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Nature and severity of menopausal symptoms and impact on quality of life and sexual function in cancer survivors compared to women without a cancer history

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Abstract:	Objective: Following cancer treatment, troublesome menopausal symptoms are common but poorly understood. Using standardized instruments, we measured differences in symptom nature, severity, impact on quality of life and sexual function between cancer survivors and non-cancer participants. Methods: The Menopausal Symptoms after Cancer (MSAC) Clinic operates within the general menopause service in a large women's hospital, providing menopause advice and management to women with menopausal symptoms and a history of cancer. Menopausal symptoms were recorded using Greene Climacteric Scale, past-week symptoms with Functional Assessment of Cancer Therapy - Breast and Endocrine Symptom Subscales, and sexual symptoms using Fallowfield's Sexual Activity Questionnaire. Results: Cancer survivors (N=934) and non-cancer participants (N=155) did not significantly differ by age at menopause (46 years) or age at first clinic visit (51 years). Cancer survivors were more likely than non-cancer participants to be severely troubled by vasomotor symptoms (hot flushes and night sweats, OR 1.71 95% CI 1.06-2.74), and reported more frequent (6.0 vs. 3.1 in 24 hours, $p<0.001$) and more severe ($p=0.008$) hot flushes. In contrast, cancer survivors were significantly less troubled by psychological and somatic symptoms and reported better quality of life than non-cancer participants. Groups did not differ significantly in physical or functional well-being, gynecologic symptom severity, or sexual function. Conclusion: Cancer survivors are more troubled by vasomotor symptoms than non-cancer participants, but non-cancer participants report greater psychological

	symptoms. Sexual function did not differ. Improved understanding of the nature and impact of menopause in cancer survivors can be used to direct patient management protocols.

Title: Nature and severity of menopausal symptoms and impact on quality of life and sexual function in cancer survivors compared to women without a cancer history

Running title: Menopausal symptoms in cancer survivors

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Key words: menopause, cancer, sexual function

ABSTRACT

Objective: Following cancer treatment, troublesome menopausal symptoms are common but poorly understood. Using standardized instruments, we measured differences in symptom nature, severity, impact on quality of life and sexual function between cancer survivors and non-cancer participants.

Methods: The Menopausal Symptoms after Cancer (MSAC) Clinic operates within the general menopause service in a large women's hospital, providing menopause advice and management to women with menopausal symptoms and a history of cancer. Menopausal symptoms were recorded using Greene Climacteric Scale, past-week symptoms with Functional Assessment of Cancer Therapy - Breast and Endocrine Symptom Subscales, and sexual symptoms using Fallowfield's Sexual Activity Questionnaire.

Results: Cancer survivors (N=934) and non-cancer participants (N=155) did not significantly differ by age at menopause (46 years) or age at first clinic visit (51 years). Cancer survivors were more likely than non-cancer participants to be severely troubled by vasomotor symptoms (hot flushes and night sweats, OR 1.71 95% CI 1.06-2.74), and reported more frequent (6.0 vs. 3.1 in 24 hours, $p<0.001$) and more severe ($p=0.008$) hot flushes. In contrast, cancer survivors were significantly less troubled by psychological and somatic symptoms and reported better quality of life than non-cancer participants. Groups did not differ significantly in physical or functional well-being, gynecologic symptom severity, or sexual function.

Conclusion: Cancer survivors are more troubled by vasomotor symptoms than non-cancer participants, but non-cancer participants report greater psychological symptoms. Sexual function did not differ. Improved understanding of the nature and impact of menopause in cancer survivors can be used to direct patient management protocols.

INTRODUCTION

Over 151,000 women in Australia, nearly 4% of the female population, are cancer survivors[1] (more than 15 million worldwide[2]). More than a third of those are breast cancer survivors[1]. In developed countries, cancer survival rates, particularly of breast cancer, have rapidly risen over the past 30 years[1, 3], emphasizing the importance of survivorship issues[4]. Menopausal symptoms are a frequent and distressing effect of cancer treatments in women[5, 6]. Ovarian tissue is highly sensitive to the radiation or cytotoxic regimens commonly used in breast, colorectal, gynecologic and hematologic cancers[7-10]. In hormone-sensitive breast and gynecologic cancers, suppression of estrogen production or action improves cancer outcomes[11].

