original article

Effect of complementary and alternative medicine on the survival and health-related quality of life among terminally ill cancer patients: a prospective cohort study

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Background: We evaluated whether complementary and alternative medicine (CAM) use influenced outcomes [survival and health-related quality of life (HRQOL)] of cancer patients whose condition had just been judged terminal.

Patients and methods: From July 2005 to October 2006, we conducted a prospective cohort study of 481 terminally ill cancer patients at 11 university hospitals and the National Cancer Center in Korea. We assessed how the use of CAM affected HRQOL and survival.

Results: In a follow-up of 481 patients and 163.8 person-years, we identified 466 deceased cases. On multivariate analyses, CAM users did not have better survival compared with nonusers [adjusted hazard ratio (aHR), 0.91; 95% confidence interval (CI) 0.74–1.10]. Among mind–body interventions, prayer showed significantly worse survival (aHR, 1.56; 95% CI, 1.00–2.43). Clinically, CAM users reported significantly worse cognitive functioning (−11.6 versus −1.3; $P < 0.05$) and fatigue (9.9 versus −1.0; $P < 0.05$) than nonusers. Compared with nonusers in subgroup analysis, users of alternative medical treatments, prayer, vitamin supplements, mushrooms, or rice and cereal reported clinically significant worse changes in some HRQOL subscales.

Conclusion: While CAM did not provide any definite survival benefit, CAM users reported clinically significant worse HRQOLs.

Key words: alternative medicine, cancer, complementary medicine, HRQOL, prospective cohort, terminal illness

introduction

The use of complementary and alternative medicine (CAM) has been increasing worldwide [1–3] over the past two decades, and an estimated 40%–60% of adult cancer patients use CAM [1, 4–7]. CAM use may improve health-related quality of life (HRQOL) and symptoms that are inadequately managed by conventional medicine [8, 9].

Substantial evidence from randomized trials among cancer patients supports the use of CAM for symptom control [6]. Acupuncture, for example, has been used with success for post-dissection neck pain [10] and chemotherapy-induced acute nausea severity [11], as has American ginseng for cancer-related fatigue [12]. Before CAM methods can be considered part of conventional medicine, however, they must be subjected to greater scientific scrutiny [13]. As 62% of patients in palliative care units (PCUs) expressed an interest in CAM [5], an investigation of its effects is warranted. Especially, more attention should be paid to the impact of CAM use on HRQOL among the terminally ill patients.

Here, we evaluated whether CAM use influenced outcomes (survival and HRQOL) of cancer patients whose condition had just been judged terminal.

methods

study design and recruitment

From July 2005 to October 2006, the Study to Understand Risks, Priority and Issues at End-of-Life (SURPRISE), a multicenter study designed to

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Table 1. Independent variables associated with baseline use of CAM in terminal cancer patients before and after adjustment for propensity scores

Variables	N (%)		P value (Wald F)[a]	P value (Wald F[a] adjusted for propensity score)[b]
	Users of CAM 202 (42.0)	Nonusers of CAM 279 (58.0)		
Sex				
Male	115 (42.0)	159 (58.0)	0.0002 (0.999)	0.0002 (0.999)
Female	87 (42.0)	120 (58.0)		
Age, years				
<65	153 (45.3)	185 (54.7)	4.955 (0.026)	1.928 (0.165)
≥65	49 (34.3)	94 (65.7)		
Mean age (SD)	55.9 (11.3)	58.2 (11.8)		
Marital status				
Not married	50 (43.5)	65 (56.5)	0.201 (0.654)	0.0001 (0.991)
Married	148 (41.1)	212 (58.9)		
Educational level				
≤Middle school	79 (36.4)	138 (63.6)	5.348 (0.021)	0.0008 (0.977)
≥High school	118 (53.0)	133 (47.0)		
Job status before cancer diagnosis				
Unemployed	82 (39.8)	124 (60.2)	0.728 (0.393)	<0.0001 (0.995)
Employed	115 (43.7)	148 (56.3)		
Having a religion				
No	56 (38.1)	91 (61.9)	1.361 (0.243)	0.0008 (0.978)
Yes	142 (43.8)	182 (56.2)		
ECOG PS				
0–2	76 (49.0)	79 (51.0)	0.013 (0.909)	0.001 (0.974)
3–4	123 (38.9)	193 (61.1)		
Metastasis				
Yes	184 (43.0)	244 (57.0)	0.803 (0.370)	0.0004 (0.985)
No	17 (36.2)	30 (63.8)		
Primary cancer site				
Lung or liver	93 (49.5)	95 (50.5)	7.031 (0.008)	0.003 (0.960)
Stomach, breast, cervix, colon, or head & neck	109 (37.2)	184 (62.8)		
Reason disease is terminal				
General prostration	48 (33.8)	94 (66.2)	–	–
Others	153 (45.3)	185 (54.7)	6.138 (0.013)	0.025 (0.875)

