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Menopausal-related Symptoms in Women One Year After Breast Cancer Surgery

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Abstract

Context—Approximately 60% to 100% of women with breast cancer experience at least one menopausal-related symptom. Little is known about associations between menopausal status and symptoms in women 12 months after breast cancer surgery.

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Objective—Purpose of this study was to evaluate for differences in occurrence, severity, and distress of symptoms between pre- and post-menopausal women 12 months after breast cancer surgery.

Methods—Women with breast cancer (n=327) completed the Menopausal Symptoms Scale, that evaluated the occurrence, severity, and distress of 46 common menopausal-related symptoms. Regression analyses were used to evaluate for between group differences in the seven symptoms that occurred in 30% of the sample (i.e., hot flashes, night sweats, depression, daytime sweats, joint pain or stiffness, wake during the night, numbness or tingling).

Results—Of the 327 breast cancer patients who completed the 12-month assessment, 35.2% were premenopausal and 64.8% were postmenopausal prior to surgery. In the conditional models, when significant interactions were found, the differences in symptom occurrence rates between pre- and postmenopausal patients depended on their age.

Conclusions—Regardless of menopausal status, women reported relatively high occurrence rates for several menopausal symptoms. Associations between symptom occurrence rates and menopausal status depended on the patient's age.

Implications for Practice—During the development of a survivorship care plan, clinicians need assess symptom burden within the context of a woman's menopausal status and salient demographic and clinical characteristics. This approach will assist with the prescription of more effective interventions.

Keywords

symptoms; premenopausal; postmenopausal; breast cancer; surgery

INTRODUCTION

Between 65% and 100% of women with breast cancer experience at least one treatment-induced, menopausal-related symptom.^{1,2} These symptoms include: sleep disturbance, musculoskeletal pain, mood changes, vasomotor symptoms, sexual dysfunction, vaginal dryness and atrophy, cognitive impairment, headaches, weight gain, and fatigue.^{3,4} These menopausal-related symptoms are some of the most common and distressing side effects of breast cancer treatment.^{2,5} Moreover, because of abrupt changes in sex steroid hormones, these symptoms are often more frequent and severe than those experienced during a natural menopausal transition.⁶ For premenopausal women, this unexpected exacerbation of symptoms can have a negative impact on their quality of life (QOL).^{6,7}

The occurrence, severity, and distress from these menopausal-related symptoms vary based on a woman's menopausal status,^{8–10} age,^{4,11} type of cancer treatment (i.e., chemotherapy (CTX), endocrine therapy (ET));^{12,13} and time since completion of treatment; as well as demographic, health and illness, and psychosocial factors.¹² For example, following breast cancer treatment, compared to postmenopausal patients, women who were premenopausal at diagnosis reported more severe vasomotor symptoms,¹⁴ sexual dysfunction,¹⁵ and sleep disturbances.¹⁴ In addition, in another study,¹⁶ the highest menopausal-related symptom burden was reported in the first six months after the completion of primary treatment.

While, the impact of menopausal-related symptoms is well documented,^{1,2,5,12,17-19} little is known about differences in the occurrence, severity, and distress of these symptoms between premenopausal and postmenopausal women one year after breast cancer surgery. The majority of these studies compared differences in the symptom experience of older versus younger women;^{4,11,20} younger women who did or did not experience treatment-induced menopause;^{1,2,10} and/or specific types of treatment (i.e., CTX, tamoxifen, aromatase inhibitors (AIs)).^{12,13,21-24} Moreover, the majority of these studies evaluated a single symptom; a single dimension of the symptom experience; included women several years after a breast cancer diagnosis; and/or did not evaluate the impact of menopausal status on differences in patients' symptom experiences. (for reviews see^{1, 3, 10}) In fact, to our knowledge, only five studies reported on differences in menopausal-related symptoms between pre- and postmenopausal women after primary breast cancer treatment.^{8,9,14,15,25}

These five studies evaluated for associations between pre-diagnosis menopausal status and symptom occurrence^{8,9,25} or severity^{14,15} in women who had received adjuvant CTX and/or ET. Two longitudinal studies evaluated symptom severity before and immediately after CTX.^{28,29} Three cross-sectional studies evaluated menopausal symptom occurrence six months²¹ to several years^{7,27} after diagnosis. Compared to postmenopausal patients, premenopausal women reported higher occurrence rates of hot flashes, night sweats,^{8,9,25} vaginal dryness, and libido reduction.⁸ In one study,⁸ while two-thirds of the menopausal-related symptoms were reported as severe by premenopausal women, differences in severity scores between pre- and postmenopausal women were not evaluated.

Findings from these five studies provide preliminary evidence of differences in the occurrence^{8,9,25} and severity^{14,15} of menopausal-related symptoms based on pre-diagnosis menopausal status. However, a number of limitations warrant consideration. These studies evaluated only a single symptom¹⁴ and/or one dimension of the symptom experience.^{8,9,14,15,25} Two studies did not include relevant covariates such as body mass index (BMI) in their analysis.^{8,25} In two studies, the assessments were done either several years after the cancer diagnosis²⁵ or the time since diagnosis was not reported.⁸ In addition, in two studies,^{14,15} the sample sizes of premenopausal women were relatively small. If differences were found in the symptom experience of pre- versus postmenopausal women after surgery, this information could be used to guide symptom management interventions.

Given the paucity of research on the association between menopausal status prior to surgery and menopausal-related symptoms after primary breast cancer treatment, the purpose of this study was to evaluate for differences in multiple dimensions of the symptom experience (i.e., occurrence, severity, distress) between pre- and postmenopausal women one year after breast cancer surgery. We hypothesized that both groups of women would report the co-occurrence of multiple menopausal-related symptoms. In addition, we hypothesized that compared to postmenopausal women, women who were premenopausal at diagnosis would report higher occurrence rates of and severity and distress ratings for vasomotor symptoms (i.e., hot flashes, night sweats, daytime sweats).

