Cost–utility analysis of individual psychosocial support interventions for breast cancer patients in a randomized controlled study

Cecilia Arving[1]*, Yvonne Brandberg[3], Inna Feldman[4], Birgitta Johansson[2] and Bengt Glimelius[2,3]

[1]*Department of Public Health and Caring Sciences, Section of Caring Sciences, Uppsala University, Uppsala, Sweden*
[2]*Department of Radiology, Oncology, and Radiation Science, Uppsala University, Uppsala, Sweden*
[3]*Department of Oncology-Pathology, Karolinska Institutet, Stockholm, Sweden*
[4]*Department of Women's and Children's Health, Social Paediatrics, Uppsala University, Uppsala, Sweden*

Correspondence to: Department of Public Health and Caring Sciences, Uppsala University, Box 564, SE-751 22 Uppsala, Sweden. E-mail: cecilia. arving@pubcare.uu.se

Abstract

Objectives: The aim was to explore the cost–utility in providing complementary individual psychosocial support to breast cancer patients compared with standard care (SC).

Methods: Patients just starting adjuvant therapy ($n = 168$) at Uppsala University Hospital, Sweden, were consecutively included and randomized into three groups: psychosocial support from a specially trained nurse (INS), from a psychologist (IPS), or SC. Psychological effects and healthcare utilization were monitored during a 2-year period. The hospital billing system provided cost estimates. Quality-adjusted life years (QALYs) were calculated using health-related quality of life data from the European Organization for Research and Treatment of Cancer Quality of Life Core Questionnaire (EORTC QLQ C-30) translated into the Euro Quality of Life- 5-Dimensional classification. On the basis of the medical cost offset, a cost–utility analysis was performed.

Results: Health care utilization was mainly related to the breast cancer diagnosis and treatment. The intervention costs amounted to about €500 or 3% of the total costs. Total health care costs, including interventions cost, were lower in the INS (€18,670) and IPS (€20,419) groups than in the SC group (€25,800). The number of QALYs were also higher in the INS (1.52 QALY) and IPS (1.59 QALY) groups, compared with the SC group (1.43 QALY).

Conclusions: The cost–utility analysis revealed that, during adjuvant treatment for breast cancer, the individual psychosocial support interventions provided here was cost effective because the health care costs were lower and QALYs were higher compared to SC alone.

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Introduction

In Sweden, breast cancer is a costly disease for the healthcare system [1]. The total cost for patients ≤65 years has been estimated to €30,435 during the first year after primary diagnosis [2]. For patients >65 years, the same cost was €8696. The total cost for following years varied between €1413–1956 [2]. The total mean cost for patients with metastatic disease has been estimated to €93,700 [3]. The largest single costs were for drugs and hospitalization constituting 36% and 22% of total costs, respectively.

Adjuvant therapy for breast cancer patients prevents recurrences and improves survival but can result in adverse effects with decreased health-related quality of life (HRQoL) and increased distress, both during treatment and afterwards [4–9]. Distress may be associated with increased utilization of healthcare resources [10–12]. In a study, breast cancer patients with anxiety and depression more often requested additional investigations to routine follow-up visits than non-distressed patients [13].

Support based on cognitive behavioral techniques may reduce psychosocial problems and increase HRQoL [14,15]. Psychosocial support may also reduce utilization of healthcare resources [16,17]. A meta-analytic review reported a cost reduction of about 20% associated with psychological interventions in various diseases [18]. Breast cancer patients have reported better psychological well-being and HRQoL, after a cognitive behavioral group, compared with a control group. There was also a 24% reduction in direct healthcare costs for the intervention group [19].

Economic analyses in psycho-oncology are rare but have been called for [16,20]. Few studies have related economic or resource utilization outcomes to psychosocial support interventions [17,19,21–23]. Carlsson and colleagues suggested that it would be of interest to conduct cost–utility analyses (CUA), which take into account both costs and improvement in HRQoL [16].