CAM, complementary and alternative medicine; ECOG, Eastern Cooperative Oncology Group.
[a]F statistic based on the Wald chi-square.
[b]The propensity score is the probability of being a CAM user on the basis of observed characteristics.

identify important issues such as use of CAM, quality of life, care burden and needs, end-of-life discussion, advance care planning, and overall satisfaction with care at the end of life, recruited terminal cancer patients for this Korean prospective cohort study from 11 university hospitals and the National Cancer Center. The details of the study design have been published elsewhere [14]. In SURPRISE, patients were eligible to participate if they were aged at least 18 years, diagnosed as terminal at an outpatient or inpatient facility, capable of filling out questionnaires or communicating with an interviewer, and competent enough to understand the intent of the study and provide informed consent. The patients were asked to identify their primary family caregiver, defined as the relative who provided them with the most assistance. The family caregivers were invited to participate in the study but were ineligible if they were not well enough to fill out questionnaires, unable to communicate with an interviewer, or unable to understand the intent of this study well enough to provide informed consent. All participants provided informed consent, and our institutional review boards approved the protocol.

The SURPRISE questionnaires were used to collect demographic data from the patients and the caregivers and clinical information from the patients. The patient and family caregiver questionnaires were similar and

took about 20 min to complete. Both the groups were followed for 2 months by mail, and the family caregivers were interviewed by telephone about 3 months after the patient died. The information presented here is based on data collected at baseline, and the QOL data were collected at baseline and again at 1 month.

data collection

Within days of a patient's being diagnosed as terminally ill, SURPRISE collected clinical information using a questionnaire designed to collect information on (i) demographics (age, sex, relationship of caregiver with the patient, level of education, income, and religiousness), (ii) CAM use (type of CAM, satisfaction with CAM used, reason for satisfaction or dissatisfaction), (iii) quality of life, and (4) other end-of-life issues. We administered the questionnaires by face-to-face interviews at an outpatient or inpatient facility to patients and family caregivers at the same time within days of the baseline time point of the study, which was when the physician judged that the cancer was refractory to the conventional anticancer therapy (surgery, radiotherapy, chemotherapy, or hormone therapy) and the patient was likely to die within months.

We used the definition of CAM adopted by the US National Center of Complementary and Alternative Medicine (NCCAM): 'CAM is a group of diverse medical and health care systems, practices, and products that are not presently considered to be part of conventional medicine' [15]. NCCAM named five major CAM categories: (i) alternative medical systems (oriental herbal medicine, acupuncture, ayurveda, and homeopathy), (ii) mind–body intervention (yoga, meditation, prayer therapy, music/dance therapy, art therapy, and horticultural therapy), (iii) biologically based therapy (medicinal herbs, vitamin supplements, hydrotherapy, dietary supplements, etc.), (iv) manipulative and body-based therapies, and (v) energy therapies. In this research, we investigated participant's use of all five categories and focused on specific therapies within each category.

All patients completed the European Organization for Research and Treatment of Cancer quality-of-life questionnaire core-30 (EORTC QLQ-C30) instrument. The EORTC QLQ-C30 is composed of five multi-item functional scales that evaluate physical, role, emotional, cognitive, and social function, and one global health status/QOL scale. Three symptom scales measure fatigue, pain, and nausea/vomiting, and six single items assess other symptoms (dyspnea, insomnia, appetite loss, constipation, and diarrhea) and financial difficulties. The Korean-language EORTC QLQ-C30 has been validated [16].

statistical analysis

CAM users were defined as those who reported using at least one form of CAM, and those with questions left unanswered on the questionnaire were defined as nonusers. We summarized the data using descriptive statistics and frequency distributions and examined the association of CAM use with patient demographics, primary cancer site, ECOG (Eastern Cooperative Oncology Group) performance status (PS), and basis of terminal status.

We used propensity scores to minimize bias in the selection of cases versus referents [17]. An individual's propensity score is the probability of being a CAM user on the basis of observed characteristics (sex, age, marital status, educational level, job status, religion, ECOG PS, metastasis, primary cancer site, and reason for terminal status).