Several small observational studies[12-16] have suggested that menopausal symptoms in cancer survivors may differ in nature and severity from those seen in non-cancer participants. However, no previous studies have compared a large population of cancer survivors with menopausal symptoms with non-cancer participants presenting for treatment of menopause symptoms in order to determine differences in the nature, severity, impact on quality of life and sexual function using standardized and validated instruments. The aim of this study was to describe how menopausal symptoms differ in cancer survivors compared to non-cancer participants in these key areas. Further information about the nature, severity and impact on quality of life is needed in order to develop appropriate services and therapeutic options for the growing population of female cancer survivors.

METHODS

Between January 2003 and November 2010, data were collected for all first visits to a multidisciplinary Menopausal Symptoms after Cancer (MSAC) clinic and, when funding became available in 2008, the Menopause clinic of the King Edward Memorial Hospital, a public tertiary women's hospital that serves a population of around 1.3 million women in Western Australia. Data were collected on marital status, occupation, smoking status, alcohol intake, family cancer history, parity, gravidity, menopausal status and date of last menstrual period. Women were considered premenopausal if they had regular menstrual periods and no vasomotor symptoms, perimenopausal if

they had changes in menstrual cycle and/or new onset vasomotor symptoms, and postmenopausal if they were more than one year past their last menstrual period[17]. Gynecologic history, history of previous hormone and non-hormone therapy for menopausal symptoms, and history of hypertension, diabetes, venous thrombotic event, anxiety and depression were recorded at the first visit. Information about the nature, stage and grade of cancer plus cancer therapy was collected from medical records. Where possible, the nature of menopause (spontaneous, surgical, chemotherapy-induced, radiation-induced) was identified from clinical history and discussion with women.

All women attending the Menopause or Menopausal Symptoms after Cancer clinic were invited to participate. The study was approved by the institutional ethics committee at King Edward Memorial Hospital in Western Australia.

Questionnaires

Participants were asked to report their symptoms currently, within the previous week, and within the previous month. Current menopausal symptoms were collected using the Greene Climacteric Scale[18], a validated self-report questionnaire for which age-specific Australian population norms have been published[19]. The Greene Scale measures the extent to which women are currently troubled ("not at all", "a little", "quite a bit", "extremely") by 21 menopause symptoms in four domains: vasomotor, psychological, sexual, and somatic.

Past-week symptoms were evaluated using the Functional Assessment of Cancer Therapy (FACT) family of instruments[20] (www.facit.org). Participants completed the 19-item Endocrine Symptom Subscale[21] and selected items from the FACT-General Scale[20] and Breast Cancer Subscale (version 4). These tools are appropriate for use in women with and without cancer[20, 22, 23]. Some items were not administered because they are not appropriate for women without cancer (e.g. "I am losing hope in the fight against my illness"). Global well-being scores were derived from these instruments[24].

Sexual function during the previous month was reported using Fallowfield's Sexual Activity Questionnaire (SAQ)[25], which has been validated in populations of women with and without cancer as well as high-risk women[26].

Detailed information regarding participant completion of components of all scale components, as well as examples of scale items, may be found in Supplementary Online Table 1.

Vasomotor symptoms

In addition to the Greene Scale assessment of current hot flushes and night sweats, participants were asked to report the number of hot flushes of each of four severities ("mild", "moderate", "severe", "very severe") they had experienced in the previous 24 hours. The Endocrine Symptom Subscale vasomotor symptom assessmentevaluates the past-week impact of hot flushes, night sweats, cold sweats and sleep disruption

Neuropsychological symptoms

The Greene Scale psychological domain includes anxiety and depression subscales. Women were also assessed with neuropsychological items from the FACT scales, and completed the Social/Family Well-being subscale. *Somatic symptoms*

The Greene Scale asks participants to describe the extent to which they are troubled by seven items in the somatic domain. We also asked items from the FACT Endocrine Symptoms Subscale pertaining to gastrointestinal function in the past week, as well as completing the Physical and Functional Well-Being Subscales.

Gynecologic symptoms and sexual function

The Greene Scale assesses the current extent to which participants are troubled by "loss of interest in sex". In addition, women reported current trouble with "vaginal dryness" and “bladder problems” ("not at all", "a little", "quite a bit" and "extremely"). In addition to the Greene and FACT scales, participants completed Fallowfield's Sexual Activity Questionnaire (SAQ).[25]. All participants complete the first section of the instrument, which investigates current sexual activity status. Section II, completed by sexually inactive women, lists reasons for the lack of sexual activity. Section III, completed by sexually active women, consists of ten Likert-format items regarding sexual feelings

and experiences the previous months, in scales of Pleasure (SAQ-), Discomfort (SAQ-D), and Habit (SAQ-H).