CUA, using quality-adjusted life years (QALYs), is a general approach in health economic evaluations [24,25]. QALY weighs the life expectancy of a patient against an

estimate of their HRQoL score (measured on a 0–1 scale). For assessment of HRQoL, economists prefer the generic instrument Euro Quality of Life-5-Dimensional Classification (EQ-5D) [26]. Population data are available, and responses to the EQ-5D can be transformed into HRQoL scores using a population 'tariff'. Generic instruments have the advantage of allowing comparisons of treatments in one disease with those of other diseases [24].

The majority of scientists prefer to measure HRQoL using disease-specific instruments, which are more sensitive to clinically important differences. The European Organization for Research and Treatment of Cancer (EORTC) developed a commonly used HRQoL questionnaire for cancer patients, the EORTC QLQ C-30 [27]. Although population values are available for some disease-specific instruments [28,29], the results cannot be used in CUA [24]. Given the extensive use of the EORTC QLQ C-30 worldwide, it has been mapped into the EQ-5D instrument [30]. QALYs calculated using predicted scores of the EQ-5D were almost identical to QALYs based on actual EQ-5D scores in that trial.

The EORTC QLQ C-30 was used in the 'Individual psychosocial support project' [31], which aimed to compare the effects of individual psychosocial support provided by the following: (i) oncology nurses trained in psychological techniques (INS) or by (ii) psychologists (IPS); and to (iii) standard care (SC) (control group) in 179 randomly assigned breast cancer patients. The results indicated that the interventions were beneficial to the patients regarding distress, HRQoL, and patient satisfaction and that INS was equally effective as IPS [31,32].

The primary aim of this study was to explore the cost–utility of INS and IPS compared with SC. The hypothesis was that the addition of individual psychosocial support could improve HRQoL and decrease health-care cost or least is cost neutral compared with SC.

Methods

Patients

During December 1997 to December 1999, consecutive breast cancer patients ($n = 425$), about to start adjuvant treatment at the Department of Oncology, Uppsala University Hospital, were considered for inclusion. On-going psychiatric illness, previous cancer, or inability to speak or understand Swedish ($n = 111$, 26%) were exclusion criteria. Twenty-six (6%) of 314 eligible patients were missed at inclusion because of administrative failure. Thus, a consecutive series of patients ($n = 288$) were approached after having received information about the adjuvant treatment. Of the 179 (62%) patients who accepted, 8 (4%) discontinued participation after randomization before responding to the baseline questionnaires. Data from the county hospitals utilization database were not retrieved

for three patients (2%) because of incorrect personal identification numbers. Thus, 168 patients were included in the study with follow-up until January 2002. Patients were randomized into one of three groups: INS ($n = 55$), IPS ($n = 57$), or SC ($n = 56$). The Research Ethics Committee at the Faculty of Medicine, Uppsala University, approved the project.

Interventions (INS and IPS)

The interventions are described in detail previously [31,32]. Both interventions took place outside the hospital, face-to-face or over the telephone, and started in median 20 days after inclusion (baseline assessment). They were intended to be similar and used the same techniques such as relaxation, distraction, activity scheduling, and ways to improve communication, methods derived from cognitive behavioral therapy [33,34].

Standard care

Standard care included contacts with medical staff according to ordinary routines. Referrals to a psychiatrist or social worker for discussion of psychosocial issues were arranged if the medical staff judged this to be necessary or if requested by the patient. These referrals were more common in the SC group ($n = 16$) than in the intervention groups together ($n = 8$) ($p < 0.02$) [31].