METHODS

The methods for the larger descriptive, longitudinal study that evaluated neuropathic pain and lymphedema in women who underwent breast cancer surgery are described in detail elsewhere.^{26–30} In brief, women were recruited from seven Breast Cancer Centers in Northern California. Women were eligible if they: were 18 years of age; were scheduled for unilateral breast cancer surgery; were able to read, write, and understand English; agreed to participate; and provided written informed consent. Patients were excluded if they had bilateral breast surgery and/or had distant metastases at the time of diagnosis.

Instruments

Patients completed a demographic questionnaire, the Karnofsky Performance Status (KPS) scale,³¹ and the Self-Administered Comorbidity Questionnaire (SCQ).³² Menopausal status was determined by the patient's response (yes/no) at the time of study enrollment to the question "Have you gone through menopause yet (stopped having your menstrual cycle)?".

The Menopausal Symptoms Scale (MSS), that was modified from the Seattle Women's Health Study questionnaire,³³ was used to evaluate the occurrence, severity, and distress of 46 menopausal-related symptoms. Women were asked to indicate whether they experienced each symptom during the past week (i.e., symptom occurrence). If they experienced the symptom, they were asked to rate its severity and distress. Symptom severity was rated on a 0 ('none') to 10 ('intolerable') numeric rating scale (NRS). Symptom distress was rated on a 0 ('not at all distressing') to 10 ('very distressing') NRS. The MSS has well established validity and reliability.³⁴

Study Procedures

The study was approved by the Committee on Human Research at the University of California, San Francisco and by the Institutional Review Boards at each of the study sites. A clinician explained the study, determined the woman's willingness to participate, and introduced her to the research nurse. All patients provided written informed consent. Women completed the enrollment questionnaire an average of four days prior to surgery. For the current study, data from the KPS, SCQ, and MSS that were obtained one year after surgery were analyzed. Medical records were reviewed for disease and treatment information.

Statistical Analysis

Data were analyzed using SPSS Version 23 (IBM, Armonk, NY). Descriptive statistics and frequency distributions were generated on sample characteristics and symptom occurrence rates, severity scores, and distress scores. Using their self-reported status, women were categorized into the premenopausal and postmenopausal groups at enrollment (i.e., prior to surgery). Independent Student t-tests, Mann-Whitney U tests, Fisher Exact tests, and Chi Square analyses were used to evaluate for differences in demographic and clinical characteristics between the two menopausal groups. Characteristics that differed significantly between the menopausal groups were considered for use as potential covariates in the logistic and linear regression analyses.

As part of the evaluation of between group differences, symptom occurrence rates were generated for each symptom and mean scores for severity and distress ratings were calculated for patients who reported a symptom. Unadjusted and adjusted logistic regression analyses were used to evaluate for between group differences in symptom occurrence rates. For symptoms that occurred in $\geq 30\%$ of the total sample, unadjusted and adjusted linear regression analyses were used to evaluate for between group differences in symptom severity and distress scores. First, menopausal status was entered into the regression analysis (unadjusted model). Then, characteristics that were found to be significantly different between the two menopausal groups and identified as potential covariates were added into the model along with menopausal status (adjusted model). Finally, the interaction between age and menopausal status group was evaluated. If the age by menopausal status group interaction was statistically significant, an adjusted stratified analysis was done for premenopausal and postmenopausal women.³⁵ The stratified analyses were done because the interaction term was significant, but the sample size was too small to generate stable combined estimates. A p-value of $<.05$ was considered statistically significant.

RESULTS

Differences in demographic characteristics

Of the 327 women with breast cancer who completed the 12-month assessment, 35.2% were premenopausal and 64.8% were postmenopausal prior to surgery. Compared to postmenopausal women, premenopausal women were significantly younger, were less likely to live alone, and were more likely to be employed (Table 1).

Differences in clinical characteristics

Compared to postmenopausal women, premenopausal women had a lower SCQ score. In addition, a lower percentage of premenopausal women reported high blood pressure, diabetes, ulcer, osteoarthritis, a prior hysterectomy, a prior oophorectomy, were on HRT prior to surgery, and had external beam radiation therapy (RT) during the prior 12 months. A higher percentage of premenopausal women had a mastectomy versus conservation surgery, had breast reconstruction during the prior 12 months, received adjuvant CTX during the prior 12 months, and had undergone genetic testing for BRCA1 and BRCA2 (Table 1).

Differences in symptom occurrence rates and total number of symptoms

Occurrence rates for the 46 symptoms on the MSS and for the top ten occurring symptoms are listed in the Supplementary Table 1 and in Table 2, respectively. No differences were found in the total number of symptoms reported by premenopausal versus postmenopausal women. The five symptoms with the highest occurrence rates in premenopausal women were: wake during the night, hot flashes, fatigue or tiredness, difficulty falling asleep, and night sweats. While wake during the night, fatigue or tiredness and hot flashes, were among the 5 most common symptoms in the postmenopausal group, they reported two different symptoms (i.e., joint pain or stiffness and waking too early).

Unadjusted and adjusted analyses of symptoms with higher occurrence rates in premenopausal women—As shown in Table 3, in the unadjusted models,

premenopausal patients reported higher occurrence rates for eating more than usual, skin breakout/acne, hostility, weight gain, irritability, and lost sexual interest. In the multivariate analyses, after adjusting for nine covariates, no differences in these symptoms' occurrence rates were found between the two menopausal groups.

Unadjusted and adjusted analyses of symptoms with higher occurrence rates in postmenopausal women—In the unadjusted and adjusted analyses, none of the symptom occurrence rates were significantly higher in the postmenopausal group.

Differences in occurrence rates for symptoms with interaction effects—As shown in Table 4, in the unadjusted models, premenopausal women reported higher occurrence rates for hot flashes, night sweats, depression, and daytime sweats. Postmenopausal women reported higher occurrence rates for joint pain or stiffness.