Statistical analyses

For demographic and lifestyle characteristics, comparisons between groups were conducted for median values of continuous variables using Fisher's exact test for the equality of medians, and for distribution of categorical variables using two-sided Fisher's exact tests.

Analyses of the Greene Scale were limited to women for whom data were complete for at least one domain. Scoring within domains was skewed for the Greene Scale and SAQ, so medians and ranges were reported to describe score distributions, and non-parametric tests used to compare scores between groups. With the exception of the sexual interest item, for Greene Scale domains, we reported the proportion of the study groups scoring above the upper bound of published 95% reference ranges[19] for postmenopausal women (who score higher on most Greene Scale domains than pre or peri-menopausal women). Differences in continuous variables were assessed using Fisher's exact test for equality of medians. Mean scores for the FACT Social/Family Well-being, Functional Well-being, and Physical Well-being subscales were compared using t-tests for unequal variances. Binary variables were derived from Greene Scale domains by grouping women who were troubled "quite a bit" or "extremely" for half the scale items or more within that domain. Similarly, women who had reported "a little" or "not at all" for three or more of the six items on the SAQ-P scale were classified as having low sexual pleasure, and those who had reported feeling pain or discomfort during penetration or dryness of the vagina "very much" were classified as having high sexual discomfort. Those who reported "quite a bit" or "very much" for symptoms derived from the FACT scales were classified as having severe symptoms, except for the item "I am sleeping well", which was classified as severe if participants endorsed "not at all" or "a little bit". Relationships between binary variables and cancer status were explored using logistic regression analysis adjusted for age at visit, age at menopause, current use of hormone therapy (HT) and current use of endocrine therapy.

Data analysis was conducted using Stata v.11.2 (StataCorp. 2009. *Stata Statistical Software: Release 11*. College Station, TX: StataCorp LP). All hypothesis tests were two-sided and p-values<0.05 were considered statistically significant.

RESULTS

Study group characteristics

Demographic and lifestyle characteristics of the study groups (934 cancer survivors, 155 non-cancer participants) are shown in Table 1. For both groups, median age at first clinic visit was 51 years, and at menopause was 46 years. Non-cancer participants were more likely to have experienced natural menopause (59% vs 33%). Non-cancer participants were more likely to have experienced surgical menopause compared to cancer survivors (41% v. 26%). Most participants were married or in de-facto relationships and had given birth to at least one child. There were no significant differences in smoking or alcohol use. Lifetime and current HT use were more common in non-cancer participants than cancer survivors (ever HT 38% cancer survivors v. 50% non-cancer participants; current HT 5% v. 13.5%). Lifetime use of clonidine was higher among cancer survivors than non-cancer participants (5.8% v. 1.3%) , but use of selective serotonin-norepinephrine reuptake inhibitors and gabapentin did not differ. Use of complementary/alternative therapies was more common among cancer survivors than non-cancer participants (17.5% v. 7.1%).

Characteristics of cancer survivors are presented in Table 2. Over half of the cancer survivors referred to the MSAC clinic for management of menopausal symptoms were peri- or postmenopausal when their cancer was diagnosed. Over half the survivors had undergone treatment more than a year before their clinic visit, and 13% had been treated five or more years previously. The great majority of survivors had a previous diagnosis of breast cancer (82%). A smaller proportion had previously had a gynecological cancer (10.5%) with the remainder (7.5%) hematological and colorectal malignancies. A small percentage (5%) had more than one previous cancer.

All participants were offered all instruments. Ninety percent (N=841) of the cancer survivors and 98.7% (N=153) of non-cancer participants completed at least part of the Greene Climacteric Scale.

The SAQ was attempted by 422 (45.1%) cancer survivors and 97 (62.6%) non-cancer participants, and the FACT questionnaire by 442 (47.3%) cancer survivors and 102 (65.8) non-cancer participants. Details regarding subscale completion are available in Supplementary Online Table 1.

Vasomotor symptoms

Seventy-nine percent of cancer survivors and 61% of non-cancer participants reported current severe vasomotor symptoms (Table 3). Thirty-six percent of cancer survivors and 23% of non-cancer participants scored in excess of the upper bound of the published reference range for vasomotor symptoms (Supplementary Online Table 2). Current severe trouble with vasomotor symptoms was more likely among cancer survivors after accounting for age at visit, age at menopause, and current HT ($p=0.027$, see Table 3). The difference between groups was attributable to greater likelihood of severe trouble with hot flushes ($p=0.022$).