Resource utilization collection and analyses

Demographic and medical data were retrieved from patient files. Data on the utilization of healthcare were derived from the computerized patient administration systems used by the county. All outpatient hospital visits, irrespective of the reason, to any healthcare professional at the oncology, internal medicine, psychiatry, and surgery departments in Uppsala County were summed up to obtain the number of 'hospital outpatient visits' (HOPV). Length of hospitalization was calculated as follows: the days of admission and discharge were counted as 1 day in all, but no days were counted if admission and discharge took place on the same day. The length of stay of each admission was added up to obtain days of 'hospital inpatient care' (HIPC). Analyses of 'sessions in the intervention' were made according to the 'intention to treat principle', that is, patients in the intervention groups were assigned a first session even if they did not attend ($n = 3$). Health utilization was collected from each patient's study enrollment date and ending 730 days later.

Cost calculations

All costs in Swedish crowns (SEK) were obtained from Uppsala University Hospital, on the basis of the fiscal period 2006, which was the year the health care utilization data was retrospectively collected. These cost estimates

were inflated to reflect 2012 costs according to the Swedish national consumer price index [35] and then transformed into Euro (€) (€1 2012 = SEK 8.71). The costs, for example, for radiation or chemotherapy, might be different today, but the charges will be the same for all groups.

Because the interventions were similar and the differences in salary between the professions limited, the cost for the intervention was estimated at €148 per session. The cost included salary, a direct hospital component and an indirect allocation, that is, supervision. No associated cost to the intervention in regard to training was included, because training was not paid for by the government or the health care services. The same sum was used in the cost calculation for psychosocial support in connection with SC.

Patients receiving radiotherapy were assigned a cost of €7723, on the basis of the average cost for postoperative breast cancer radiation to 50–54 Gy given in 25–27 fractions, including visits to medical staff, radiation planning costs, equipment, X-ray, and overhead costs.

The most frequently used regime (77%) included 5-fluorouracil, epirubicin, and cyclophosphamide, was chosen to evaluate costs. The cost for eight cycles of 5-fluorouracil, epirubicin, and cyclophosphamide was €6113, including drugs, an implantable port, staff fees, standard antiemetics (steroids, a $5HT_3$-receptor antagonist, and metochlopramide), pharmacy salaries, laboratory tests, equipment, consultants, X-ray, and overhead costs.

The cost of a 20-min outpatient hospital visit was €280 being the cost of a standard visit to a physician. This sum was chosen because, in more than 95% of the cases, the patients consulted a physician when visiting a healthcare professional.

The hospitalization cost was based on the billing system for admissions used by the hospital. For a standard patient with complications, the most common reason for admission, the cost was €961 per day.

Costs for the patients and society because of disability and productivity loss are not included in the analyses. The total costs are reported as mean values with 95% confidence intervals (CIs).

Health utilities

Health utilities were obtained using the EORTC QLQ-C30 [27,36]. Measurements were made at seven assessment points, at baseline and at 1, 3, 6, 9, 12, and 24 months. Substitution of missing values was carried out according to the scoring manual [36]. Individual scores on the EORTC QLQ C-30 at each assessment point were multiplied by the β values from the regression analysis described in McKenzie and van der Pol's study [30]. Their study provides important support for the validity of our study, as the present results are based on predicted EQ-5D values. On the basis of recommendations for technology appraisal [25], a British National Health Service perspective was adopted. Missing EQ-5D values were interpolated or replaced so that the last observation was carried forward. QALYs were calculated on three tolerance levels. In low level, only cases were used in which all seven EQ-5D values existed. In high-level tolerance, all cases were included in which at least one EQ-5D value existed. An alternative tolerance level (the base case) required existence of at least one observation per year during the 24 months. The number of QALYs gained/lost relative to baseline was calculated for each patient, for the base case and for low and high tolerance levels, respectively.

Cost–utility analyses

Differences between randomization groups regarding resource use, costs, utility scores, and QALYs were analyzed using SPSS® version 20, Chi-2 test for categorical data, and one-way analysis of variance for continuous variables. For the three groups, values of total healthcare costs (healthcare costs + intervention costs) were calculated. Mean differences in costs between groups and 95% CIs were obtained by non-parametric bootstrap with 1000 replications [37]. Because of the short-time horizon, discounting of costs was not considered necessary.

