRW (≥ US\$6894). The most common treatment-related side effects were anxiety/distress and fatigue.

Table 1
Characteristics of the 2017 online survey participants (n = 100).

Characteristics	Mean/N ¹	SD/%
Age (years), mean and SD	55.0	6.2
Age at diagnosis (years), mean and SD	50.5	5.9
Sex		
Female	100	100.0
Marital status		
Single	3	3.0
Married	80	80.0
Divorced/widowed/separated	17	17.0
Occupation status		
Employed	15	15.0
Unemployed	85	85.0
Household income per month ²		
< 2 million KRW	24	24.0
2-4 million KRW	33	33.0
4-6 million KRW	27	27.0
6-8 million KRW	7	7.0
≥ 8 million KRW	9	9.0
Insurance type		
National Health Insurance	95	95.0
Medical Aid	5	5.0
Private insurance		
Yes	77	77.0
No	23	23.0
Breast cancer stage		
0	1	1.0
I	25	25.0
II	34	34.0
III	38	38.0
IV	2	2.0
Types of treatment-related side effects ³		
Anxiety/distress	52	52.0
Fatigue	52	52.0
Depression	42	42.0
Pain	39	39.0
Edema	32	32.0
Hot flashing	19	19.0
Nausea/vomiting	10	10.0
Skin problem	1	1.0
Arthritis	1	1.0
Gum problem	1	1.0
Toothache	1	1.0
Epistaxis	1	1.0
Hair loss	1	1.0
Anal problem	1	1.0
Constipation	1	1.0

KRW, Korean Won.

¹ Data are presented as mean/SD for continuous variables and N/percentage for categorical variables.

² The exchange rate of Korean won to the US dollar was 1160.5 Korean won/US dollar in 2016.

³ Multiple responses were allowed and percentages were calculated based on 100 patients.

3.2. Direct medical costs for breast cancer treatment-related side effects

The average numbers of outpatient, inpatient, and emergency department visits to utilize Korean medicine were 22, 15, and 15 during the previous 12 months. Fig. 1 shows the Korean medicine used for treatment-related side effects by patients with breast cancer in 2016. Physical therapy was the most commonly used Korean medicine during that year. The most expensive Korean medicine was uninsured herbal medicine. The mean annual cost for uninsured herbal medicine was US \$1281.78, while the annual costs of the rest of the Korean medicine were all below US\$926.32 (Table 2). The total out-of-pocket cost of Korean medicine for treatment-related side effects per patient per year was calculated to be US\$829.10.

Table 3 shows the mean annual costs for the use of OTC products, dietary supplements, and folk remedies by patients with breast cancer who experienced treatment-related side effects. The annual cost for

bamboo salt was the highest, followed by selenium supplements (Table 3). The total mean cost for using OTC products, dietary supplements, and folk remedies per patient per year was calculated to be US\$754.95. Thus, the total direct medical cost of complementary medicine per patient per year was calculated to be US\$1,584.05.

3.3. Direct non-medical costs for breast cancer treatment-related side effects

The mean costs of transportation, time, and nursing care per year expended to visit the hospital for treatment-related side effects were US \$170.68, US\$820.93, and US\$1358.86, respectively. Thus, the total direct non-medical cost per patient per year was calculated to be US \$2,350.47.

3.4. Indirect costs for breast cancer treatment-related side effects

Approximately 12% of the participants of this survey were employed. On average, they reported missing 17.2 h of work during the previous 7 days due to treatment-related side effects (Table 4). The impact of productivity loss on the mean annual cost per patient is illustrated in Fig. 2. The total indirect cost due to breast cancer was estimated to be US\$6988.40 per patient per year.

3.5. Total economic burden of breast cancer treatment-related side effects

Considering the number of patients who were diagnosed with breast cancer in Korea in 2014 (n = 158,916) and the prevalence rate of complementary medicine use by patients with breast cancer in Korea (67%), it can be estimated that the total economic burden of treatment-related side effects in patients with breast cancer is US\$1,163,006,984 per year (Table 5). The proportion of presenteeism cost to total cost was the highest (62%), followed by direct non-medical cost (22%).