In the prior 24 hours, cancer survivors were more likely to report hot flushes ($p<0.001$) than non-cancer participants. Cancer survivors were more likely than non cancer participants to report severe or very severe flushes ($p=0.008$) in the last 14 hours, after adjusting for the same factors. Cancer survivors also reported more frequent flushes than non-cancer participants (mean, 95% CI cancer survivors: 6.0, 5.6-6.4; non-cancer participants 3.1, 2.4-3.8, t-test $p<0.001$) and were substantially more likely to report ten or more hot flushes in the previous 24 hours compared to non-cancer participants (Table 3, $p=0.004$).

Neuropsychological symptoms

Cancer survivors were much less likely to report that they were severely troubled by psychological symptoms compared to non-cancer participants. This difference between groups was attributable to differences in the depression subscore of the Greene Climacteric Scale (Table 4). Sixteen percent of cancer survivors and 27% of non-cancer participants scored in excess of the upper bound of the published reference range for psychological symptoms (Supplementary Online Table 1).

Over the prior week, cancer survivors were less likely to have severe mood swings (p=0.004), irritability (p=0.003), or sadness (p=0.024) than non-cancer participants (Table 4). Cancer survivors also scored significantly better in social/family well-being than non-cancer participants (p=0.002) (Table 4).

Somatic symptoms

Somatic symptoms were less troublesome for cancer survivors compared to non-cancer participants (p<0.001), a difference consistent across all items except breathing difficulties and muscle/joint pains (Table 5). Twelve percent of cancer survivors and 24% of non-cancer participants scored in excess of the upper bound of the published reference range for somatic symptoms (Supplemental Online Table 1). Cancer survivors were less likely than non-cancer participants to report severe headaches (p=0.04), weight gain (p=0.01) or bloating (p=0.02) in the previous week (Table 5). Mean Physical Well-Being and Functional Well-Being scores did not differ between cancer and non-cancer participants.

Gynecologic symptoms and sexual function

Although 79% of all participants were currently in relationships, only 59% were sexually active. Overall no significant differences in sexual activity or function were observed between cancer and non-cancer participants. However, cancer survivors were significantly more likely to attribute their sexual inactivity to a "physical problem that makes sexual relations difficult or uncomfortable" compared to non-cancer participants (21% v. 3%, p=0.013). (Table 6).

Thirty-seven percent of cancer survivors and 34% of non-cancer participants scored in excess of the upper bound of the published reference range for loss of interest in sexual activity (Supplementary Online Table 1) but this should be interpreted cautiously as the range for this domain of the Green Scale is very small (0 to 3) and so score variability is limited.

Severe vaginal dryness troubled 49% of this study population but did not differ significantly between cancer and non-cancer populations. Severe loss of sexual interest was also common, troubling 65% of participants and affecting 45% within the past week, but did not differ by cancer status.

DISCUSSION

This is the first large clinic-based study to measure the nature, severity and impact of menopausal symptoms on sexual function and quality of life in cancer survivors compared to non-cancer participants. The most striking observation was that, after accounting for age and use of menopausal hormone therapy (HT), hot flushes were more troublesome, severe and frequent among cancer survivors compared to non-cancer patient, consistent with previous smaller studies[12, 27]. It is notable that many cancer survivors presented with menopausal symptoms many years since their original diagnosis, indicating the persistence and prevalence of menopausal symptoms in this population. Although HT use at the first clinic visit was over twice as frequent among non-cancer participants as cancer survivors (13.5% v. 5%), HT use was uncommon and did not account for differences in multivariate analysis. Although lifetime clonidine use was more common among cancer survivors, indication information was not available, and lifetime use of other non-hormonal medications for vasomotor symptoms did not differ between groups. Complementary and alternative therapies, including use of herbal preparations, were more common among cancer survivors, but this finding should be taken cautiously because, if survivors are more focused on maintaining health, they might be more likely to recall and report these and other therapies than other patients. Data were not available regarding body mass index, which could potentially have impacted on vasomotor symptoms.

The observation that psychological symptoms, particularly depressive symptoms, were more prevalent in non-cancer participants than cancer survivors was unexpected. Over a quarter of the non-cancer participants scored above the reference range for psychological symptoms[19]. However, this observation is consistent with recent reports that over one third of gynecologic outpatients meet diagnostic criteria for an anxiety or depressive disorder[28]. The reason for this difference in emotional well-being is not known, but may be attributable to the better social and psychological support associated with a cancer diagnosis compared to that of menopause[20].