The basic task of health economic evaluations is to measure and to compare the costs and consequences of the alternatives, in our case, INS and IPS compared with SC. In this evaluation, a so-called incremental analysis, mean differences in costs are compared with mean differences in health consequences, and the results are expressed as an incremental cost-effectiveness ratio\ for INS and IPS compared with SC. An intervention is defined as dominant when its costs are less and it's at least as effective as the comparator [25]. Effect size was calculated as 0.2 (medium) and statistical power as 0.316. To obtain a power of 0.8 (with an alpha level $p < 0.05$), 76 individuals are needed for each group [38].

Sensitivity analyses

Sensitivity analyses are needed to handle uncertainties in health economic evaluations. They systematically examine the influence of the variables and assumptions employed for the estimated cost-effectiveness results [39]. Most commonly, each uncertainty component of the evaluation are varied individually, whereas the others are held at their baseline values, to establish the separate effects of each component on the results.

In the present study several one-way sensitivity analyses were performed. Firstly, the QALY calculations were investigated on the two extreme tolerance levels, low and high. Secondly, separate analyses were performed for patient subgroups depending on tumor size (T1 and T2) and on lymph node metastases (N0, N1, and N2), that is, disease severity. Thirdly, outliers in INS or IPS sessions (>10, $n = 12$), outliers in HOPV (>56 visits, $n = 8$), and

outliers in HIPC (>83 days, *n* = 3) were excluded to check sensitivity to resource utilization calculation.

Results

Participants

More INS patients were diagnosed in stage N0 compared to the other groups (INS 67%, IPS 46% and SC 52%, *p* = 0.01). However, no statistically significant difference in number of patients receiving adjuvant chemotherapy was found (Table 1).

Health service resource use and costs

There were no statistically significant between-group differences in number of HOPV or HIPC during the two-year period (Table 2), although numerically more HIPCs were seen in SC. Thus; the costs for hospitalization and the total healthcare costs were higher in the SC group. The total health care costs (healthcare costs + intervention costs) were € 18 670 for INS, € 20 419 for IPS and for SC € 25 800 (Table 2).

Health utilities

Utility scores for seven assessment points are presented in Table 3. Missing rates were similar across groups at every point and increased from 0-2% at baseline to 30-40% at the last measurement. There were no statistically significant differences in HRQoL at baseline or in health improvement between groups. The number of QALY was numerically highest in the INP group (1.59) compared with the INS group (1.52) and the SC group (1.43) (Table 4).

Cost–utility analysis

The base-case analysis (Table 4) showed that, on average, the total healthcare costs in SC were higher compared to both intervention groups. The differences between the INS and SC were estimated as of €-7130 (95% CI €-4 286 to €-11 532) and between IPS and SC €-5 381 (95% CI €-2 732 to €-9 524), respectively (Figure 1). Since the number of QALYs was higher and the total health care costs were lower in both INS and IPS, both interventions were dominant compared to the SC.

Sensitivity analyses

The results of the sensitivity analyses generally confirmed the base-case statement, i.e. that both INS and IPS were dominant compared to SC (Table 4). For patients with no regional lymph node metastasis, the difference in total healthcare costs between IPS and SC was not as evident, but otherwise the INS and IPS were dominant compared to the SC for patients with and without regional lymph node metastasis. Exclusion of outliers in number of INS or IPS sessions, HOPV and HIPC did not influence the base-case statement.