Fig. 3 shows the patient-reported financial burden of complementary medicine use for patients with breast cancer. Almost one-third of participants reported a substantial-to-heavy burden related to the use of complementary medicine to manage treatment-related side effects (Fig. 3A). In the no burden group, the proportions of patients whose monthly household income was < 2 million KRW was 12.5%. In the substantial-to-heavy burden group, the proportions of patients whose monthly household income was < 2 million KRW was 41.2% (Fig. 3B).

In addition, survey participants reported that they wished to spend US\$95 per month for complementary medicine use (data not shown).

3.6. Costs spent in non-medical institutions to utilize complementary medicine for breast cancer treatment-related side effects

Of the 100 survey participants, 6 patients used complementary medicine at non-medical institutions. They spent US\$460 as direct medical costs per patient per year in these institutions (data not shown).

3.7. Information sources about complementary medicine of patients with breast cancer

When multiple responses were allowed, patients with breast cancer who experienced breast cancer treatment-related side effects used the following information sources to utilize complementary medicine: other breast cancer patients (83%); internet (41%); television (29%); and family or friends (20%). Patients who got the information through their physician were only 17% (data not shown).

3.8. Effect of complementary medicine overall on symptom

When we surveyed the effect of complementary medicine overall on symptom, 51% of survey participants reported they experienced

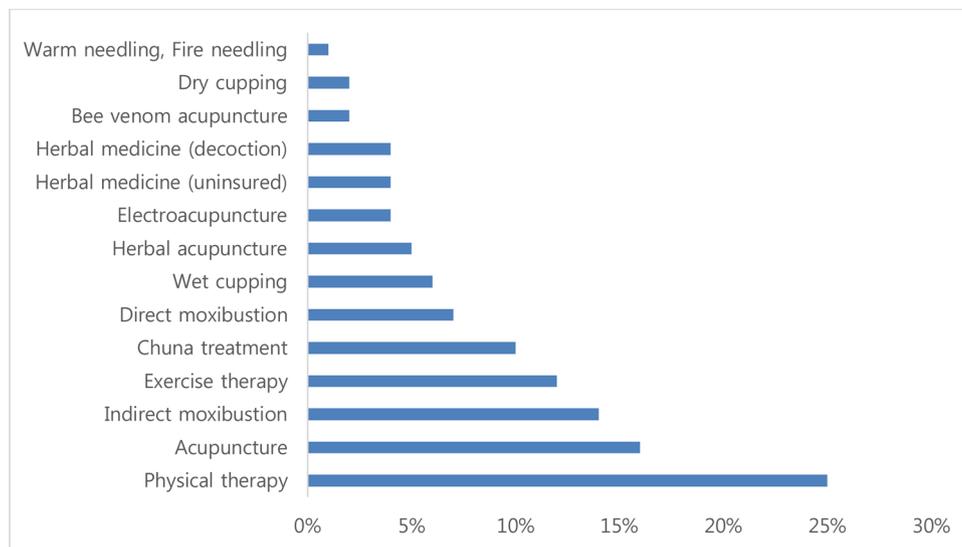


Fig. 1. Types of complementary medicine used for treatment-related side effects by breast cancer patients¹.

Table 2

Annual out-of-pocket costs of complementary medicine per patient for breast cancer treatment-related side effects.

Complementary medicine ¹	Annual costs per patient ²	
	Mean	SD ³
Acupuncture	\$130.22	120.76
Electroacupuncture	\$46.32	29.72
Warm and fire needling	\$25.85	ND
Herbal acupuncture	\$336.06	326.20
Bee venom acupuncture	\$47.39	54.84
Direct moxibustion	\$263.90	461.67
Indirect moxibustion	\$305.96	467.93
Dry cupping	\$142.18	164.51
Wet cupping	\$237.68	345.69
Chuna treatment	\$633.35	726.95
Exercise therapy	\$392.07	482.11
Physical therapy	\$287.43	379.09
Herbal medicine (uninsured)	\$1281.78	890.22
Herbal medicine (decoction)	\$926.32	618.88

¹ Multiple responses were allowed.

² The exchange rate of Korean won to the US dollar was 1160.5 Korean won/US dollar in 2016.

³ ND indicates that the data were insufficient.

symptom relief, 6% of the survey participants reported they underwent symptom exacerbation, and 43% of the survey participants reported that they felt no change in symptom after using complementary medicine (data not shown).