This is the first time that psychological symptoms have been compared between these groups using validated instruments. A small study from Brazil, using a non-standardized measurement tool, reported no differences in "nervousness, headache, depression and insomnia" between cancer

survivors and controls with menopausal symptoms [13]. We used a validated menopause scale with a psychological symptoms domain (Greene Climacteric Scale) rather than a mental health tool to measure psychological symptoms. Further comparative studies using validated measurement scales for anxiety and depression are needed. Both cancer and non-cancer survivors had considerably more severe psychological symptoms than published norms[19], although the 20-25% prevalence of severe trouble with menopausal symptoms in these mental health domains in cancer survivors is consistent with previous studies of menopausal breast cancer survivors[29, 30]. We were surprised to find that cancer survivors were less likely to report psychological symptoms. Psychological support through hospital services and consumer organisations is available for cancer survivors in Australia, particularly breast cancer survivors. It is possible that cancer survivors referred to the MSAC service had already received psychological support which may explain the lower reports of psychological symptoms in this population. Also, many survivors were some years from their cancer diagnosis. Psychological morbidity is common at diagnosis of breast and gynaecological cancers but symptoms improve significantly over time[31], and the early psychological symptoms associated with a cancer diagnosis may have resolved. Also, it is well recognised that symptoms of anxiety and depression are common in women at menopause[32, 33]. Furthermore, those women attending a gynaecology outpatient clinic may be more likely to report psychological symptoms than women in the general community [34].

Somatic symptoms measured by the Greene Climacteric Scale (e.g. “pressure or tightness in head or body" and "headaches") were also more common in non-cancer participants, as were some of the somatic symptoms measured by the FACT Breast Cancer Subscale (e.g. "weight gain" and "bloating"). These somatic symptoms are nonspecific, not clearly attributable to endocrine changes at menopause[35] and may further reflect the worse psychological condition of non-cancer participants undergoing menopause.

We were surprised to find that symptoms of sexual dysfunction symptoms did not differ by cancer status but severe vaginal dryness, pain during sexual intercourse, and loss of interest in sex were very common and troublesome in both groups. This contrasts with the few studies comparing women with a breast cancer history[12, 36, 37] or cervical cancer[16, 38, 39], which found worse gynecologic and sexual

function, but most of these studies did not account for menopausal status[36-39]. A relatively high proportion of non-cancer participants (41%) had gone through surgical menopause. It is well recognized that surgical menopause may be more likely to lead to sexual dysfunction than natural menopause[40] and this may have contributed to our observations. Cancer survivors were more likely to attribute their sexual inactivity to a "physical problem that makes sexual relations difficult or uncomfortable" compared to non-cancer participants. This does not appear to reflect increased levels of vaginal dryness in the cancer participants, as this was common in both groups. Further qualitative studies may shed further light on the physical problems which negatively impacted on sexual function in these cancer patients

The current study has certain limitations. This was a convenience sample and the cancer participants are skewed towards the most common types of cancer in women. As close to 90% of the survivors had a history of breast cancer, our findings mainly reflect this population. Ethnicity data are not available for individual participants, but the hospital serves a population who are 90% White. Menopausal symptoms are known to differ in nature and severity according to ethnicity [41], but our ethnically homogenous sample minimizes these variations.

Conclusion

In summary, this large comparative observational study has shown that in clinical populations, menopausal symptoms differ significantly between cancer survivors, some many years after their cancer diagnosis and non-cancer participants in both their severity and impact. Hot flushes were more troublesome and severe among cancer survivors, but psychological and somatic symptoms and measures of were more marked in women with no cancer history going through menopause. The safe and effective management of menopausal symptoms after cancer is a considerable clinical challenge[35]. The majority of cancer survivors with clinically significant menopause symptoms have a breast cancer history and should avoid hormonal products since these may impact negatively on cancer prognosis[42]. Accurate information about the nature and severity of menopausal symptoms after cancer is needed to inform the development of appropriate evaluation and management protocols.

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Table

Table 1. Participant characteristics, Menopause and Menopausal Symptoms after Cancer clinics, King Edward Memorial Hospital.