We measured survival time from the date of enrollment in the study and used the Kaplan–Meier method to trace survival curves by major CAM categories. We used the Wilcoxon test to estimate the differences in survival for univariate analysis and, for variables that showed statistical significance at the 0.10 level, carried out multivariable analyses using the Cox proportional hazards model to estimate adjusted hazard ratios (aHRs) and 95% confidence intervals (CIs) after adjusting for propensity scores and ECOG PS.

We scored EORTC QLQ-C30 responses according to EORTC scoring manual 3.0 [18] and linearly transformed the data to yield scores from 0 to 100, with a higher functional scores representing better functioning and a high symptom score indicating more severe symptoms. We handled incomplete questionnaires for EORTC QLQ according to the developers' recommendations: if at least half the items in a scale were present, we used their mean as the missing value. We used analysis of covariance to determine significant differences in changes of the HRQOL mean from baseline to 1 month between users of five major categories of CAM and CAM nonusers, adjusting for baseline HRQOL and propensity scores. All statistical tests were two-sided and carried out using SAS version 9.2 (SAS Institute, Inc., Cary, NC). We considered $P < 0.05$ to be statistically significant, and we defined a 'clinically significant' difference in HRQOL as a 10-point difference in the mean score [18, 19].

results

Among the study population, 42% used CAM. They had a median age of 58.2 years, compared with 59.0 years for

nonusers. Table 1 summarizes the demographic and clinical characteristics for CAM users and nonusers. There was a trend for higher education level to be associated with a higher chance of CAM usage ($P = 0.02$). After weighting according to propensity scores, the two groups of patients did not differ substantially in any other characteristic (Table 1).

The proportion of patients who used CAM among the categories of terminal status was 45.7% among those 'Refractory to chemotherapy', 44.6% among those who registered a 'Refusal of further chemotherapy', and 3.8% among those who reported 'General prostration'.

The most frequently used CAMs were biologically based therapies (84.2%). Mind–body interventions were used with higher frequency (18.3%) than alternative medical systems (12.9%). A few used body-based therapy and energy-based therapy.

We found no difference in overall survival between CAM users and nonusers in univariate analysis and in subgroup analysis of each major CAM category (Table 2). In multivariate analysis adjusting for propensity scores and ECOG PS, CAM users did not have better survival compared with nonusers (aHR, 0.91; 95% CI, 0.74–1.10). Body-based therapy did not show significantly better survival compared with nonusers. (aHR, 0.55; 95% CI, 0.30–1.01) (Figure 1).

Changes in the adjusted mean of most EORTC QLQ-C30 subscale scores were similar for CAM users and nonusers, except for cognitive functioning and fatigue, where CAM users reported a clinically significant greater worsening of both (Table 3). Changes in the adjusted mean of most EORTC QLQ-C30 subscale scores did not differ significantly for CAM subcategory users and nonusers. In subgroup analysis by CAM category, users of alternative medical systems reported a clinically significant greater worsening in insomnia subscale

Table 2. Univariate analysis of use of CAM compared with nonuse of CAM

Variables	N (%)	Median survival, days (95% CI)	P value
Use of CAM			
No	279 (58.0)	67.0 (61.0–78.0)	0.07
Yes	202 (42.0)	76.0 (69.0–97.0)	
Alternative medical system			
No	140 (69.3)	74.0 (65.0–93.0)	0.4
Yes	62 (12.9)	86.5 (69.0–22.0)	
Mind–body intervention			
No	165 (81.7)	79.0 (69.0–101.0)	0.563
Yes	37 (18.3)	74.0 (51.0–121.0)	
Biologically based therapy			
No	32 (15.8)	74.5 (55.0–121.0)	0.118
Yes	170 (84.2)	78.0 (69.0–100.0)	
Body-based therapy			
No	188 (93.1)	74.0 (68.0–89.0)	
Yes	14 (2.9)	163.5 (75.0–301.0)	0.057
Energy-based therapy			
No	201 (99.5)	–	–
Yes	1 (0.5)	–	–

