

Complementary and alternative medicines use by Scottish women with breast cancer. What, why and the potential for drug interactions?

J. S. McLay · D. Stewart · J. George · C. Rore ·
S. D. Heys

Received: 3 October 2011 / Accepted: 21 November 2011 / Published online: 14 December 2011
© Springer-Verlag 2011

Abstract

Background Despite the increased use of complementary and alternative medicine (CAM) by breast cancer patients, there is little published information regarding CAM use in the Scottish breast cancer population.

Methods A questionnaire comprising five sections—demographics; perceived health status, prescribed medicines; use, indications, satisfaction and expenditure on CAMs; attitudes towards and factors associated with CAM use; and attitudinal statements—was issued to patients attending the Aberdeen Breast Clinic.

Results A total of 453 questionnaires were distributed and 360 (79.5%) returned. Respondents were prescribed a mean of 3.2 medicines (95% CI 2.83–3.47). With regard to CAM use, 33.1% of respondents reported current use, 36.4% prior use, and 30.6% reported never having used CAMs. The key indications for use were general well being, boosting immune system and cancer prophylaxis, with high levels of satisfaction reported. The strongest association for CAM use was use by friends and family and higher educational attainment ($p < 0.001$). Supplements with estrogenic activity, such as soya or

red clover, were taken by 29% of respondents. Herbs (echinacea, pomegranate, peppermint, chamomile, grapefruit, garlic, ginseng) that have the potential to interact with adjuvant endocrine therapies (tamoxifen, anastrozole, letrozole, exemestane) were being taken by 38% of treated patients.

Conclusion The level of CAM use by Scottish breast cancer patients is similar to that reported from other countries, although there are marked differences in the type, nature and frequency of specific CAM therapies. Higher patient education level and use by family and friends were significantly associated with CAM use. The high level of use of potentially disease modifying or interacting herb supplements may be of concern.

Keywords Attitudes · Satisfaction · Expenditure · Indications · Disease modifying activity · Herb-drug interaction · Phytoestrogen

Introduction

Alternative therapy, also known as complementary medicine, refers to a variety of therapies and practices that are not usually provided by physicians. The World Health Organisation suggests that the terms “complementary medicine” or “alternative medicine” are commonly used interchangeably with traditional medicine in some countries and that they refer to a broad set of health care practices that are not part of that country’s own tradition and are not integrated into the dominant healthcare system [1]. These health practices, which include acupuncture, homeopathy, herbal medicine, special diets, aromatherapy, energy flow control within the body and psychological therapies, are frequently used in

J. S. McLay (✉) · S. D. Heys
Division of Applied Health Sciences, University of Aberdeen,
Aberdeen AB25 2ZG, UK
e-mail: j.mclay@abdn.ac.uk

C. Rore
NHS Grampian,
Aberdeen, UK

D. Stewart · J. George
Robert Gordon University,
Aberdeen, UK

addition to, and sometimes in place of, conventional treatment. Women are larger consumers of healthcare than men, and this extends to their utilisation of complementary and alternative medicine (CAM) [2].

The reasons why women turn to CAM are unclear. However, the desire to have personal control over one's own health, dissatisfaction with conventional treatment and the perception that conventional medicine has a disregard for a holistic approach, together with concerns about the side effects of prescribed medications have been cited as some of the reasons. However the majority of CAM users do not appear to be dissatisfied with conventional medicine, but find these health care alternatives more congruent with their own values, beliefs and philosophical orientations toward health and life [3]. Whatever the reasons, the prevalence of CAM use as a self-selected component of a particular patient's treatment regimen is increasing in developed countries [4], with 8–76% of the general population reporting CAM use [5–7].

A similar situation exists amongst specific patient groups, such as those with cancers of various types, who are also reported to be frequent users of complementary therapies [7–10]. The highest use, however, is reported to be amongst women who have been diagnosed with breast cancer. A high proportion of such patients use CAMs, with figures ranging from 17 to 84% [4, 10–21]. Recent results would further suggest that CAM use has increased significantly over the last decade amongst patients with breast cancer from 67% in 1998 to 74% in 2005 [22]. Caution should be exercised, however, in interpreting the results of different CAM studies due to the lack of clear and consistent definitions of CAM used by the authors. The reasons for the widespread and increasing use of CAMs, despite a lack of evidence for benefit, but with evidence from well conducted studies that various complementary therapies are ineffective or, more importantly, may have harmful effects when used in patients with cancer, are unclear [23–33]. However, it is possible that the tacit acknowledgement /approval of CAM use in European Guidelines [34] for the treatment of breast cancer together with the holistic approach adopted by CAM practitioners, which many patients may find rewarding, may be partially responsible for this increasing usage. Two further issues of importance are the potential for herbal remedies to interact with concomitant drug therapies or to exert an unknown/adverse effect on the disease process. Herb-drug interactions are most likely to occur with herbs which induce or inhibit the cytochrome P450 (CYP450) hepatic enzymes and so alter drug metabolism. In particular this may be of importance when considering drugs such as tamoxifen, exemestane, letrozole and toremifene, agents which rely on the CYP450 enzymes either wholly or in part for metabolism [35]. Many supplements also contain phytoestrogens or isoflavones which possess estrogen-like activity, and

the potential roles of such agents in the genesis and treatment of breast cancer is complex and far from clear [36, 37].