In the adjusted models that evaluated seven symptoms for which significant interactions were found between age and menopausal status (i.e., hot flashes, night sweats, depression, daytime sweats, joint pain or stiffness, wake during the night, numbness or tingling), the differences in symptom occurrence rates between pre- and post-menopausal women depended on their age. In the premenopausal group, as age increased, women were significantly more likely to report depression and joint pain or stiffness. In the postmenopausal group, as age increased, women were significantly less likely to report hot flashes, night sweats, depression, daytime sweats, wake during the night, and numbness or tingling.

Differences in symptom severity scores

The severity scores for the 46 as well as for the ten symptoms with the highest mean severity scores are listed in the Supplementary Table 1 and in Table 2, respectively. For premenopausal women, the five symptoms with the highest severity scores were: cramps, diarrhea, lost sexual interest, fatigue or tiredness, and mood swings. While lost sexual interest and cramps were among the five most severe symptoms in the postmenopausal group, they reported three different symptoms (i.e., abdominal bloating, vaginal dryness, hot flashes).

Unadjusted and adjusted analyses of symptoms with higher severity scores in premenopausal women—As shown in Table 5, in the unadjusted models for symptoms that occurred in >30.0% of the sample, premenopausal women reported higher symptom severity scores for impatience and irritability. In the adjusted analysis, premenopausal women reported higher symptom severity scores for fatigue.

Unadjusted and adjusted analyses of symptoms with higher severity scores in postmenopausal women—In the unadjusted and adjusted analyses, none of the severity scores were significantly higher in the postmenopausal group.

Differences in symptom distress scores

The distress scores for the 46 symptoms, as well as for the ten symptoms with the highest mean distress scores, are listed in the Supplementary Table 1 and in Table 2, respectively. For premenopausal women, the five symptoms with the highest distress scores were: weight gain, diarrhea, swollen hands/feet, hostility, and tearful/crying spells. While weight gain was one of the five most distressing symptoms in the postmenopausal women, they reported four different symptoms (i.e., lost sexual interest, cramps, abdominal bloating, eating more than usual).

Unadjusted and adjusted analyses of symptoms with higher distress scores in premenopausal women—As shown in Table 5, in the unadjusted analyses for symptoms that occurred in >30% of the sample, premenopausal women reported higher distress scores for impatience. In the adjusted analyses, none of the distress scores were significantly higher in premenopausal women.

Unadjusted and adjusted analyses of symptoms with higher distress scores in postmenopausal women—In the unadjusted and adjusted analyses, none of the symptom distress scores were significantly higher in the postmenopausal women.

DISCUSSION

This study is the first to describe associations between preoperative menopausal status and symptom occurrence, severity, and distress in women one year after breast cancer surgery. Consistent with previous studies,^{1,2,4,36} our first hypothesis was supported. All women, regardless of menopausal status, reported an average of 11 co-occurring symptoms (range of 0 to 38). Our second a priori hypothesis was only partially supported. After accounting for multiple demographic, clinical, and treatment characteristics, the relationship between menopausal status and the occurrence rates for vasomotor symptoms was dependent on women's age. In terms of severity, fatigue was the only symptom that was more severe in premenopausal women. Of note, no differences in symptom distress ratings were found between the menopausal groups.

Findings from this study have a number of clinical implications. For example, our findings suggest that women who used HRT prior to their breast cancer diagnosis were two to three times more likely to report vasomotor symptoms even one year after stopping the medication. Therefore, previous use of HRT should be assessed as part of survivorship care. Given the large number of symptoms and dimensions evaluated, the discussion will focus primarily on significant differences in symptom dimensions found between pre- and postmenopausal women and the interaction of age and menopausal status.

Symptom Occurrence

Differences in the occurrence of symptoms with interaction effects—One of the strengths of this study is that for each of the symptoms, after controlling for clinically meaningful characteristics, the interaction between menopausal status and age was evaluated. For example, significant interactions were found between age and menopausal

status for all three vasomotor symptoms (i.e., hot flashes, night and daytime sweats). While this specific interaction was not reported previously, relative to younger and older premenopausal women, it is common for older premenopausal and younger postmenopausal women to report vasomotor symptoms.^{36,37} Similarly, in our study, as premenopausal women aged, they were 25% to 48% less likely to report vasomotor symptoms. However, contrary to previous findings,¹ as premenopausal women's age increased, they did not report higher occurrence rates for vasomotor symptoms. Our sample size may have been too small to detect the effects of age on the occurrence of hot flashes in our premenopausal women.

While the occurrence of nighttime awakenings was the most common symptom in both pre- and postmenopausal women, a significant interaction was found between menopausal status and age. While no studies evaluated for interaction effects, in previous reports, pre- and postmenopausal women differed on post-treatment occurrence rates for restless sleep¹⁰ and insomnia.⁸ Moreover, consistent with prior reports,¹⁵ none of the other covariates in the multivariate analysis predicted variations in the occurrence of wake during the night. Given the high occurrence rates of nighttime awakenings in women with and without breast cancer, the causes for this symptom warrant additional investigation so that appropriate interventions can be prescribed.¹⁵

Numbness and tingling are associated with the neurotoxic effects of CTX.³⁸ Therefore, it is not surprising that women in our study who were treated with CTX in the past 12 months were 2.5 times more likely to report this symptom. Given that numbness and tingling can be related to hormonal changes during menopause³⁹ and/or the neurotoxicity of CTX,³⁸ the etiology of these symptoms warrant evaluation in future studies.

Symptom Severity

Fatigue was the only symptom that was more severe in premenopausal women and in women with a higher level of comorbidity. Consistent with a previous report,⁴⁰ premenopausal women were more likely to report the occurrence as well as more severe fatigue after CTX and during the first three years of hormone therapy. Given that fatigue is common, moderately severe, persists over time,¹⁹ and may be associated with a higher symptom burden,⁴¹ it warrants ongoing assessment and management.