3.9. Prevalence of integrative therapy use by patients with breast cancer

Of the 41 patients with breast cancer who were discharged from the Korean medicine hospitals in the Patient Survey 2014 data, 20 (49%) indicated that integrative therapies for breast cancer had been used (Table 6).

4. Discussion

This study shows the overall trends in the use of complementary medicine in patients with breast cancer. It also provides the first

¹ Multiple responses were allowed and percentages were calculated based on 100 patients.

Table 3

Annual costs of over-the-counter products, supplements, and folk remedies for breast cancer treatment-related side effects.

Categories ¹	Annual costs per patient ²	
	Mean	SD ³
Bamboo salt	\$8,617	0.00
Selenium supplements	\$2,154	ND
Red ginseng	\$1,122	1609.97
Propolis	\$830	1916.92
Glutathione	\$560	ND
Aloe	\$384	448.85
Mushroom	\$374	329.51
Silicone implants	\$367	119.96
Detoxification	\$345	ND
Omega-3 supplements	\$200	277.02
Nutritional supplements	\$190	111.25
Bandage	\$172	ND
Circulatory drugs	\$172	ND
Onion	\$155	ND
Dietary therapy	\$150	176.17
Fermented food	\$129	ND
Vitamins	\$102	62.31
Radiofrequency hyperthermia treatment	\$98	43.87
Aronia	\$95	12.19
Hot massage	\$92	103.29
Foot bath	\$86	ND
Calcium supplements	\$80	44.22
Salt	\$65	18.28
Spirulina	\$62	58.49
Hemp seeds	\$56	22.80
Circulatory device	\$52	72.51
Graviola	\$51	11.76
Lower-body bathing	\$29	19.50
Dietary sulfur	\$26	ND
Yeast	\$9	ND
Gastrointestinal drugs	\$5	ND
Pain medications	\$3	ND
Exercise	\$0	0.61
Meditation	ND	ND

¹ Multiple responses were allowed.

² The exchange rate of Korean won to the US dollar was 1160.5 Korean won/US dollar in 2016.

³ ND indicates that the data were insufficient.

estimates of direct and indirect costs for patients with breast cancer who experienced treatment-related side effects. Patients with breast cancer who experienced treatment-related side effects spent US\$1,584

Table 4
Lost work productivity for patients with breast cancer treatment-related side effects.

Types of productivity loss	Productivity loss
<i>Absenteeism</i>	
%, mean (SD) ¹	5.29 (14.35)
Hours/week, mean (SD)	0.58 (1.44)
<i>Presenteeism</i>	
%, mean (SD) ¹	35.83 (28.11)
Hours/week, mean (SD)	16.58 (18.10)
<i>Overall productivity loss</i>	
%, mean (SD) ¹	38.59 (29.87)
Hours/week, mean (SD)	17.16 (15.35)
<i>Daily activity impairment</i>	
%, mean (SD) ¹	41.20 (22.03)

¹ Higher percentages indicate greater impairment.

as direct medical costs per patient per year. In a previous study that reported the economic burden of breast cancer in Korea, the estimated total direct medical costs were US\$399.22 million in 2010.⁹ However, there were only 77,809 patients with breast cancer in 2010 in Korea, almost half the number in 2014. Furthermore, the direct medical costs in the previous study did not include any complementary medicine.⁹ Therefore, our study is meaningful because it estimates costs that were not considered in earlier studies.

The costs of productivity loss at work due to treatment-related side effects in patients with breast cancer were more than 1.5 times greater than the direct costs. To the best of our knowledge, no reports have examined the economic burden of patients with breast cancer who experience treatment-related side effects. According to a previous study on the economic burden of patients with breast cancer, the total indirect costs are almost two times greater than the total direct costs.¹⁰ However, a direct comparison to our study is difficult because the direct cost in our study is the cost to manage treatment-related side effects, not to treat breast cancer itself; the costs reported in the previous study are from 2002, so they are outdated; and the costs and insurance coverage vary from country to country. Annual direct non-medical costs (i.e., transportation costs, time costs, and nursing costs) were also high and were similar to direct medical costs. This may be due to relatively frequent visits to medical institutions to manage treatment-related side effects. Furthermore, most patients were elderly, with more than half of

survey participants being accompanied by caregivers when they visited a physician.