The aims of the present study, therefore, were to describe CAM use, reasons for use and factors associated with use by a well described population of women with breast cancer in Scotland, to assess their views and attitudes towards CAM use, and to assess the potential for drug interactions with concomitant adjuvant therapies.

Methods

A questionnaire comprising open and closed questions and attitudinal items on five- or six-point Likert scales was developed to explore the use of CAMs by breast cancer patients who attended the Breast Clinic, Aberdeen Royal Infirmary during a 6 month period. We defined CAM use as referring to “the diagnosis, the treatment, and/or the prevention of illness using any means other than an orthodox or conventional medical approach”. The diagnosis, treatment and prevention of medical conditions by practitioners such as acupuncturists, chiropractors, homeopaths or naturopaths as well as the use of herbal products, natural products, minerals or vitamins purchased from a pharmacy, health food outlet or supermarket without a prescription were considered to be CAM.

The questionnaire was reviewed for face and content validity by five doctors and pharmacists and piloted at the Aberdeen Breast Clinic prior to use. The final questionnaire comprised five sections: demographics (seven items); perceived health status, concurrently prescribed medicines (eight items); use of specific CAMs in the previous 24 months including average cost per month (six items); attitudes towards CAM use in general and factors associated with CAM use (four items); attitudinal statements from the multidimensional health locus of control questionnaire (MHLC) covering three six-item subscales: internality, powerful others externality and chance externality [38].

Nursing staff at the clinic provided patients with a pack containing an introductory letter from the clinic consultant, study information leaflet, questionnaire and reply-paid envelope. Questionnaire distribution took place over a 24 week period. Anonymity precluded follow up of non-respondents. Data were analysed using SPSS for Windows version 17.0 (SPSS, Chicago, IL). Chi-squared test, Student's *t*-test and Mann Whitney *U*-test were used to compare users and non-users of CAMs for parametric and non-parametric data where appropriate. *P* values <0.05 were considered statistically significant. The potential for CAM-drug and CAM-disease interactions was assessed with reference to the Natural Medicines Comprehensive Database, which grades known interactions as major, moderate or minor and then discusses the theoretical

potential for interactions or disease modification [35]. This study was approved by the North of Scotland Research Ethics Committee.

Results

Demographics

A total of 453 questionnaires were distributed over a period of 6 months to eligible patients attending the breast clinic and 360 (79.5%) were returned. Most respondents were over 55 years of age (255, 70.8%) with their breast cancer diagnosed more than 3 years previously (3 months to 9 years).

Concurrent medication

Respondents reported taking a mean of 3.2 prescribed medicines (95% CI 2.83–3.47). Two hundred and twenty-two patients (61.7%) were currently taking specific adjuvant endocrine treatments (106 tamoxifen, 79 anastrozole, 31 letrozole, 8 exemestane), or trastuzumab (8). Ten patients reported taking two of these medicines concurrently.

Complementary and alternative medicine used

Throughout this paper we classify current and previous CAM users as “Ever Users” and those who have never used CAMs as “Never Users”. One-third (119, 33.1%) of respondents reported current CAM use, and an additional one-third (131, 36.4%) reported use within the previous 24 months. The remainder (110, 30.6%) reported never having used CAMs. Of the CAMs reported used by Ever Users (69.5%, $n=250$), the 10 most commonly reported were vitamins and minerals (50.0%), herbal medicines (38.4%), massage (24.4%), reflexology (14.4%), relaxation and visualisation (13.2%), reiki (10.4%), homeopathic medicines (10.0%), aromatherapy (9.6%), acupuncture (6.4%) and chiropractic (3.6%). One-quarter of Ever Users (26.1%) reported the use of other unlisted CAM therapies such as prayer, crystal therapy and yoga. The median number of CAMs reported for Ever Users was 1 [interquartile range (IQR) 1–2]. Table 1 provides detail of the frequency of specific product use by Ever Users. Of the current users, 52.6% were spending up to 10 GBP per month on CAM therapies, 27.6% 11–20 GBP, and 13.8% over 20 GBP per month.

Reasons for CAM use and level of satisfaction

The specific reasons for use of CAM products such as herbal medicines and homeopathy are reported in Table 1, highlighting a range of indications including those related to

cancer treatment and prophylaxis. The key reasons given for using other CAM therapies were relaxation and general well being (massage, relaxation and visualisation, reiki, aromatherapy), pain and nausea (reflexology, acupuncture) and back pain (chiropractic). Ever Users reported high levels of satisfaction for all CAM modalities [median 4–5, on a scale of 1 (low) to 5 (high)].