While we hypothesized that premenopausal women would report higher severity scores for vasomotor symptoms, our findings are not consistent with previous reports. In previous studies, compared to postmenopausal women with breast cancer, premenopausal women reported more severe vasomotor symptoms¹⁵ and hot flashes¹⁴ after CTX and were more likely to report severe hot flashes while taking tamoxifen.²⁵ These inconsistent findings may be related to differences in how symptoms were assessed and categorized, the timing of the assessments, and failure to control for significant covariates in the analyses.

The ranking of the five most severe symptoms differed by menopausal group. Moreover, regardless of menopausal status, the ten most severe symptoms were in the moderate severity range. In fact, for the entire sample, using a moderate cutoff score of >4.0,⁴² 13 of the 46 symptoms were in the moderate to severe range. A survivorship care plan, that

includes aggressive symptom management interventions, is warranted after surgery to prevent the escalation of symptoms during the subsequent year.

Symptom Distress

No between group differences in symptom distress scores were identified. In contrast, previous reports suggested that younger women were more bothered by menopausal symptoms than older women.^{21,43–45} For example, compared to women older than 60, younger women reported that vasomotor symptoms, vaginal symptoms, and weight problems were more bothersome.²¹ However, the influence of menopausal status was not evaluated in this study.

In our study, the analysis of severity and distress ratings included only those women who reported the occurrence of the symptom. The exclusion of women who did not experience the symptom provides a more accurate evaluation of the impact of each symptom.³ However, in most of the previous studies, the analyses included women who did not have the symptom. In addition, one of the most common instruments used to evaluate menopausal-related symptoms in breast cancer patients is the Breast Cancer Prevention Trial (BCPT) checklist.^{4,46} The BCPT assesses “bother” using a 0 “not at all” to 4 “extremely” Likert scale. While this instrument is valid and reliable,⁴⁶ the term “bother” is used interchangeably with “severity”,^{10,21} “intensity”,⁴⁷ and “distress”.⁴⁸ These differences make comparisons of severity and distress scores across studies difficult.

Similar to severity, the rankings of the five most distressing symptoms differed by menopausal status. Regardless of menopausal status, many of the ten most distressing symptoms were in the moderate range. While both menopausal groups reported approximately 11 symptoms, premenopausal women reported a higher number of distressing symptoms. This difference highlights the importance of comprehensive assessments of all symptom dimensions in women after breast cancer treatment.

Limitations

Several limitations warrant consideration. The woman’s self-report of menopausal status at diagnosis was used to create the two groups. Moreover, the inclusion of five women who were on HRT in the premenopausal group suggests that some women may have been perimenopausal. While the gold standard for determining menopausal status includes an assessment of menstrual cycle, hormonal levels, and symptoms,⁴⁹ previous studies support the validity and reliability of self-report.^{18,50} Moreover, while menopausal status was not re-evaluated at 12 months, this study’s aim was to compare pre-surgical menopausal status and women’s symptom experience at 12 months after surgery. In addition, testing for interactions between age and menopausal status accounted for variations between younger and older pre- and postmenopausal women. Some of the symptoms on the MSS (e.g., cramps) may be interpreted differently by pre- (i.e., menstrual cramps) versus post- (i.e., gastrointestinal cramps) menopausal women. Lastly, the majority of women in this study was Caucasian and well educated, which limits the generalizability of our findings.

Implications for Clinical Practice and Research

Regardless of menopausal status, at one year following surgery, our patients experienced multiple co-occurring symptoms that were in the moderate to severe range for both severity and distress. Moreover, similar to previous reports of women after breast cancer treatment,^{2,10,11} the occurrence of menopausal-related symptoms varied based on menopausal status, as well as demographic (e.g., age), clinical (e.g., level of comorbidity), and treatment (e.g., prior HRT use, receipt of adjuvant CTX in prior 12 months) characteristics. Of note, all of the differences in symptom occurrence rates depended on the interaction between age and menopausal status. Accordingly, both characteristics warrant consideration during the assessment of symptom burden. Given that these menopausal symptoms negatively impact women's well-being after primary breast cancer treatment, assessment and education prior to and during therapy may help manage expectations of symptom burden over time. Findings from this study can be used by clinicians to focus their assessments and individualize patient education and interventions.

Given the various etiologies for menopausal-related symptoms, longitudinal evaluations of how symptoms change from pre- to post-treatment are warranted. These time-sensitive evaluations may identify other causal associations between menopausal status and symptom burden (e.g., pre-surgical anxiety). Moreover, studies of the inter-relationships among symptoms (i.e., symptom clusters) using multiple dimensions of the symptom experience are warranted. Increased information on menopausal symptom clusters could be used to support future studies on the common and distinct mechanisms that underlie these symptom clusters, well as interventions to manage single and multiple menopausal-related symptoms.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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References

1. Howard-Anderson J, Ganz PA, Bower JE, Stanton AL. Quality of life, fertility concerns, and behavioral health outcomes in younger breast cancer survivors: a systematic review. *J Natl Cancer Inst.* 2012; 104:386–405. [PubMed: 22271773]
2. Leining MG, Gelber S, Rosenberg R, et al. Menopausal-type symptoms in young breast cancer survivors. *Ann Oncol.* 2006; 17:1777–1782. [PubMed: 16971671]
3. Barton DL, Ganz PA. Symptoms: Menopause, Infertility, and Sexual Health. *Adv Exp Med Biol.* 2015; 862:115–141. [PubMed: 26059933]
4. Ganz PA, Rowland JH, Desmond K, Meyerowitz BE, Wyatt GE. Life after breast cancer: understanding women's health-related quality of life and sexual functioning. *J Clin Oncol.* 1998; 16:501–514. [PubMed: 9469334]