Table 1. Demographic and medical background data of the study sample. Numbers in parentheses indicate percentages unless otherwise indicated

	INS	IPS	SC	Total
n	55	57	56	168
Age, years				
Mean (range)	55 (34–72)	55 (23–75)	55 (25–87)	55 (23–87)
Social status				
Married/cohabitant	45 (82)	43 (75)	40 (71)	128 (77)
Employed	36 (65)	36 (63)	37 (66)	109 (65)
Working at home/unemployed/student	5 (9)	5 (9)	4 (7)	14 (8)
Retired	11 (20)	15 (26)	11 (20)	37 (22)
Stage				
T 1	41 (74)	42 (74)	40 (71)	123 (73)
T2	11 (20)	11 (19)	12 (21)	34 (20)
N 0	37 (67)*	26 (46)	29 (52)	92 (55)
Type of surgery				
Sector resection + ax. diss.	48 (87)	43 (75)	41 (73)	132 (78)
Mastectomy + ax. diss.	7 (13)	13 (23)	15 (27)	35 (21)
Adjuvant polychemotherapy	15 (27)	28 (49)	21 (38)	64 (38)
Radiotherapy (RT)	54 (98)	56 (98)	52 (93)	162 (96)
Hormone therapy	23 (42)	29 (51)	32 (57)	84 (50)
2 Years after diagnosis				
Recurrence	1 (2)	1 (2)	2 (4)	4 (2)
Deceased	1 (2)	1 (2)	3 (5)	5 (3)

SD, standard deviation.
*Statistically significant group difference, p = .05.

Table 2. Mean (SD) and median values for utilization of health care resources and health care costs/patient during a two-year period in Euro (€) for the three randomization groups

	Groups	N	Mean (SD)/Median	Min	Max
Health care resource utilization					
Sessions with the INS or IPS	INS	55	3.8 (3.4)/2.0	1	16
	IPS	57	4.4 (4.4)/3.0	1	23
	SC	0			
Hospital outpatient visits	INS	55	50.5 (14.3)/45.0	13	84
	IPS	57	56.5 (20.2)/51.0	22	125
	SC	56	52.9 (18.9)/52.5	8	102
Hospital outpatient visits including sessions	INS	55	54.3 (15.0)/49.0	18	85
	IPS	57	60.9 (22.2)/56.0	23	137
	SC	56	52.9 (18.9)/52.5	8	102
Hospital inpatient days at county hospitals	INS	18	12.7 (17.9)/4.0	1	58
	IPS	21	11.2 (15.7)/5.0	0	48
	SC	23	27.8 (33.9)/11.0	0	122
Costs for					
Hospital outpatient visits (HOPV)	INS	55	14127 (4000)/12585	3636	23494
	IPS	57	15800 (5650)/14263	6153	34960
	SC	56	14803 (5287)/14683	2237	28528
Breast cancer treatment[a]	INS	55	7475		
	IPS	57	7969		
	SC	56	7332		
Other hospital outpatient visits	INS	55	*6652 (3002)/5594*	2237	14263
	IPS	57	*7831 (4955)/6712*	0	25731
	SC	56	*7472(3945)/6992*	0	19299
Hospital inpatient care (HIPC)	INS	55	3989 (11268)/0	0	55808
	IPS	57	3967 (10455)/0	0	46186
	SC	56	10996 (245274)/0	0	117390
Psychosocial intervention	INS	55	560 (507)/297	148	2381
	IPS	57	653 (656)/446	148	3423
	SC	56	0	0	0
Total health care costs including, breast cancer treatment, other hospital outpatient visits, hospital inpatient treatment and intervention	INS	55	18670 (12761)/13574	9379	76653
	IPS	57	20419 (14030)/16445	6302	77880
	SC	56	25800 (26178)/16361	2237	129416

SD, standard deviation.
[a]Sum based on the average cost for radiation therapy and adjuvant FEC chemotherapy and number of individuals scheduled for each treatment in the groups.