Comparison of Ever Users and Never Users

There were no significant differences between Ever Users and Never Users in terms of age, duration of diagnosis, employment status, health score rating, or number of prescribed medicines (Table 2). However, Ever Users were significantly more likely to report a university education ($P=0.007$) and CAM use among their close family ($P<0.001$) or friends ($P<0.001$).

When asked whether they believed that CAM therapy kept them “well”, half (50.8%) of Ever Users and 3.7% of Never Users replied “yes” ($P<0.001$; chi-squared). When asked whether CAMs improved their health, 45.6% of Ever Users and 3.8% of Never Users responded “yes” ($P<0.001$; chi-squared). Within the Ever User group, further analysis confirmed that a positive response for both statements was significantly more common in current users when compared to previous users (both, $P<0.001$, chi-squared).

Attitudes towards CAM use

Table 3 reports the responses of Ever Users and Never Users towards a series of attitudinal statements on aspects of CAM safety and efficacy. Significantly more Ever Users agreed with the statements “using prescription medicine and complementary and alternative medicine is better than using either one alone” ($P=0.05$) and “complementary and alternative medicine should be made available through the NHS” ($P=0.01$). Significantly more Ever Users also disagreed with the statement that “patients should only use traditional prescription medicines recommended by their doctors, pharmacists or nurses” ($P=0.002$).

Multi-dimensional health locus of control

When asked to respond to a series of statement relating to “internal control” (self) over their disease process, there were no significant differences between Ever and Never Users (Appendix 1). However, when asked to rate statements concerning the role of “powerful others” such as doctors in the disease process, significantly more Ever Users agreed with the statement “following doctor's orders to the letter is the best way to keep my condition from getting any worse” ($P=0.041$). There were no significant differences

Table 1 Specific CAM preparations and reasons for use by “Ever Users” ($n=250$)

CAM	Number (%)	Reasons for use ^a
Vitamins and minerals		
Multivitamin	64 (25.6)	Boost immune system, general well being
Calcium preparations	52 (20.8)	Osteoporosis, bone protection
Vitamin C preparations	36 (14.4)	Boost immune system, prevent colds
Iron preparations	16 (6.4)	Anaemia
Zinc preparations	15 (6.4)	Boost immune system, general well being
Selenium	7 (2.8)	Antioxidant, combat effects of cancer
Others	22 (8.8)	Combat cancer, boost immune system
Herbal medicines		
Cod liver oil	96 (38.4)	Joint related
Glucosamine	74 (29.6)	Joint related
Cranberry	60 (24.0)	Urinary tract related, antioxidant
Evening primrose oil	41 (16.4)	Menopausal symptoms
Fish oil	38 (15.2)	Combat effects of cancer treatment, boost immune system, well being
Echinacea	36 (14.4)	Immune system
Soy milk	35 (14.0)	Alternative to dairy products; cancer prophylaxis
Pomegranate	34 (13.6)	Antioxidant, well being, combat effects of cancer
Tea tree oil	29 (11.6)	Skin, antiseptic
Peppermint	25 (10.0)	Indigestion
Chamomile	22 (8.8)	Relaxation
Grapefruit	16 (6.4)	Healthy diet
Green tea	7 (2.8)	Antioxidant
Garlic	7 (2.8)	Coughs and colds
Others	30 (12.0)	General health, dietary supplement, boost immune system
Homeopathic medicines		
Arnica	35 (14.0)	Skin disorders, bruising, post surgery
Mistletoe	11 (4.4)	Boost immune system, combat cancer
Rhus tox	2 (0.8)	Arthritis
Others	3 (1.2)	Menopausal symptoms

^aKey themes are reported

between Ever and Never Users for any other MHLC statements. However, irrespective of CAM use, a high proportion of respondents agreed that “powerful others” played a key role in determining disease outcomes.

Potential for interaction with adjuvant endocrine and trastuzumab therapy

Of the 360 respondents, a total of 105 individuals reported the use of a supplement with possible estrogenic activity including soya, evening primrose, chamomile, garlic, black cohosh and red clover. Of the 222 patients who were currently using adjuvant endocrine and trastuzumab therapy, 84 reported concurrent use of herbal CAM therapies, resulting in a total of 119 possible herb-drug interactions (55 with tamoxifen, 66 with anastrozole, 6 with letrozole and 2 with exemestane).

The herbal supplements most commonly implicated were soya, cranberry, echinacea, glucosamine, grapefruit and garlic.