5. Anderson DJ, Yates P, McCarthy A, et al. Younger and older women's concerns about menopause after breast cancer. *Eur J Cancer Care (Engl)*. 2011; 20:785–794. [PubMed: 21883565]
6. Ruddy KJ, Gelber S, Ginsburg ES, et al. Menopausal symptoms and fertility concerns in premenopausal breast cancer survivors: a comparison to age- and gravidity-matched controls. *Menopause*. 2011; 18:105–108. [PubMed: 21243735]
7. Rosenberg SM, Partridge AH. Premature menopause in young breast cancer: effects on quality of life and treatment interventions. *J Thorac Dis*. 2013; 5(Suppl 1):S55–61. [PubMed: 23819028]
8. Biglia N, Cozzarella M, Cacciari F, et al. Menopause after breast cancer: a survey on breast cancer survivors. *Maturitas*. 2003; 45:29–38. [PubMed: 12753941]
9. Dorjgochoo T, Gu K, Kallianpur A, et al. Menopausal symptoms among breast cancer patients 6 months after diagnosis: a report from the Shanghai Breast Cancer Survival Study. *Menopause*. 2009; 16:1205–1212. [PubMed: 19590459]
10. Crandall C, Petersen L, Ganz PA, Greendale GA. Association of breast cancer and its therapy with menopause-related symptoms. *Menopause*. 2004; 11:519–530. [PubMed: 15356404]
11. Ganz PA, Greendale GA, Petersen L, Kahn B, Bower JE. Breast cancer in younger women: reproductive and late health effects of treatment. *J Clin Oncol*. 2003; 21:4184–4193. [PubMed: 14615446]
12. Duijts SF, Stolk-Vos AC, Oldenburg HS, van Beurden M, Aaronson NK. Characteristics of breast cancer patients who experience menopausal transition due to treatment. *Climacteric*. 2011; 14:362–368. [PubMed: 21401440]
13. Fallowfield LJ, Kilburn LS, Langridge C, et al. Long-term assessment of quality of life in the Intergroup Exemestane Study: 5 years post-randomisation. *Br J Cancer*. 2012; 106:1062–1067. [PubMed: 22353807]
14. Berger AM, Treat Marunda HA, Agrawal S. Influence of menopausal status on sleep and hot flashes throughout breast cancer adjuvant chemotherapy. *J Obstet Gynecol Neonatal Nurs*. 2009; 38:353–366.
15. Rissling MB, Liu L, Natarajan L, He F, Ancoli-Israel S. Relationship of menopausal status and climacteric symptoms to sleep in women undergoing chemotherapy. *Support Care Cancer*. 2011; 19:1107–1115. [PubMed: 20508951]
16. Ganz PA, Kwan L, Stanton AL, Bower JE, Belin TR. Physical and psychosocial recovery in the year after primary treatment of breast cancer. *J Clin Oncol*. 2011; 29:1101–1109. [PubMed: 21300931]
17. Glaus A, Boehme C, Thurlimann B, et al. Fatigue and menopausal symptoms in women with breast cancer undergoing hormonal cancer treatment. *Ann Oncol*. 2006; 17:801–816. [PubMed: 16507565]
18. Conde DM, Pinto-Neto AM, Cabello C, et al. Menopause symptoms and quality of life in women aged 45 to 65 years with and without breast cancer. *Menopause*. 2005; 12:436–443. [PubMed: 16037759]
19. Mortimer J, Behrendt CE. Severe menopausal symptoms are widespread among survivors of breast cancer treatment regardless of time since diagnosis. *J Palliat Med*. 2013; 16:1130–1134. [PubMed: 23947627]
20. Rosenberg SM, Partridge AH. New insights into nonadherence with adjuvant endocrine therapy among young women with breast cancer. *J Natl Cancer Inst*. 2015; 107
21. Ganz PA, Cecchini RS, Julian TB, et al. Patient-reported outcomes with anastrozole versus tamoxifen for postmenopausal patients with ductal carcinoma in situ treated with lumpectomy plus radiotherapy (NSABP B-35): a randomised, double-blind, phase 3 clinical trial. *Lancet*. 2016; 387:857–865. [PubMed: 26686960]
22. Cella D, Fallowfield L, Barker P, et al. Quality of life of postmenopausal women in the ATAC (“Arimidex”, tamoxifen, alone or in combination) trial after completion of 5 years’ adjuvant treatment for early breast cancer. *Breast Cancer Res Treat*. 2006; 100:273–284. [PubMed: 16944295]
23. Marino JL, Saunders CM, Emery LI, et al. How does adjuvant chemotherapy affect menopausal symptoms, sexual function, and quality of life after breast cancer? *Menopause*. 2016; 23:1000–1008. [PubMed: 27272225]