In addition, we found that some patients with breast cancer receive complementary medicine at non-medical institutions. In our study, 6% of patients used complementary medicine at non-medical institutions and the total cost spent at these non-medical institutions per patient per year was US\$460. Although we did not assess the detailed information, including frequency, types, and consequences of complementary medicine use at non-medical institutions, it is questionable whether complementary medicine provided by unqualified persons are effective. Furthermore, although several complementary medicines, such as acupuncture, moxibustion, cupping, and physical therapy are covered by National Health Insurance in Korea, patients who use complementary medicine at non-medical institutions would not receive these benefits. Thus, strategies for guiding patients to receive evidence-based and cost-effective complementary medicine from qualified doctors may be needed. In addition, we found that patients with breast cancer reported a considerable financial burden to utilize complementary medicine, but only 17% of patients got information about complementary medicine through their physician, while 83% of patients got information through other breast cancer patients. Thus, clinical practice guidelines or other strategies are needed to inform patients with breast cancer and physicians about cost-effective complementary medicine that are reimbursed by National Health Insurance. Of the uninsured complementary medicines, cost-effective therapies should be discovered and reimbursed. We thought that if there are efforts to support studies on complementary medicine, to develop evidence-based clinical practice guideline, to establish and inform cost-effective strategies, and to approve reimbursement (National Health Insurance) based on pharmacoeconomic evidences by government and related institutions, the financial burden in patients with cancer-treatment related side effects can be reduced.

The estimated total cost (sum of direct and indirect cost) per patient per year in patients with breast cancer who experienced treatment-related side effects was US\$10,922. Although this study does not include the cost of conventional treatments for the treatment of breast cancer itself, it is significant because many patients with breast cancer experience treatment-related side effects due to surgery, radiation, or anticancer drugs and show interest in the use of complementary medicine to alleviate their side effects.

Regarding integrative medicine use, we found that 49% of patients

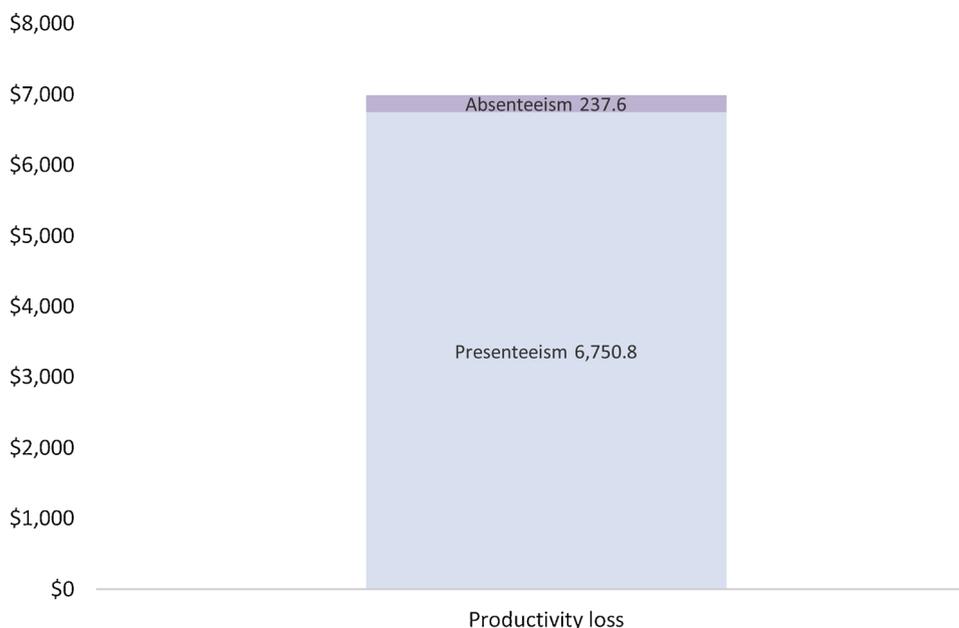


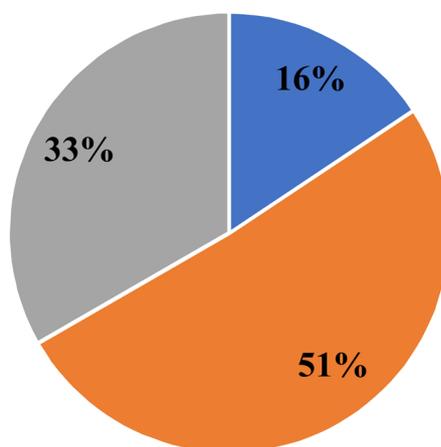
Fig. 2. Annual indirect costs (costs of productivity loss) per patient with breast cancer.