Discussion

This research was carried out within a breast cancer out-patient clinic at Aberdeen Royal Infirmary to determine types of CAM therapies and products being used by patients together with indications, levels of satisfaction and monthly expenditure. In addition, we assessed the attitudes of CAM Ever Users (current and past users of CAMs) and CAM Never Users to a range of attitudinal items relating to aspects of CAM use and personal health beliefs. CAM use by close family ($P<0.001$) or friends ($P<0.001$), and university education ($P=0.007$) were associated with personal CAM use. Most patients (69.4%) had tried at least one form of CAM over the past 24 months, the three most commonly reported being vitamins and minerals (50.0%), herbal medicines (38.4%) and massage (24.4%).

Ever Users were significantly more likely to agree that CAMs should be supplied by the NHS and that using CAMs in combination with prescribed medicines was better than

Table 2 Demographics of “Ever Users” and “Never Users”

	Ever Users (n, %)	Never Users (n, %)	P-value
Total number	250	110	
Age (years)			
25–34	5 (2.0)	1 (0.9)	0.221 ^a
35–44	14 (5.6)	5 (4.5)	
45–54	58 (23.2)	20 (18.2)	
55–64	90 (36.0)	34 (30.9)	
≥64	81 (32.4)	50 (45.5)	
Employment status			
Full-time	59 (23.6)	15 (13.6)	0.192 ^a
Part-time	44 (17.6)	24 (21.8)	
Retired	125 (50.0)	58 (52.7)	
Unemployed	17 (6.8)	9 (8.2)	
Education level			
University			
Yes	51 (20.4)	8 (7.3)	0.007 ^a
No	194 (77.6)	101 (91.2)	
Median (IQR) health scores (1, as bad as it can be, to 5, as good as it can be)	4 (4, 5)	5 (4, 5)	0.681 ^b
Mean (SD) number of medicines prescribed by doctor	3.2 (2.9)	2.9 (2.9)	0.378 ^c
Median (IQR) years since breast cancer diagnosed	4 (2–7)	4 (2–6)	0.528 ^b
Spouse uses CAMs			
Yes	54 (21.6)	7 (6.4)	<0.001 ^a
No	196 (78.4)	102 (92.7)	
Other family members use CAMs			
Yes	69 (27.6)	7 (6.4)	<0.001 ^a
No	181 (72.4)	102 (92.7)	
Friends use CAMs			
Yes	117 (46.8)	15 (13.6)	<0.001 ^a
No	133 (53.2)	94 (85.5)	

^aChi-squared^bMann Whitney *U*-test^cStudent's *t*-test

using either alone. They were more likely to disagree with the statements that CAM should only be used when recommended by healthcare professionals and that “following doctor’s orders to the letter is the best way to keep my condition from getting any worse”.

The high level of CAM use by Scottish women with a diagnosis of breast cancer, identified in this study, is similar to those reported by studies from Europe, Australasia and North America [4, 5, 10–20], indicating that the relevance and importance of such therapies to individual patients transcends national barriers. The role of education level as a key factor in determining CAM use is also consistent with other multinational studies; however of note there was a marked difference in the frequency with which specific CAM therapies were used by the Scottish population. The Scottish clinic population placed a greater emphasis on specific CAM products such as vitamins and minerals and herbal remedies rather than therapies such as spiritual healing and massage [22, 39, 40]. Similarly differences were noted in the types of specific CAM preparations used [22, 39, 40], which is

surprising given that these studies were all reporting on patients with a diagnosis of breast cancer. The reasons for these differences are not clear but may reflect local culture, CAM practice and fads. Given the lack of evidence of benefit and the potential for harm with some therapies [41–43], this high level use of CAM may reflect a widespread patient-perceived need for supportive therapy and help.

In this study the most significant determinant for CAM use was use by family and friends, indicating the potential importance of social networks in determining health behaviours. This finding in relation to CAM use has not been previously reported, and although our study does not allow us to comment further on the causal nature of this association, further studies are required to evaluate this. In this study we did not ask respondents about their sources of information for CAM use. However in light of the report by Schmidt et al. concerning the number of CAM sites on the internet and the extensive use of these sources by patients and CAM users, coupled with the resulting potential for misinformation and ensuing dangers, it is important for the clinician to be alert to these issues [44].