CAM, complementary and alternative medicine; CI, confidence interval; NA, not available.
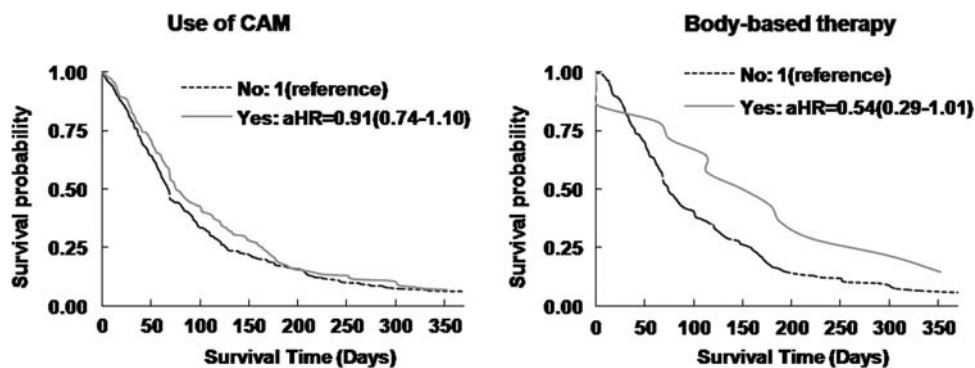
Figure 1. Adjusted survival curves for users of CAM versus non-users of CAM. CAM, complementary and alternative medicine; aHR, hazard ratio adjusted for Eastern Cooperative Oncology Group performance status (ECOG PS) and propensity scores.

Table 3. Adjusted[a] quality-of-life scores change[b] in users of CAM when compared with nonusers of CAM

EORTC QLQ-C30	LS mean									
	Users of CAM		Alternative medical system		Mind–body intervention		Biologically based therapy		Body-based therapy	
	n = 316		n = 316		n = 316		n = 316		n = 316	
	No	Yes	No	Yes	No	Yes	No	Yes	No	Yes
Function scales										
Physical functioning	−3.7	−3.2	−2.5	−4.9	−2.7	−6.2	2.6	−4.4	−3.9	7.0
Role functioning	−2.0	−6.3	−1.0	−6.3	0.0	−14.9	−6.7	−1.9	−4.6	10.4
Emotional functioning	0.4	−6.2	−0.5	−4.8	0.6	−13.6	−10.5	−0.3	−3.0	4.2
Cognitive functioning	**−1.3**	**−11.6**[c]	−7.2	−15.8	−7.7	−20.6	−15.6	−8.9	−6.7	5.6
Social functioning	−4.1	−6.0	−4.3	−2.6	−3.8	−3.7	5.5	−5.6	−5.2	0.1
Global QOL	2.0	−2.6	2.1	−7.3	**3.0**	**−17.9**[c]	−11.5	1.0	−0.3	1.0
Symptom scales										
Fatigue	**−1.0**	**9.9**[‡]	5.9	9.2	5.6	13.0	11.1	6.3	4.3	−3.0
Nausea/vomiting	−1.3	5.3	−0.3	14.6	3.0	10.7	15.3	2.3	1.1	18.6
Pain	−6.7	3.4	0.6	0.6	−1.1	8.6	−5.3	1.7	−1.5	−14
Dyspnea	10.6	15.8	13.1	21.5	15.5	17.1	20.4	14.9	13.5	0.9
Insomnia	−2.6	3.0	**−4.8**	**16.1**[c]	0.8	6.3	−2.7	2.6	0.5	−12
Appetite loss	−2.4	1.0	−3.7	6.1	0.5	−5.7	−1.8	−0.3	−0.6	−5.5
Constipation	0.5	11.3	6.1	11.1	8.6	3.1	14.9	6.5	6.5	−17.6
Diarrhea	4.3	8.2	2.2	15.8	6.5	7.5	9.3	6.2	6	8.5
Financial difficulties	4.8	5.8	5.0	4.1	2.3	15.7	7.6	4.1	5.4	2.9

CAM, complementary and alternative medicine; LS Mean, least squares mean.
[a]Adjusted for baseline QOL and propensity scores.
[b]Difference in mean QOL from baseline to 1 month.
[c]$P < 0.05$. Bold type characters indicate statistically significant and clinically meaningful difference (10 of 100 points).

score than nonusers. The users of mind–body interventions showed significantly greater impairment of HRQOL in global QOL than nonusers (Table 3). The use of biologically based and body-based therapies was not associated with worse impairment in any HRQOL subscale (Table 3). As only one patient used energy-based therapy, it was not possible to investigate its effect.