	Non-cancer participants	Cancer survivors	p
Total (N)	155	934	-
Median age at visit (IQR[a], range)	51 (46-56, 27-72)	51 (45-57, 17-83)	1.00
Median age at menopause (IQR[a], range)	46 (39-50, 21-59)	46 (41-50, 16-60)	0.92
Cause of menopause, N (%)			
Natural only	91 (58.7)	305 (32.7)	**<0.001**[b]
Surgical	63 (40.6)	241 (25.8)	**<0.001**[c]
Chemotherapy	-	247 (26.4)	
Radiation	-	7 (0.7)	
More than one cancer-related cause	-	43 (4.6)	
Missing/unreported	1 (0.6)	91 (9.7)	
Marital status, N (%)			
Never married	13 (8.4)	124 (13.3)	**0.04**
Married/de facto	103(66.5)	655 (70.1)	
Widowed/separated/divorced	25 (16.1)	99 (10.6)	
Missing	14 (9.0)	56 (6.0)	
Gravidity, N (%)			0.82
0	26 (16.7)	131 (14.0)	
1	19 (12.3)	91 (9.7)	
2	33 (21.3)	203 (21.7)	
3+	58 (37.4)	326 (34.9)	
Missing	20 (12.9)	183 (19.6)	
Parity, N (%)			0.29
0	32 (20.6)	175 (18.7)	
1	19 (12.3)	125 (13.4)	
2	41 (26.5)	327 (35.0)	
3+	50 (32.3)	269 (28.8)	
Missing	13(8.4)	38 (4.1)	
Smoking, N (%)			0.32
Never	118 (76.1)	684 (73.2)	
Former	4 (2.6)	51 (5.5)	
Current	26 (16.8)	149 (16.0)	
Missing	7 (4.5)	50 (5.4)	
Alcohol use, N (%)			0.44
None	49 (31.6)	264 (28.3)	
Any	97 (62.6)	611 (65.4)	
Missing	9 (5.8)	59 (6.3)	
Ever HT[d], N (%)	78 (50.3)	364 (39.0)	**0.010**
HT[d] use at clinic visit, N (%)	21 (13.5)	45 (4.8)	**<0.001**
Ever SSNRI/SSRI[e], N(%)	22 (14.2)	186 (19.9)	0.10
Ever gabapentin, N(%)	2 (1.3)	10 (1.1)	0.68
Ever clonidine, N(%)	2 (1.3)	54 (5.8)	**0.017**
Ever CAT[f], N(%)	11 (7.1)	163 (17.5)	**0.001**
Ever herbal remedies[g], N(%)	11 (7.1)	145 (15.5)	**0.004**
Vitamin/mineral supplement use, N(%)	29 (18.7)	225 (24.1)	0.15

a. IQR: interquartile range. b. Natural menopause frequency comparison only. c. Surgical menopause frequency comparison only. d. Hormone therapy. e. SSNRI: selective serotonin-norepinephrine reuptake inhibitors f. SSRI: selective serotonin reuptake inhibitors. f. CAT: complementary or alternative therapy, including herbal remedies, acupuncture, meditation, yoga, reiki, bowen therapy, aromatherapy, reflexology, homeopathy, naturopathic, immune system boosters, or natural therapy. g. Herbal remedies include unspecified herbs, evening primrose oil, black cohosh, red clover, wild yam, soy, echinacea, rosehip, St Johns wort, barley, spirulina, ginkgo, dong quai, garlic, licorice, acai berry,

linseed, flaxseed oil, chia seed, Nature's Way Menopause, Promensil, Remifemin, Meno-Health, Meno-Eze, Zen Harmony, Stress No More from Totally Natural, Crampeze, Femarelle.

Table 2. Clinical characteristics of cancer survivors, Menopausal Symptoms after Cancer clinic, King Edward Hospital.

	N (%)
Menopause status at cancer diagnosis	
Premenopausal	433 (46.4)
Perimenopausal	110 (11.8)
Postmenopausal	391 (41.9)
Time since cancer treatment	
Less than 1 year	405 (43.4)
1 to <2 years	196 (21.0)
2 to <5 years	202 (21.6)
5 to <10 years	90 (9.6)
10 years or longer	32 (3.4)
Missing	9 (1.0)
Cancer site	
Breast only	764 (81.8)
Gynecologic only	98 (10.5)
Ovarian only	47 (5.0)
Cervical only	25 (2.7)
Endometrial only	26 (2.8)
Other	21 (2.2)
Colorectal only	9 (1.0)
Hematologic only	4 (0.4)
Other only	8 (0.9)
More than one site/type	51 (5.5)
Ever endocrine therapy	593 (63.5)
Endocrine therapy at clinic visit	396 (42.4)

Table 3. Vasomotor symptoms, Menopause and Menopausal Symptoms after Cancer clinics, King Edward Memorial Hospital.