Table 3 Attitudes of “Ever Users” and “Never Users” towards CAMs

	Strongly agree/ agree (%)		Unsure (%)		Disagree/strongly disagree (%)		P-value
	Ever	Never	Ever	Never	Ever	Never	
Complementary and alternative medicines are safer than other medicines prescribed by my doctors (<i>n</i> =310)	13.9	5.1	45.0	53.2	45.1	41.8	0.402
Using traditional prescription medicine and complementary and alternative medicine is better than using either one alone (<i>n</i> =305)	33.5	19.2	46.7	57.7	19.8	23.1	0.05
Patients should only use complementary and alternative medicines recommended by their doctor, pharmacist or nurses (<i>n</i> =313)	35.5	48.8	13.9	23.2	50.6	28.0	0.002
Complementary and alternative medicines are more effective than traditional prescription medicines prescribed by my doctors (<i>n</i> =304)	4.8	1.3	37.6	41.3	57.6	57.3	0.860
Complementary and alternative medicines are a cheaper alternative to traditional prescription medicines (<i>n</i> =306)	9.6	5.2	30.6	48.1	59.8	46.8	0.134
Complementary and alternative medicines can interfere with traditional prescription medicines prescribed by my doctors (<i>n</i> =307)	40.4	44.2	43.0	51.9	16.5	3.9	0.126
Complementary and alternative medicines can cause side effects (<i>n</i> =306)	44.1	37.7	44.5	58.4	11.4	3.9	0.822
Use of complementary and alternative medicines can result in decreased use of traditional prescription medicines (<i>n</i> =304)	38.1	20.5	43.4	64.1	18.6	15.4	0.077
Doctors should be informed about the use of any complementary and alternative medicine (<i>n</i> =319)	91.1	91.5	5.5	7.3	3.4	1.2	0.890
Complementary and alternative medicine should be made available through the NHS (<i>n</i> =319)	73.1	56.4	18.5	33.3	8.4	10.3	0.010

It has been suggested by Astin that patients use CAM because of dissatisfaction with medical treatment and that they offer greater personal autonomy and control and are seen as compatible with their values and beliefs [3]. The results of the attitudinal statements and the MHLC in our population add some support to these suggestions in that Ever Users did believe that the use of CAM together with medical therapies was beneficial and that they did not need professional medical advice prior to use. However, in terms of the MHLC, which assesses the role of self, other people and luck in health, health management and outcomes, few differences were observed between Ever Users and Never Users indicating that personal autonomy is not a major association with CAM use. Paradoxically, Never Users were significantly more likely to agree with the statement that “following doctor’s orders to the letter is the best way to keep my condition from getting any worse”, clearly indicating that patient responses to attitudinal statements such as these are complex and deserve further exploration using a qualitative approach.

The potential for herbs to interact with current drug therapies or to modify disease process is recognised although significantly under researched. Herbal supplements such as soya, red clover and ginseng are reported to have direct estrogenic activity, however their actions appear complex and often contradictory [45]. Nevertheless such supplements could have the potential to promote breast cancer in patients when taken singly or, as is often the case, in combination with other sources of phytoestrogens. At present, however, there is no good evidence to confirm or refute these concerns. A further issue is the use of supplements which may directly affect the

metabolism or activity of adjuvant endocrine chemotherapy. In this study 52% of patients were currently using adjuvant endocrine (tamoxifen, anastrozole, letrozole or exemestane) and trastuzumab therapy. Of these, 40% were using herbal supplements, either singly or in combination, which reportedly have the potential to disrupt the CYP450 enzyme system. The situation however is complex and far from clear as neither the exact metabolic pathways of the adjuvant chemotherapy or of the herbal supplements used by women in this study have been fully elucidated. The metabolism of tamoxifen, anastrozole, letrozole and exemestane appears to rely on a combination of CYP450s including 1A1, 1A2, 2A6, 3A4, 3A5, 2B6, 2C6 and 2D6 [46–49]. Much of the CYP450 metabolic data have been obtained from in vitro human microsome studies, which may not be directly translatable into clinical practice. Several of the herb supplements commonly used in this study, such as echinacea, garlic, ginkgo biloba, valerian and St Johns Wort, have been reported to possess CYP450 enzyme-inducing activity, raising the possibility of reduced chemotherapeutic plasma levels and treatment failure. Although in the case of tamoxifen, which may act at least as a prodrug, increased therapeutic activity could possibly be observed. Similarly grapefruit, peppermint, chamomile, ginkgo biloba, valerian and black cohosh have been reported to inhibit a variety of CYP450 enzymes raising the possibility of impaired metabolism and resultant toxicity. However the potential for such interactions and the possible therapeutic outcomes have not been formally assessed and are far from clear. In the absence of robust data on the potential outcomes of such herb/medication interactions, it would seem more appropriate to avoid herbal supplements until

there is good evidence to ensure that neither safety nor efficacy are impaired.

Given these issues and the view of Ever Users that the use of CAM together with medical therapies was beneficial and that they did not need professional medical advice prior to use, there is a clear need for discussion between patients with breast cancer and healthcare professionals on the safe and informed use of CAMs.

There are several strengths to this study. We have added to the sparse published literature relating to use of CAMs, indications for use, levels of satisfaction, expenditure, and factors associated with patient use of CAMs. A high response rate together with a diverse population in relation to the demographic variables makes findings generalisable to other populations of breast cancer patients. However, there are limitations which we acknowledge. Our sample of patients was clustered around one breast cancer out-patient clinic and hence the findings may reflect medical and patient practice in this centre. Although our response rate was high, non-respondents may have replied very differently, and we had no data to compare respondents and non-respondents in terms of demographics. As there was no standard validated questionnaire in the literature (apart from the MHLC), a specific CAM survey tool was developed and piloted for

this study. However before use the questionnaire was tested for face and content validity.