24. Ganz PA, Rowland JH, Meyerowitz BE, Desmond KA. Impact of different adjuvant therapy strategies on quality of life in breast cancer survivors. *Recent Results Cancer Res.* 1998; 152:396–411. [PubMed: 9928575]
25. Moon Z, Hunter MS, Moss-Morris R, Hughes LD. Factors related to the experience of menopausal symptoms in women prescribed tamoxifen. *J Psychosom Obstet Gynaecol.* 2016:1–10.
26. Kyranou M, Paul SM, Dunn LB, et al. Differences in depression, anxiety, and quality of life between women with and without breast pain prior to breast cancer surgery. *Eur J Oncol Nurs.* 2013; 17:190–195. [PubMed: 22892272]
27. McCann B, Miaskowski C, Koetters T, et al. Associations between pro- and anti-inflammatory cytokine genes and breast pain in women prior to breast cancer surgery. *J Pain.* 2012; 13:425–437. [PubMed: 22515947]
28. Doong SH, Dhruva A, Dunn LB, et al. Associations between cytokine genes and a symptom cluster of pain, fatigue, sleep disturbance, and depression in patients prior to breast cancer surgery. *Biol Res Nurs.* 2015; 17:237–247. [PubMed: 25304131]
29. Langford DJ, West C, Elboim C, et al. Variations in potassium channel genes are associated with breast pain in women prior to breast cancer surgery. *J Neurogenet.* 2014; 28:122–135. [PubMed: 24392765]
30. Van Onselen C, Aouizerat BE, Dunn LB, et al. Differences in sleep disturbance, fatigue and energy levels between women with and without breast pain prior to breast cancer surgery. *Breast.* 2013; 22:273–276. [PubMed: 22858121]
31. Karnofsky D, Abelmann WH, Craver LV, Burchenal JH. The use of nitrogen mustards in the palliative treatment of carcinoma. *Cancer.* 1948; 1:634–656.
32. Sangha O, Stucki G, Liang MH, Fossel AH, Katz JN. The Self-Administered Comorbidity Questionnaire: a new method to assess comorbidity for clinical and health services research. *Arthritis Rheum.* 2003; 49:156–163. [PubMed: 12687505]
33. Woods NF, Mitchell ES, Lentz M. Premenstrual symptoms: delineating symptom clusters. *J Womens Health Gend Based Med.* 1999; 8:1053–1062. [PubMed: 10565663]
34. Woods NF, Mitchell ES, Schnall JG, et al. Effects of mind-body therapies on symptom clusters during the menopausal transition. *Climacteric.* 2014; 17:10–22. [PubMed: 23937432]
35. Singer, JD., Willett, JB. *Applied longitudinal data analysis: Modeling change and event occurrence.* 1st. New York, NY: Oxford University Press; 2003.
36. Gupta P, Sturdee DW, Palin SL, et al. Menopausal symptoms in women treated for breast cancer: the prevalence and severity of symptoms and their perceived effects on quality of life. *Climacteric.* 2006; 9:49–58. [PubMed: 16428125]
37. Freeman EW, Sherif K. Prevalence of hot flushes and night sweats around the world: a systematic review. *Climacteric.* 2007; 10:197–214. [PubMed: 17487647]
38. Hershman DL, Weimer LH, Wang A, et al. Association between patient reported outcomes and quantitative sensory tests for measuring long-term neurotoxicity in breast cancer survivors treated with adjuvant paclitaxel chemotherapy. *Breast Cancer Res Treat.* 2011; 125:767–774. [PubMed: 21128110]
39. Sievert LL, Anderson D, Melby MK, Obermeyer CM. Methods used in cross-cultural comparisons of somatic symptoms and their determinants. *Maturitas.* 2011; 70:127–134. [PubMed: 21852054]
40. Huang X, Zhang Q, Kang X, Song Y, Zhao W. Factors associated with cancer-related fatigue in breast cancer patients undergoing endocrine therapy in an urban setting: a cross-sectional study. *BMC Cancer.* 2010; 10:453. [PubMed: 20731876]
41. Ho SY, Rohan KJ, Parent J, Tager FA, McKinley PS. A longitudinal study of depression, fatigue, and sleep disturbances as a symptom cluster in women with breast cancer. *J Pain Symptom Manage.* 2015; 49:707–715. [PubMed: 25461671]
42. Woo A, Lechner B, Fu T, et al. Cut points for mild, moderate, and severe pain among cancer and non-cancer patients: a literature review. *Ann Palliat Med.* 2015; 4:176–183. [PubMed: 26541396]
43. Knobf MT. “Coming to grips” with chemotherapy-induced premature menopause. *Health Care Women Int.* 2008; 29:384–399. [PubMed: 18389434]

44. Knopf MT. Reproductive and hormonal sequelae of chemotherapy in women. Premature menopause and impaired fertility can result, effects that are especially disturbing to young women. *Am J Nurs*. 2006; 106:60–65.
45. Knopf MT. Carrying on: the experience of premature menopause in women with early stage breast cancer. *Nurs Res*. 2002; 51:9–17. [PubMed: 11822573]
46. Stanton AL, Bernards CA, Ganz PA. The BCPT symptom scales: a measure of physical symptoms for women diagnosed with or at risk for breast cancer. *J Natl Cancer Inst*. 2005; 97:448–456. [PubMed: 15770009]
47. Lobchuk MM. The memorial symptom assessment scale: modified for use in understanding family caregivers' perceptions of cancer patients' symptom experiences. *J Pain Symptom Manage*. 2003; 26:644–554. [PubMed: 12850647]
48. Heidrich SM, Egan JJ, Hengudomsu P, Randolph SM. Symptoms, symptom beliefs, and quality of life of older breast cancer survivors: a comparative study. *Oncol Nurs Forum*. 2006; 33:315–322. [PubMed: 16518447]
49. Harlow SD, Gass M, Hall JE, et al. Executive summary of the Stages of Reproductive Aging Workshop + 10: addressing the unfinished agenda of staging reproductive aging. *J Clin Endocrinol Metab*. 2012; 97:1159–1168. [PubMed: 22344196]
50. Colditz GA, Stampfer MJ, Willett WC, et al. Reproducibility and validity of self-reported menopausal status in a prospective cohort study. *Am J Epidemiol*. 1987; 126:319–325. [PubMed: 3605058]

Table 1

Differences in demographic and clinical characteristics between premenopausal and postmenopausal women 12 months after breast cancer surgery