discussion

In this large multicenter study, we have described associations between the use of CAM by terminal cancer patients in Korea and their HRQOL and survival. Our finding that 42% of

terminal cancer patients used CAM is consistent with the findings of another Korean study [4–7] and the findings of the population-based palliative care research network (PoPCRN) [20] as well as of studies in Japan [4–7], and the USA [6], despite cultural differences. Our finding that the order of frequency of CAM use was biologically based therapies (especially dietary supplements) > alternative medical systems > mind–body interventions was also consistent with findings from other studies [7, 21]. While patients often use CAM in the hope that it will lead to tumor growth suppression and cure [5, 22], our study showed that CAM users did not have better survival than nonusers. Moreover, among mind–body interventions, those who prayed showed marginally worse

survival. Although no reliable, well-designed clinical trials on the efficacy of CAM in cancer patients have been carried out, earlier studies have also shown complementary therapies to be associated with worse outcomes [23, 24]. That CAM therapies have the potential to maintain or to enhance the quality of life [8], however, has been supported by randomized, controlled trials of acupuncture [10, 11], and ginseng [12]. The use of mind–body interventions was associated with more clinically significant impairment in global QOL. The use of prayer, for example, was associated with more impairment of QOL changes in global QOL and emotional functioning (data not shown). That finding was consistent with those of a previous study, showing that the use of complementary medicine by cancer patients was associated with severe depression [25]. Such findings suggest the possibility that the use of complementary medicine might not only be a marker of greater psychological distress in this group of patients [25], but might also cause impairment of QOL. Additionally, the use of biologically based therapies was associated with greater impairment of dyspnea and greater clinically significant impairment of physical functioning and pain. Recent phase I studies with advanced cancer patients also showed that biologically based CAM was associated with poorer overall QOL [2]. Ginseng, in particular, is commonly used by patients with cancer-related fatigue [12], but it was not associated with any statistically significant benefit in this study (data not shown).

Recently, combining Pan-Asian medicine + vitamins (PAM + V) with the conventional therapy improved survival compared with the conventional therapy alone, suggesting that prospective trials of that combination regimen are justified [26]. Furthermore, acupuncture appears to be a safe and effective treatment for pain [10], nausea and vomiting [11], and vasomotor symptoms [27–28], and yoga might enhance emotional well-being and serve to buffer QOL deterioration [29]. Therefore, this study, together with the earlier ones, suggests that well-designed clinical trials of CAM in terminally ill patients should be carried out.

Our study had some limitations. First, the nonrandomized study design made it is difficult to draw firm conclusions from the findings. Second, due to the small size sample available for analysis of CAM subcategories, the statistical power might not have been adequate to detect benefits of CAM use. No CAM had a significant effect on HRQOL after the Bonfferoni correction for multiple comparisons with an adjusted α level of 0.003 ($\alpha' = 0.05/15 = 0.003$). Since our multiple comparisons of the effects of CAM on QOL increase the likelihood of a Type 1 error, we defined a 'clinically significant' difference in HRQOL as a 10-point difference in the mean score. Third, it could be argued that the 1-month timeframe was not long enough for changes to become manifest, and a longer study period (3–6 months) is necessary. Additionally, the therapy might be more efficacious among treatable cancer patients than among terminal ones.

While CAM did not provide any definite survival benefit, CAM users reported clinically significant worse HRQOLs. We believe that there is a need for well-designed double-blind randomized clinical trials to evaluate the potential benefits and safety of CAM for terminal cancer patients.

disclosure

The authors have declared no conflicts of interest.