Conclusions

The level of CAM use by Scottish breast cancer patients is similar to that reported from other countries although there are marked differences in the type, nature and frequency of specific CAM therapies and preparations. A higher patient education level and use by family and friends were significantly associated with CAM use. Few differences between views and attitudes towards CAM use and health were observed, however where they did occur they served to underline the complex nature of the patient. The use of specific herbal supplements with the potential to interact with adjuvant endocrine chemotherapy appears common and in light of the paucity of data concerning such interactions the precautionary principle should be adopted.

Conflict of interest All authors state that they have no conflicts of interest to declare.

Appendix 1

Table 4 Multidimensional health locus of control. Comparison of “Ever Users” with “Never Users”

	Strongly agree (%)		Moderately agree/ somewhat agree (%)		Somewhat disagree/ moderately disagree (%)		Strongly disagree (%)		P-value ^a
	Ever	Never	Ever	Never	Ever	Never	Ever	Never	
Scale A, internal									
If my condition worsens, it is my own behaviour which determines how soon I will feel better again (n=327)	15.3	19.6	77.0	76.1	7.7	4.3	0	0	0.119
I am directly responsible for my condition getting better or worse (n=326)	12.4	6.5	69.2	73.9	18.4	19.6	0	0	0.306
Whatever goes wrong with my condition is my own fault (n=329)	3.8	2.2	53.1	53.3	43.1	44.4	0	0	0.728
The main thing which affects my condition is what I myself do (n=331)	16.9	12.8	58.2	57.4	20.7	20.2	4.2	9.6	0.187
I deserve the credit when my condition improves and the blame when it gets worse (n=326)	3.9	5.3	20.7	18.1	45.3	39.4	30.2	37.2	0.386
If my condition takes a turn for the worse, it is because I have not been taking proper care of myself (n=331)	4.2	7.4	26.3	20.0	43.6	45.3	25.8	27.4	0.728
Scale B, powerful others									
If I see my doctor regularly, I am less likely to have problems with my condition (n=331)	21.9	25.8	68.4	68.1	9.7	6.4	0	0	0.311
Whenever my condition worsens, I should consult a medically trained professional (n=338)	79.2	80.6	19.6	19.4	1.3	0	0	0	0.728

Table 4 (continued)

	Strongly agree (%)		Moderately agree/ somewhat agree (%)		Somewhat disagree/ moderately disagree (%)		Strongly disagree (%)		P-value ^a
	Ever	Never	Ever	Never	Ever	Never	Ever	Never	
Other people play a big role in whether my condition improves, stays the same or gets worse (<i>n</i> =326)	12.4	14.1	74.8	70.7	12.8	15.2	0	0	0.915
In order for my condition to improve, it is up to other people to see that the right things happen (<i>n</i> =322)	8.2	14.4	37.9	37.8	32.3	31.1	21.6	16.7	0.151
Following doctor's orders to the letter is the best way to keep my condition from getting any worse (<i>n</i> =338)	40.8	54.1	48.3	36.7	9.2	8.2	1.7	1.0	0.041
The type of help I receive from other people determines how soon my condition improves (<i>n</i> =328)	17.5	23.4	62.8	59.6	15.8	11.7	3.8	5.3	0.288
Scale C, chance									
As to my condition, what will be will be (<i>n</i> =323)	12.6	15.1	69.1	71.0	18.3	14.0	0	0	0.318
Most things that affect my condition happen to me by chance (<i>n</i> =318)	7.9	11.0	75.3	68.1	16.7	20.9	0	0	0.820
Luck plays a big part in determining how my condition improves (<i>n</i> =329)	8.5	7.4	32.3	33.0	33.2	28.7	26.0	30.9	0.592
Whatever improvement occurs with my condition is largely a matter of good fortune (<i>n</i> =326)	6.4	3.3	30.8	31.5	39.3	40.2	23.5	25.0	0.537
If my condition worsens, it's a matter of fate (<i>n</i> =328)	7.2	10.8	46.8	43.0	26.4	25.8	19.6	20.4	0.844
If I am lucky, my condition will get better (<i>n</i> =323)	15.9	18.9	44.6	36.7	24.9	30.0	14.6	14.4	0.818