Demographic characteristics	Premenopausal n=115 (35.2%)	Postmenopausal n=212 (64.8%)	Statistics
	Mean (SD)	Mean (SD)	
Age (years)	45.2 (6.2)	61.0 (10.4)	t=-17.21; p<.001
Education (years)	15.9 (2.4)	15.6 (2.8)	t=1.04; p=.296
	% (n)	% (n)	
Ethnicity			
White	63.5 (73)	68.9 (146)	FE; p=.328
Non-white	36.5 (42)	31.1 (66)	
Lives alone (% yes)	13.9 (16)	28.4 (60)	FE; p=.004
Married/partnered (% yes)	35.7 (41)	44.8 (95)	FE; p=.127
Currently working for pay (% yes)	60.5 (69)	44.5 (94)	FE; p=.007
Total annual household income			U; p=.150
< \$10,000 to \$19,999	6.9 (7)	5.4 (9)	
\$20,000 to \$99,000	47.5 (48)	59.9 (100)	
\$100,000	45.5 (46)	34.7 (58)	
Clinical characteristics	Mean (SD)	Mean (SD)	
Body mass index (kg/m ²)	25.9 (5.6)	27.1 (6.1)	t=-1.82; p=.069
Karnofsky Performance Status score	94.2 (9.8)	93.6 (10.0)	t=0.50; p=.620
Self-Administered Comorbidity Scale score	3.1 (2.2)	4.4 (3.4)	t=-4.02; p<.001
Number of menopausal symptoms	12.0 (8.7)	10.3 (8.0)	t=1.83; p=.068
Months since diagnosis	13.6 (2.9)	13.8 (2.3)	t=-0.52; p=.601
	% (n)	% (n)	
Occurrence of comorbid conditions (% and number of women who reported each comorbid condition from the Self-Administered Comorbidity Questionnaire)			
Heart disease	1.7 (2)	5.7 (12)	FE; p=.150
High blood pressure	14.8 (17)	38.7 (81)	FE; p<.001
Lung disease	1.7 (2)	2.4 (5)	FE; p=1.000
Diabetes	1.7 (2)	12.7 (27)	FE; p<.001
Ulcer	0.0 (0)	5.2 (11)	FE; p=.010
Kidney disease	0.0 (0)	0.0 (0)	FE; p=1.00
Liver disease	0.0 (0)	1.9 (4)	FE; p=.302

Demographic characteristics	Premenopausal n=115 (35.2%)	Postmenopausal n=212 (64.8%)	Statistics
	Mean (SD)	Mean (SD)	
Anemia	5.2 (6)	4.3 (9)	FE; p=.783
Depression	13.0 (15)	16.5 (35)	FE; p=.427
Osteoarthritis	9.6 (11)	22.2 (47)	FE; p=.004
Back pain	22.6 (26)	24.1 (51)	FE; p=.787
Rheumatoid arthritis	3.5 (4)	5.2 (11)	FE; p=.588
Diagnosed with mastitis (% yes)	13.0 (15)	12.7 (27)	FE; p=1.000
Diagnosed with fibrocystic disease (% yes)	15.8 (18)	23.4 (48)	FE; p=.115
Exercise on a regular basis (% yes)	77.4 (89)	73.5 (155)	FE; p=.525
Ever breast fed (% yes)	50.4 (58)	43.4 (92)	FE; p=.246
Prior hysterectomy (% yes)	4.3 (5)	17.9 (38)	FE; p<.001
Prior oophorectomy (% yes)	4.3 (5)	13.7 (29)	FE; p=.008
Type of surgery			
Breast conservation	72.2 (83)	84.4 (179)	X ² ; p=.009
Mastectomy	27.8 (32)	15.6 (33)	
Sentinel lymph node biopsy (% yes)	86.1 (99)	84.0 (178)	FE; p=.748
Axillary lymph node dissection (% yes)	35.1 (40)	31.6 (67)	FE; p=.538
Re-excision or mastectomy during the 12 months (% yes)	33.9 (39)	27.4 (58)	FE; p=.254
Breast reconstruction during the 12 months (% yes)	20.9 (24)	9.0 (19)	FE; p=.003
Received neoadjuvant chemotherapy (% yes)	15.8 (18)	19.8 (42)	FE; p=.454
Received adjuvant chemotherapy during the 12 months (% yes)	42.6 (49)	28.3 (60)	FE; p=.010
Received external beam radiation therapy during the 12 months (% yes)	65.2 (75)	76.9 (163)	FE; p=.027
On hormonal therapy during the 12 months (% yes)	65.2 (75)	62.3 (132)	FE; p=.632
On HRT prior to surgery (% yes)	4.4 (5)	24.6 (52)	FE; p<.001
Stage of disease			
Stage 0	21.6 (25)	18.0 (38)	U; p=.264
Stage I	41.4 (48)	39.3 (83)	
Stage IIA and IIB	31.9 (37)	35.5 (75)	
Stage IIIA, IIIB, IIIC, and IV	5.2 (6)	7.1 (15)	
Estrogen receptor positive (% yes)	78.3 (90)	76.8 (162)	FE; p=.784
Progesterone receptor positive (% yes)	77.4 (89)	67.3 (142)	FE; p=.057

Demographic characteristics	Premenopausal n=115 (35.2%)	Postmenopausal n=212 (64.8%)	Statistics
	Mean (SD)	Mean (SD)	
HER2/neu receptor positive (% yes)	16.5 (17)	16.9 (32)	FE; p=1.000
BRCA1 and BRCA2 genetic testing			X ² =10.78; p=.004
Positive	2.6 (3)	1.0 (2)	
Negative	18.4 (21)	7.2 (15)	
Not done	78.9 (90)	91.9 (192)	

Abbreviations: BRCA = breast cancer; FE = Fisher's Exact; HER2/neu = human epidermal growth factor receptor 2; HRT = hormone replacement therapy; kg = kilogram; m² = meters squared; SD = standard deviation; U = Mann Whitney U test

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Table 2

Differences between premenopausal and postmenopausal women in rankings of symptoms with the highest occurrence, severity, and distress ratings 12 months after breast cancer surgery