Table 3. Mean values (SD) for utilities and missing values frequencies (%) per randomization group

	Value					
EQ-5D utilities QALYs	INS		IPS		SC	
Baseline	0.60(0.24)	0%	0.64(0.23)	2%	0.56(0.25)	0%
1 month	0.71(0.22)	2%	0.70(0.25)	3%	0.64(0.28)	0%
3 month	0.76(0.23)	7%	0.67(0.24)	2%	0.68(0.21)	3%
6 month	0.77(0.19)	7%	0.75(0.22)	3%	0.66(0.27)	10%
12 month	0.78(0.20)	12%	0.73(0.30)	5%	0.76(0.23)	12%
18 month	0.82(0.16)	12%	0.82(0.22)	8%	0.71(0.26)	10%
24 month	0.86(0.16)	38%	0.81(0.23)	30%	0.76(0.23)	32%
Difference (24 month -baseline)	0.26 (0.20)		0.17(0.26)		0.20(0.24)	

SD, standard deviation.

Discussion

The primary aim was to explore the cost–utility of providing individual psychosocial support given by nurses or psychologists as a compliment to SC, compared to SC alone. The INS and IPS were dominant compared to the SC in the CUA. Thus, the study showed that the intervention is cost-effective for breast cancer patients during adjuvant treatment.

Table 4. Base-case and sensitivity analysis showing cost, QALYs and cost–utility data for randomization groups

Group	Total health care cost (€)	QALY	Incremental costs (€)	Incremental effect (QALY)	Incremental cost per QALY gained (€)(ICER)
Base-case analyses					
INS (n = 55)	18670	1.52	−7 130	0.09	Dominant
IPS (n = 57)	20419	1.59	−5 381	0.16	Dominant
SC (n = 56)	25800	1.43			
Sensitivity analyses					
QALY. high tolerance level[a]					
INS (n = 55)	18670	1.63	−7 130	0.19	Dominant
IPS (n = 57)	20419	1.55	−5 381	0.11	Dominant
SC (n = 56)	25800	1.44			
QALY. low tolerance level[b]					
INS (n = 55)	18670	1.48	−7 130	0.06	Dominant
IPS (n = 57)	20419	1.48	−5 381	0.07	Dominant
SC (n = 56)	25800	1.41			
T1[c]					
INS (n = 41)	15141	1.57	−3 363	0.11	Dominant
IPS (n = 42)	18501	1.58	−3	0.12	Dominant
SC (n = 40)	18504	1.46			
T2[d]					
INS (n = 11)	27266	1.59	−8 989	0.31	Dominant
IPS (n = 11)	27326	1.54	−8 929	0.26	Dominant
SC (n = 12)	36255	1.28			
N0[e]					
INS (n = 37)	15395	1.57	−474	0.14	Dominant
IPS (n = 26)	16372	1.53	502	0.09	5308
SC (n = 29)	15870	1.43			
N1-2[f]					
INS (n = 11)	31109	1.61	−6 946	0.24	Dominant
IPS (n = 25)	26037	1.44	−12 018	0.07	Dominant
SC (n = 23)	38055	1.37			
Outliers 1[g]					
INS (n = 50)	18463	1.58	−7 337	0.14	Dominant
IPS (n = 50)	18471	1.55	−7 329	0.12	Dominant
SC (n = 56)	25800	1.43			
Outliers 2[h]					
INS (n = 55)	18670	1.59	−4 908	0.11	Dominant
IPS (n = 54)	18622	1.52	−4 955	0.05	Dominant
SC (n = 51)	23578	1.47			
Outliers 3[i]					
INS (n = 55)	18670	1.59	−1 954	0.14	Dominant
IPS (n = 57)	20419	1.52	−204	0.07	Dominant
SC (n = 53)	20624	1.44			

[a]High level tolerance means that calculations were made for those cases in which at least one of the EQ-5D values existed.
[b]Low level means that calculations were made for those cases in which all seven EQ-5D values existed.
[c]Patients with a tumor 2 cm or less in greatest dimension.
[d]Patients with a tumor between 2–5 cm in greatest dimension.
[e]Patients with no regional lymph node metastasis.
[f]Patients with movable/fixed metastasis to ipsilateral axillary node(s).
[g]Patients who had fewer than 10 sessions with the INS or IPS.
[h]Patients who had fewer than 56 HOPV.
[i]Patients who had fewer than 83 HIPC.