Table 5
Total economic burden of treatment-related side effects for patients with breast cancer per year.

Type of cost	Total economic burden ^{4,5}	Mean annual costs per patients ⁵	Proportion of total costs (%)
<i>Direct cost</i>	\$418,924,082.48	\$3,934.52	36.0
Direct medical cost ¹	\$168,660,139.70	\$1,584.05	14.5
Direct non-medical cost ²	\$250,263,942.78	\$2,350.47	21.5
<i>Indirect cost³</i>	\$744,082,901.60	\$6,988.40	64.0
Absenteeism	\$25,297,157.66	\$237.59	2.2
Presenteeism	\$718,786,808.68	\$6,750.82	61.8
Total cost	\$1,163,006,984.08	\$10,922.92	100.0

¹ Direct medical cost includes out-of-pocket costs for using Korean medicine, over-the-counter products, dietary supplements, and folk remedies.
² Direct non-medical cost includes time costs and transportation costs.
³ Total economic burden due to absenteeism and presenteeism was calculated using the employment rate of women in 2016.
⁴ Total economic burden was calculated assuming that 158,916 patients were diagnosed with breast cancer and 106,474 (67%) patients utilized complementary medicine for treatment-related side effects.
⁵ The exchange rate of Korean won to the US dollar was 1160.5 Korean won/US dollar in 2016.

A Financial burden



■ No burden ■ Moderate burden ■ Substantial-to-heavy burden

B Monthly household income distribution by each financial burden

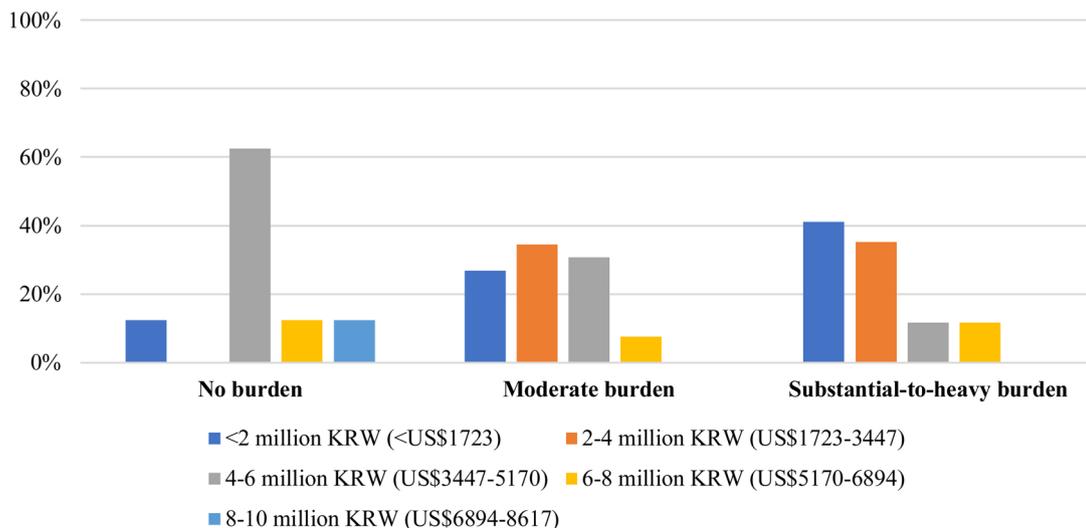


Fig. 3. Patient-reported financial burden of complementary therapy use for treatment-related side effects.

Table 6
Characteristics of breast cancer patients who participated in the Patient Survey 2014 (n = 41).