^a Mann Whitney *U*-test

References

- The World Health Organisation (2000) <http://www.who.int/medicines/areas/traditional/definitions/en/> Accessed 12.09.2010.
- Low Dog T (2009) The use of botanicals during pregnancy and lactation. *Altern Ther Health Med* 15(1):54–61.
- Astin AJ (1998) Why patients use alternative medicine. *JAMA* 279(19):1548–1553
- Bensoussan A, Marigliani R, Zorbas H (2008) Use of complementary therapies by Australian women with breast cancer. *Breast* 17:387–394
- Barnes PM, Powell-Griner E, McFann K, Nahin RL (2004) Complementary and alternative medicine use among adults: United States, 2002. *Adv Data* 27(343):1–19
- Yamashita H, Tsukayama H, Sugishita C (2002) Popularity of complementary and alternative medicine in Japan: a telephone survey. *Complement Ther Med* 10(2):84–93
- Menniti-Ippolito F, Gargiulo L, Bologna E, Forcella E, Raschetti R (2002) Use of unconventional medicine in Italy: a nation-wide survey. *Eur J Clin Pharmacol* 58(1):61–64
- Ernst E, Cassileth BR (1998) The prevalence of complementary/alternative medicine in cancer: a systematic review. *Cancer* 83(4):777–782
- Goldstein MS, Brown ER, Ballard-Barbash R, Morgenstern H, Bastani R, Lee J et al (2005) The use of complementary and alternative medicine among California adults with and without cancer. *Evid Based Complement Alternat Med* 2(4):557–565
- Morris KT, Johnson N, Homer L, Walts D (2000) A comparison of complementary therapy use between breast cancer patients and patients with other primary tumor sites. *Am J Surg* 179(5):407–411
- Molassiotis A, Scott JA, Keamey N, Pud D, Magri M, Selekerova S et al (2005) Complementary and alternative medicine use in breast cancer patients in Europe. *Support Care Cancer* 14(3):260–267
- Boon H, Stewart M, Kennard MA, Pud D, Magri M, Selvekerova S et al (2000) Use of complementary/alternative medicine by breast cancer survivors in Ontario: prevalence and perceptions. *J Clin Oncol* 18(13):2515–2521
- Nagel G, Hoyer H, Katenkamp D (2004) Use of complementary and alternative medicine by patients with breast cancer: observations from a health-care survey. *Support Care Cancer* 12(11):789–796
- Shen J, Andersen R, Albert PS, Wenger N, Glaspy J, Cole M et al (2002) Use of complementary/alternative therapies by women with advanced-stage breast cancer. *BMC Complement Altern Med* 2:8
- Helyer LK, Chin S, Chui BK, Fitzgerald B, Verma S, Rakovitch E et al (2006) The use of complementary and alternative medicines among patients with locally advanced breast cancer—a descriptive study. *BMC Cancer* 6:39
- DiGianni LM, Garber JE, Winer EP (2005) Complementary and alternative medicine use among women with breast cancer. *J Clin Oncol* 20(Suppl 18):34–38
- Crocetti E, Crotti N, Feltrin A, Ponton P, Geddes M, Buiatti E (1998) The use of complementary therapies by breast cancer patients attending conventional treatment. *Eur J Cancer* 34(3):324–328
- Rees R, Feigel I, Vickers A, Zollman C, McGurk R, Smith C (2000) Prevalence of complementary therapy use by women with breast cancer: a population-based survey. *Eur J Cancer* 36:1359–1364
- Moschen R, Kemmler G, Schweigkofler H, Holzner B, Dunser M, Richter R et al (2001) Use of alternative / complementary therapy