The study is one of the first randomized controlled trials to report results from a CUA of an individual psychosocial intervention as a compliment to SC. Because studies investigating the effects of psychosocial interventions on healthcare utilization, specifically using CUA, are scarce in cancer care, the positive cost–utility result presented here stands alone. However, studies [17,18,20] in other clinical contexts indicate that psychosocial care as a compliment to SC can decrease the overall cost burden to the healthcare system and improve HRQoL among cancer patients. This strengthens the credibility of our results.

Breast cancer is a costly disease both for the Swedish healthcare system and for other systems around the world [2]. It is therefore important for healthcare managers to consider the most cost-effective treatments
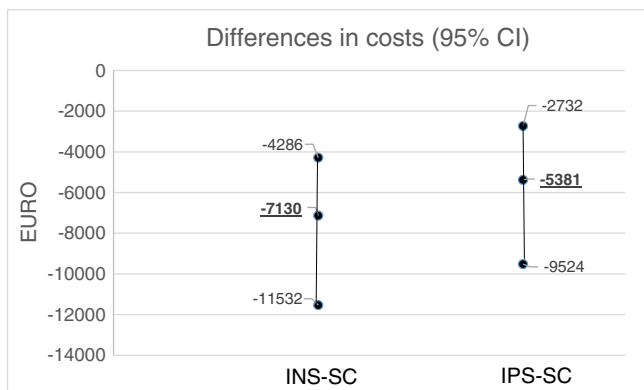
Figure 1. The differences in costs between INS vs. SC and IPS vs. SC within a 95% CI

and additional interventions that may reduce costs. The intervention carried out in the present study has reduced psychological symptoms during adjuvant treatment to a statistically significant degree, a time when the total burden for the patients was pronounced [31]. The cost for the intervention was about €500, or 3% of the total costs, which is quite a substantial sum. Yet, despite the cost for the intervention, total healthcare costs were lower in the INS and IPS groups than in the SC group. In-hospital care (HIPC) seems to be the main driver of the higher costs. Maybe unmet needs for psychosocial support in SC are associated with increased utilization of healthcare resources. Similar conclusions have been drawn by others [10–12].

A limitation of our study is the small number of patients [38]. The large amount of missing data may also decrease the credibility of our results. In addition, data on indirect costs were lacking, costs that overshadow the total costs of breast cancer care [2]. In future studies, data on indirect costs should be prospectively collected, along with measures of HRQoL and psychological effects. There were no statistically significant differences between groups regarding healthcare utilization and costs. This suggests that the cost-saving result presented here could have occurred by chance. However, within the 95% CI the differences in costs in favor of the interventions groups compared to SC were confirmed. Here we present one of

the first CUAs to explore the cost–utility of an individual psychosocial intervention for breast cancer patients, and it needs to be challenged. Can our results be replicated in other studies? Moreover, in health economic analyses the interventions can be considered cost-effective even if there are no statistically significant results. Briggs and colleagues [39] argue that since data are synthesized from different sources, like health care utilization, questionnaires, and medical records, common statistical methods cannot be employed. Due to uncertainties within data, they have to be explored and quantified in other ways, chiefly by the use of sensitivity analyses including bootstrapping of incremental costs. Although our study lacked sufficient statistical power, our findings were basically replicated in all of the sensitivity analyses performed at different tolerance levels, tumor stages and exclusion of outliers, indicating fairly robust results in the main analyses.

Conclusions

For breast cancer patients during adjuvant treatment, individual psychosocial support given by nurses or psychologists, as a compliment to SC, was cost-effective since the health care costs were lower and QALYs were higher compared to SC alone. However, the positive cost–utility result presented here stands alone, and thus more cost–utility studies of psychosocial interventions with larger samples are needed.

Conflict of interest

None declared.

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