references

1. Cassileth B. Complementary therapies: The American experience. Support Care Cancer 2000; 8: 16–23.
2. Eisenberg DM, Davis R, Ettner SL et al. Trends in alternative medicine use in the United States, 1990–1997: results of a follow-up national survey. JAMA 1998; 280: 1569–1575.
3. DiGianni LM, Garber J, Winer EP. Complementary and alternative medicine use among women with breast cancer. J Clin Oncol 2002; 20: 34S–48S.
4. Kim SG, Park EC, Park JH et al. Initiation and discontinuation of complementary therapy among cancer patients. J Clin Oncol 2007; 25: 5267–5274.
5. Hyodo I, Amano N, Eguchi K et al. Nationwide survey on complementary and alternative medicine in cancer patients in Japan. J Clin Oncol 2005; 23: 2645–2654.
6. Cassileth BR, Vickers AJ. High prevalence of complementary and alternative medicine use among cancer patients: implications for research and clinical care. J Clin Oncol 2005; 23: 2590–2592.
7. McDermott CL, Blough DK, Fedorenko CR et al. Complementary and alternative medicine use among newly diagnosed prostate cancer patients. Support Care Cancer 2010; 20: 65–73.
8. Cleeland CS. Symptom burden: Multiple symptoms and their impact as patient-reported outcomes. J Natl Cancer Inst 2007; 37: 16–21.
9. Hlubocky FJ, Ratain MJ, Wen M et al. Complementary and alternative medicine among advanced cancer patients enrolled on phase I trials: a study of prognosis, quality of life, and preferences for decision making. J Clin Oncol 2007; 25: 548–554.
10. Pfister DG, Cassileth BR, Deng GE et al. Acupuncture for pain and dysfunction after neck dissection: results of a randomized controlled trial. J Clin Oncol 2010; 28: 2565–2570.
11. Ezzo J, Vickers A, Richardson MA et al. Acupuncture-point stimulation for chemotherapy-induced nausea and vomiting. J Clin Oncol 2005; 23: 7188–7198.
12. Barton DL, Soori GS, Bauer BA et al. Pilot study of Panax quinquefolius (American ginseng) to improve cancer-related fatigue: a randomized, double-blind, dose-finding evaluation: NCCTG trial N03CA. Support Care Cancer 2010; 18: 179–187.
13. Schofield P, Diggens J, Charleson C et al. Effectively discussing complementary and alternative medicine in a conventional oncology setting: communication recommendations for clinicians. Patient Educ Couns 2010; 79: 143–151.
14. Yun YH, Kwon YC, Lee MK et al. Experiences and attitudes of patients with terminal cancer and their family caregivers toward the disclosure of terminal illness. J Clin Oncol 2010; 28: 1950–1957.
15. National Cancer for Complementary and Alternative Medicine (NCCAM). (2008). CAM Basics: What is CAM? (p. 1). Retrieved August 13, 2008, from http://nccam.nih.gov/health/whatiscam.
16. Yun YH, Park YS, Lee ES et al. Validation of the Korean version of the EORTC QLQ-C30. Qual Life Res 2004; 13: 863–868.
17. Robins JM, Hernan MA, Brumback B. Marginal structural models and causal inference in epidemiology. Epidemiology 2000; 11: 550–560.
18. Fayers PM, Aaronson N, Bjordal K et al. The EORTC QLQ-C30 scoring manual, 3rd edition. Brussels, Belgium: European Organization for Research and Treatment of Cancer 2001.

19. Fayers PM. Interpreting quality of life data: population-based reference data for the EORTC QLQ-C30. Eur J Cancer 2001; 37: 1331–1334.

20. Corbin LW, Mellis BK, Beaty BL et al. The use of complementary and alternative medicine therapies by patients with advanced cancer and pain in a hospice setting: a multicentered, descriptive study. J Palliat Med 2009; 12: 7–8.

21. Wyatt G, Sikorskii A, Wills CE et al. Complementary and alternative medicine use, spending, and quality of life in early stage breast cancer. Nurs Res 2010; 59: 58–66.

22. Frenkel M, Ben-Arye E, Cohen L. Communication in cancer care: discussing complementary and alternative medicine. Integr Cancer Ther 2010; 9: 177–185.

23. Han E, Johnson N, DelaMelena T et al. Alternative therapy used as primary treatment for breast cancer negatively impacts outcomes. Ann Surg Oncol 2011; 18: 912–916.

24. Kristoffersen AE, Fonnebo V, Norheim AJ. Do cancer patients with a poor prognosis use complementary and alternative medicine more often than others? J Altern Complement Med 2009; 15: 35–40.

25. Montazeri A, Sajadian A, Ebrahimi M et al. Depression and the use of complementary medicine among breast cancer patients. Support Care Cancer 2005; 13: 339–342.

26. McCulloch M, Broffman M, van der Laan M et al. Colon cancer survival with herbal medicine and vitamins combined with standard therapy in a whole-systems approach: ten-year follow-up data analyzed with marginal structural models and propensity score methods. Integr Cancer Ther 2011; 10: 240–259.

27. Crew KD, Capodice JL, Greenlee H et al. Randomized, blinded, sham-controlled trial of acupuncture for the management of aromatase inhibitor-associated joint symptoms in women with early-stage breast cancer. J Clin Oncol 2010; 28: 1154–1160.

28. Deng G, Vickers A, Yeung S et al. Randomized, controlled trial of acupuncture for the treatment of hot flashes in breast cancer patients. J Clin Oncol 2007; 25: 5584–5590.

29. Moadel AB, Shah C, Wylie-Rosett J et al. Randomized controlled trial of yoga among a multiethnic sample of breast cancer patients: effects on quality of life. J Clin Oncol 2007; 25: 4387–4395.