	Non-cancer participants	Cancer survivors	
	N (%) Reference category	N (%) OR (95% CI)	p
Current severe trouble with:			
Vasomotor symptoms	**89 (61.0)**	**639 (78.7)** **1.71 (1.06-2.74)**	**0.027**
Hot flushes	**84 (56.4)**	**622 (75.1)** **1.70 (1.08-2.67)**	**0.022**
Night sweats	82 (55.0)	555 (67.7) 1.41 (0.90-2.18)	0.13
Past 24 hours:			
Any hot flushes	**83 (54.2)**	**639 (76.0)** **2.56 (1.67-3.93)**	**< 0.001**
Mild or moderate flushes	74 (89.2)*	506 (79.2)[a] 0.60 (0.26-1.36)	0.22
Severe or very severe flushes	**33 (39.8)***	**386 (60.4)[a]** **2.18 (1.23-3.87)**	**0.008**
10+ flushes	**13 (15.7)***	**201 (31.5)[a]** **3.61 (1.50-8.73)**	**0.003**
Past week severe:			
Poor sleep	62 (60.8)	266 (61.3) 0.77 (0.44-1.36)	0.37
Hot flushes	55 (53.9)	326 (74.6) 1.65 (0.93-2.91)	0.09
Night sweats	47 (46.1)	252 (57.5) 1.14 (0.66-1.97)	0.64
Cold sweats	22 (22.0)	104 (24.8) 0.82 (0.44-1.53)	0.54

OR: odds ratio. CI: confidence interval.
a. Denominator is women within category reporting any hot flushes in past 24 hours.
Odds ratios adjusted for age at menopause, age at visit, and current use of hormone therapy.
Denominators vary according to completion of instrument.

Table 4. Neuropsychological symptoms, Menopause and Menopausal Symptoms after Cancer clinics, King Edward Memorial Hospital.

	Non-cancer participants	Cancer survivors	
	N (%) Reference category	N (%) OR (95% CI)	p
Current severe trouble with:			
Psychological symptoms	**41 (31.8)**	**138 (19.8)** **0.42 (0.26-0.68)**	**< 0.001**
Depressive symptoms	**56 (39.7)**	**186 (23.9)** **0.44 (0.28-0.68)**	**< 0.001**
Anxiety symptoms	43 (31.6)	177 (24.7) 0.68 (0.42-1.10)	0.12
Past week severe:			
Mood swings	**44 (43.1)**	**120 (27.5)** **0.46 (0.26-0.78)**	**0.004**
Irritability	**41 (40.6)**	**105 (24.1)** **0.49 (0.27-0.87)**	**0.014**
Nervousness	17 (16.7)	73 (16.9) 0.93 (0.47-1.85)	0.84
Lack of energy	45 (44.1)	185 (42.1) 1.05 (0.61-1.82)	0.86
Sadness	**35 (34.3)**	**95 (21.8)** **0.51 (0.29-0.92)**	**0.024**
Past week social/family well-being (mean, SD)	**16.61, 6.39**	**18.92, 6.22**	**0.002**

OR: odds ratio. CI: confidence interval. SD: standard deviation.
Odds ratios adjusted for age at menopause, age at visit, current use of hormone therapy and current use of endocrine therapy.

Table 5. Somatic symptoms, Menopause and Menopausal Symptoms after Cancer clinics, King Edward Memorial Hospital.