- in breast cancer patients—a psychological perspective. *Support Care Cancer* 9:267–274
20. Burstein HJ, Gelber S, Guadagnoli E, Weeks JC (1999) Use of alternative medicine by women with early stage breast cancer. *N Engl J Med* 340(22):1733–1759
 21. Balneaves LG, Bortorff JL, Hislop TG, Herbert C (2006) Levels of commitment: exploring complementary therapy use by women with breast cancer. *J Altern Complement Med* 12(5):459–466
 22. Boon HS, Olatunde F, Zick SM (2007) Trends in complementary/alternative medicine use by breast cancer survivors: comparing survey data from 1998 and 2005. *BMC Womens Health* 7:4. doi:10.1186/1472-6874-7-4
 23. Vickers AJ, Kup J, Cassileth BR (2006) Unconventional anticancer agents; a systematic review of clinical trials. *J Clin Oncol* 24(1):136e40
 24. Miller DR, Anderson GT, Stark JJ, Granick JL, Richardson D (1998) Phase I/II trial of the safety and efficacy of shark cartilage in the treatment of advanced cancer. *J Clin Oncol* 16(11):3649–3655
 25. Moertel CG, Fleming TR, Creagan ET, Rubin J, O'Connell MJ, Ames MM (1985) High dose vitamin C versus placebo in the treatment of patients with advanced cancer who have had no prior chemotherapy. A randomised double-blind comparison. *N Engl J Med* 312(3):137–141
 26. Creagan ET, Moertel CG, O'Fallon JR, Schutt AJ, O'Connell MJ, Rubin J et al (1979) Failure of high-dose vitamin C (ascorbic acid) therapy to benefit patients with advanced cancer. A controlled trial. *N Engl J Med* 301(13):687–690
 27. Werneke U, Earl J, Seydel C, Horn O, Crichton P, Fannon D (2004) Potential health risks of complementary alternative medicines in cancer patients. *Br J Cancer* 90(2):408–413
 28. Cassileth BR, Vickers AJ (2005) High prevalence of complementary and alternative medicine use among cancer patients: implications for research and clinical care. *J Clin Oncol* 23(12):1–3
 29. Labriola D, Livingstone R (1999) Possible interactions between dietary antioxidants and chemotherapy. *Oncology* 13(7):1003e8
 30. Boyle FM (1997) Adverse interaction of herbal medicine with breast cancer treatment. *Med J Aust* 167(5):286
 31. Bairati I, Meyer F, Gelinat M, Fortin A, Nabid A, Brochet F et al (2005) A randomized trial of antioxidant vitamins to prevent second primary cancers in head and neck cancer patients. *J Natl Cancer Inst* 97(7):481–488
 32. Cassidy A (2003) Are herbal remedies and dietary supplements safe and effective for breast cancer patients? *Breast Cancer Res* 5(6):300–302
 33. Meijerman I, Beijnen JH, Schellens (2006) Herb-drug interactions in oncology: focus on mechanisms of induction. *Oncologist* 11(7):742–752
 34. Baum M, Ernst E, Lejeune S, Horneber M (2006) Role of complementary and alternative medicine in the care of patients with breast cancer: report of the European Society of Mastology (EUSOMA) Workshop, Florence, Italy, December 2004. *Eur J Cancer* 42:1702–1710
 35. Therapeutic Research Faculty (2011) Natural medicines comprehensive database. <http://naturaldatabase.therapeuticresearch.com/home.aspx?cs=&s=ND>. Accessed August 2011
 36. Dong JY, Qin LQ (2011) Soy isoflavones consumption and risk of breast cancer incidence or recurrence: a meta-analysis of prospective studies. *Breast Cancer Res Treat* 125:315–323
 37. Patisaul HB, Jefferson W (2010) The pros and cons of phytoestrogens. *Front Neuroendocrinol* 31:400–419
 38. Wallston KA (2007) The multidimensional health locus of control. <http://www.vanderbilt.edu/nursing/kwallston/mhlc/scales.htm>. Accessed 2011
 39. Myers CD, Jacobsen PB, Huang Y, Frost MH, Patten CA, Cerhan JR, Sellers TA (2008) Familial and perceived risk of breast cancer in relation to use of complementary medicine. *Cancer Epidemiol Biomarkers Prev* 17(6):1527–1534
 40. Mueller CM, Mai PI, Bucher J, Peters JA, Loud JT, Greene MH (2008) Complementary and alternative medicine use among women at increased genetic risk of breast and ovarian cancer. *BMC Complement Altern Med* 8:17
 41. Werneke U, Earl J, Seydel C, Horn O, Crichton P, Fannon D (2004) Potential health risks of complementary alternative medicines in cancer patients. *Br J Cancer* 90:408–413
 42. Monroe KR, Murphy SP, Kolonel LN, Pike MC (2007) Prospective study of grapefruit intake and risk of breast cancer in postmenopausal women: the Multiethnic Cohort Study. *Br J Cancer* 97:440–445
 43. Spencer EA, Key TJ, Appleby PN, van Gils CH, Olsen A, Tjonneland A, Clavel-Chapelon F, Boutron-Ruault MC, Touillaud M, Sanchez MJ, Bingham S, Khaw KT, Slimani N, Kaaks R, Riboli E (2009) Prospective study of the association between grapefruit intake and risk of breast cancer in the European Prospective Investigation into Cancer and Nutrition (EPIC). *Cancer Causes Control* 20(6):803–809
 44. Schmidt K, Ernst E (2004) Assessing websites on complementary and alternative medicine for cancer. *Ann Oncol* 15:733–742
 45. Helferich WE, Andrade JE, Hoagland MS (2008) Phytoestrogens and breast cancer: a complex story. *Inflammopharmacology* 16:219–226
 46. Kamdem LK, Liu Y, Stearns V et al (2010) In vitro and in vivo oxidative metabolism and glucuronidation of anastrozole. *Br J Clin Pharmacol* 70(6):854–869
 47. Desta Z, Ward BA, Flockhart DA (2005) In vitro letrozole N-dealkylation is mainly catalyzed by human cytochrome P450 (CYP) 3A. *Clin Pharm Ther* 77:79
 48. Kamdem LK, Flockhart DA, Desta Z (2011) In vitro cytochrome P450-mediated metabolism of exemestane. *Drug Metab Dispos* 39(1):98–105
 49. Crewe HK, Notley LM, Wunsch RM et al (2002) Metabolism of tamoxifen by recombinant human cytochrome P450 enzymes: formation of the 4-hydroxy, 4'-hydroxy and N-desmethyl metabolites and isomerization of trans-4-hydroxytamoxifen. *Drug Metab Dispos* 30(8):869–874