Characteristics	Mean/N ¹⁾	SD/%
Age (years), mean and SD	51.73	6.73
Age (years), minimum and maximum	34	67
Sex		
Male	1	2.4
Female	40	97.6
Length of stay (days), mean and SD	11.95	9.22
Integrative medicine use		
Yes	20	48.8
No	7	17.1
Types of insurance		
National Health Insurance	37	90.2
Medical Aid	4	9.8

¹ Data are presented as mean/SD for continuous variables and N/percentage for categorical variables.

with breast cancer who admitted in the Korean medicine hospital utilized integrative medicine. However, due to the limitation of the data sources, the utilization rate of integrative medicine in whole breast cancer patients could not be calculated. Further researches are warranted to explore the overall trend and the levels of benefit of integrative medicine in patients with breast cancer.

Our study has several limitations. First, recall bias may exist because the recall period was one year and we did not have access to information on patients' receipts on complementary medicine. However, to minimize any possible missing elements, we used a structured questionnaire form to identify the direct medical and non-medical costs, which was developed based on the standard question forms in the Korea National Health and Nutrition Examination Survey (KNHANES). KNHANES is a nationwide cross-sectional survey which have been regularly conducted by the Korea Centers for Disease Control and Prevention. To assess direct medical costs (i.e., costs for complementary medicine), questions about average annual frequency of complementary medicine use and average cost per use were developed. To assess direct nonmedical cost (i.e., transportation, time, and nursing costs), questions about types and costs of transportation to the hospital, time required for visiting the hospital, types of caregiver, and time and costs spent with caregiver(s) were developed. Second, the small sample size of this study may have biased the estimates of annual costs. Third, we did not ask the effect of complementary medicine on symptom by each complementary medicine that they used. Because the purpose of this survey was to identify an unlimited range of complementary medicine used by patients, we used multiple response questions and additionally asked how they benefited from the used complementary medicine overall. Thus, it was difficult to measure each complementary medicine-specific effect on symptom. Further studies need to be conducted to measure the effect of each complementary medicine that patients experienced. Fourth, we did not have access to medical records on the treatment-related side effects and the reason to use complementary medicine. However, we specified 'treatment-related side effects' as 'side effects occurred during anticancer treatment for breast cancer' and 'complementary medicine' as 'complementary medicine used to alleviate the treatment-related side effects' in all questions to ascertain the correlation between the complementary medicine and treatment-related side effects. Fifth, the estimated total economic burden in this study might not be completely extrapolated to represent all patients with breast cancer in Korea since we did not survey all breast cancer patients in Korea. However, since surveying the entire patients were not possible, we used a representative sample and estimated total economic burden by using the prevalence rate of complementary medicine in patients with breast cancer in Korea (67%) multiplied by the number of patients who were diagnosed with breast cancer in Korea (n = 158,916). Sixth, these cost issues and results in

this study should be limited to patients with breast cancer who experienced treatment-related side effects in Korea. Other countries may have different cost estimation related to the complementary medicine. Last, because only 2% of the survey participants had breast cancer stage IV, the treatment pattern in patients with metastatic breast cancer might not be represented well in this study. However, considering the proportion of patients with breast cancer stage IV (1.2%) in 2014 in Korea,² the impact of this limitation may not be significant, but further study is needed including more patients with advanced cancer.

Nevertheless, this study has significance as the first study to estimate the economic burden of patients with breast cancer who experienced treatment-related side effects.

5. Conclusion

Korean patients with breast cancer who experienced treatment-related side effects spent US\$1,584 per patient per year to utilize complementary medicine and 6% of patients utilized complementary medicine at the non-medical institutions and spent additionally US \$460. Indirect cost due to productivity losses was US\$6,988 per patient per year. Furthermore, patients with breast cancer reported a considerable financial burden to utilize complementary medicine, but only 17% of patients got information about complementary medicine through their physician, while 83% of patients got information through other breast cancer patients. Thus, clinical practice guidelines or other strategies are needed to inform patients with breast cancer and physicians about cost-effective complementary medicine that are reimbursed by National Health Insurance. Of the uninsured complementary medicines, cost-effective therapies should be discovered and reimbursed.

Authors' contributions

SH contributed to the data analysis, data interpretation, drafting, and revision of the manuscript. BHJ, HSS, and DSH contributed to the conception and design of the study, data analysis, data interpretation, and critical revision of the manuscript. All authors participated in the interpretation of results and critically revised the manuscript for intellectual content.

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Conflicts of interest

None.

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