	Non-cancer participants	Cancer survivors	
	N (%) Reference category	N (%) OR (95% CI)	p
Current severe trouble with:			
Any somatic symptoms	**31 (23.0)**	**71 (10.2)** **0.30 (0.18-0.52)**	**<0.001**
Headaches	**51 (33.8)**	**183 (23.0)** **0.46 (0.28-0.72)**	**0.001**
Pressure or tightness in head or body	**47 (31.3)**	**129 (16.2)** **0.40 (0.25-0.63)**	**<0.001**
Parts of body feel numb or tingling	**45 (30.4)**	**162 (20.1)** **0.53 (0.33-0.85)**	**0.008**
Feeling dizzy or faint	**27 (18.5)**	**96 (12.0)** **0.47 (0.27-0.80)**	**0.006**
Loss of feeling in hands or feet	**26 (17.3)**	**83 (11.8)** **0.47 (0.27-0.80)**	**0.005**
Muscle and joint pains	76 (50.3)	366 (45.9) 0.77 (0.50-1.17)	0.22
Breathing difficulties	20 (13.5)	62 (7.9) 0.60 (0.31-1.16)	0.13
Past week severe:			
Headaches	**29 (28.4)**	**87 (19.95)** **0.53 (0.29-0.97)**	**0.038**
Dizziness	20 (19.6)	50 (11.3) 0.73 (0.35-1.55)	0.42
Weight gain	**49 (48.0)**	**149 (34.4)** **0.56 (0.33-0.95)**	**0.033**
Bloating	**42 (41.6)**	**131 (30.1)** **0.52 (0.30-0.89)**	**0.018**
Vomiting	2 (2.0)	4 (0.9) 0.45 (0.04-4.68)[a]	0.51
Diarrhea	6 (5.9)	17 (3.9) 0.53 (0.18-1.59)	0.26
Joint pain	48 (47.1)	178 (40.8) 0.78 (0.45-1.33)	0.36
Breast tenderness[b]	24 (23.5)	85 (19.7) 0.73 (0.40-1.35)	0.32
Past week physical well-being (mean, SD)	18.85, 6.68	20.15, 6.16	0.08
Past week functional well-being (mean, SD)	16.18, 6.18	16.37, 6.03	0.78

OR: odds ratio. CI: confidence interval. SD: standard deviation.
Odds ratios adjusted for age at menopause, age at visit, and current use of hormone therapy except where otherwise noted.
a. Rarity of this outcome did not permit fully-adjusted analysis. Estimate adjusted only for age at visit and age at menopause.
b. 34 cancer survivors with history of bilateral mastectomy omitted

Table 6. Gynecologic symptoms and sexual function, Menopause and Menopausal Symptoms after Cancer clinics, King Edward Memorial Hospital.

	Non-cancer participants	Cancer survivors	
	N (%) OR (95% CI)	N (%) OR (95% CI)	p
Current severe trouble with:			
Loss of interest in sex	101 (68.2)	497 (63.8) 0.91 (0.58-1.43)	0.70
Vaginal dryness	68 (47.2)	383 (48.9) 0.94 (0.61-1.45)	0.77
Bladder problems	39 (26.9)	179 (22.6) 0.67 (0.42-1.08)	0.10
Past week severe:			
Vaginal discharge	10 (9.8)	30 (6.9) 0.72 (0.28-1.87)	0.50
Vaginal itching/irritation	8 (7.9)	36 (8.2) 0.89 (0.36-2.20)	0.81
Vaginal bleeding/spotting	7 (6.9)	7 (1.6) 0.45 (0.08-2.51)[a]	0.36
Vaginal dryness	27 (26.7)	138 (32.2) 0.93 (0.52-1.65)	0.79
Pain/discomfort with intercourse	20 (22.0)	105 (26.9) 1.13 (0.59-2.17)	0.70
Loss of interest in sex	48 (49.0)	183 (43.8) 0.83 (0.48-1.43)	0.50
Past month:			
In a relationship, N (%)	76 (77.6)	337 (79.5)	0.68
Sexually active, N (%)	63 (64.9)	244 (57.8)	0.21
Low sexual pleasure	33 (54.1)	121 (50.4) 0.81 (0.41-1.63)	0.56
High sexual discomfort	23 (36.5)	128 (52.0) 1.41 (0.71-2.80)	0.32
Less frequent sexual activity	48 (77.4)	155 (65.7) 0.57 (0.26-1.24)	0.16
Reasons for inactivity, N (%)			
No partner	17 (50.0)	72 (40.4)	0.34
Too tired	9 (26.5)	59 (33.1)	0.55
Partner too tired	2 (5.9)	13 (7.3)	1.00
Not interested in sex	16 (47.6)	95 (53.4)	0.58
Partner not interested in sex	5 (14.7)	25 (14.0)	1.00
Physical problem	**1 (2.9)**	**37 (20.8)**	**0.013**
Partner physical problem	5 (14.7)	19 (10.7)	0.55

OR: odds ratio. CI: confidence interval.
Odds ratios adjusted for age at menopause, age at visit, and current use of hormone therapy except where otherwise noted.
a. Rarity of this outcome did not permit fully-adjusted analysis. Estimate adjusted only for age at visit and age at menopause.