Occurrence Rates				
Rank	Premenopausal	% of women	Postmenopausal	% of women
	Symptom		Symptom	
1	Wake during the night	61.7	Wake during the night	63.7
2	Hot flashes	58.3	Joint pain or stiffness	51.9
3	Fatigue or tiredness	54.8	Fatigue or tiredness	50.0
4	Difficulty falling asleep	44.3	Hot flashes	45.3
5	Night sweats	44.3	Waking too early	42.9
6	Impatience	43.5	Difficulty falling asleep	42.0
7	Irritability	41.7	Backache or neckache	35.8
8	Waking too early	41.7	Impatience	34.4
9	Anxiety	40.9	Night sweats	32.5
10	Backache or neckache	40.9	Anxiety	31.6
Severity Rating [†]				
Rank	Symptom	Mean (SD)	Symptom	Mean (SD)
1	Cramps	5.1 (2.5)	Lost sexual interest	6.2 (2.6)
2	Diarrhea	5.0 (3.0)	Cramps	4.6 (2.8)
3	Lost sexual interest	4.7 (2.6)	Abdominal bloating	4.6 (2.7)
4	Fatigue or tiredness	4.7 (2.6)	Vaginal dryness	4.6 (2.9)
5	Mood swings	4.5 (2.8)	Hot flashes	4.4 (2.1)
6	Hot flashes	4.4 (2.5)	Night sweats	4.3 (2.0)
7	Headache	4.4 (2.6)	Joint pain or stiffness	4.2 (2.3)
8	Backache or neckache	4.3 (2.9)	Difficulty falling asleep	4.2 (2.6)
9	Daytime sweats	4.3 (2.4)	Daytime sweats	4.2 (1.8)
10	Joint pain or stiffness	4.3 (2.3)	Wake during the night	4.1 (2.5)
Distress Rating ^{††}				
Rank	Symptom	Mean (SD)	Symptom	Mean (SD)
1	Weight gain	5.1 (3.3)	Lost sexual interest	5.6 (3.4)
2	Diarrhea	5.1 (3.8)	Cramps	5.3 (3.3)
3	Swollen hands/feet	4.9 (2.9)	Abdominal bloating	4.8 (3.7)
4	Hostility	4.8 (3.2)	Weight gain	4.4 (3.4)
5	Tearful/crying spells	4.5 (2.9)	Eating more than usual	4.2 (3.1)
6	Anger	4.5 (3.0)	Joint pain or stiffness	4.0 (2.7)
7	Mood swings	4.5 (3.2)	Panic feelings	4.0 (2.3)
8	Anxiety	4.3 (3.0)	Difficulty falling asleep	4.0 (2.8)
9	Headache	4.2 (3.0)	Depression	3.9 (2.9)

Occurrence Rates				
Rank	Premenopausal	% of women	Postmenopausal	% of women
	Symptom		Symptom	
10	Nausea/upset stomach	4.2 (3.0)	Vaginal dryness	3.9 (2.9)

Abbreviation: SD = standard deviation

⁺Symptom severity scores ranged from 0 (none) to 10 (intolerable).

⁺⁺Symptom distress scores ranged from 0 (not at all distressing) to 10 (very distressing).

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Table 3

Results of unadjusted and adjusted logistic regression analyses that evaluated for differences in symptom occurrence rates between premenopausal and postmenopausal women 12 months after breast cancer surgery

SYMPTOM OCCURRENCE			LOGISTIC REGRESSION RESULTS																
Symptom	Occurrence rate %		Covariate	Unadjusted Model			Adjusted Model												
	PRE (n=115)	POST (n=212)		OR	CI	p-value	OR	CI	p-value										
Eating more than usual	25.0	12.3																	Overall Model X ² =19.33; p=.036
			Menopausal status *	0.41	0.23, 0.75	.004	0.43	0.19, 1.00	.050										
			Age (in 5 year increments)				0.95	0.79, 1.14	.565										
			Lives alone				0.72	0.32, 1.62	.429										
			Working for pay				0.75	0.4, 1.42	.384										
			SCQ score				1.13	1.00, 1.26	.044										
			Prior HRT				0.86	0.32, 2.28	.761										
			Adjuvant chemotherapy during 12 months				1.30	0.68, 2.47	.425										
			Radiation therapy during 12 months				1.33	0.58, 3.01	.501										
			Reconstruction during 12 months				0.85	0.29, 2.49	.771										
			Type of surgery: conservation (ref) vs mastectomy				2.08	0.82, 5.27	.125										
Skin breakout/acne	17.2	7.1																	Overall Model X ² =24.11; p=.007
			Menopausal status *	0.39	0.19, 0.79	.009	1.00	0.38, 2.66	.999										
			Age (in 5 year increments)				0.71	0.56, 0.89	.003										
			Lives alone				2.58	1.09, 6.1	.031										
			Working for pay				1.33	0.6, 2.92	.480										
			SCQ score				1.06	0.91, 1.24	.450										
			Prior HRT				0.71	0.18, 2.69	.610										
			Adjuvant chemotherapy during 12 months				1.12	0.51, 2.45	.786										
			Radiation therapy during 12 months				0.73	0.29, 1.86	.514										
			Reconstruction during 12 months				1.40	0.43, 4.59	.577										
			Type of surgery: conservation (ref) vs mastectomy				1.20	0.39, 3.68	.745										

SYMPTOM OCCURRENCE			LOGISTIC REGRESSION RESULTS									
Symptom	Occurrence rate %		Covariate	Unadjusted Model			Adjusted Model					
	PRE (n=115)	POST (n=212)		OR	CI	p-value	OR	CI	p-value			
Hostility	16.5	7.1								Overall Model X ² =15.12; p=.128		
			Menopausal status *	0.38	0.19, 0.79	.009	0.59	0.23, 1.54	.284			
	Age (in 5 year increments)				0.77	0.62, 0.96	.021					
	Lives alone				0.96	0.36, 2.52	.926					
	Working for pay				0.85	0.40, 1.80	.667					
	SCQ score				1.09	0.94, 1.26	.240					
	Prior HRT				1.56	0.51, 4.75	.433					
	Adjuvant chemotherapy during 12 months				0.83	0.38, 1.82	.637					
	Radiation therapy during 12 months				1.54	0.55, 4.25	.410					
	Reconstruction during 12 months				1.31	0.36, 4.83	.680					
	Type of surgery: conservation (ref) vs mastectomy				1.05	0.31, 3.54	.940					
	Weight gain	37.1	24.6									Overall Model X ² =17.02; p=.074
Menopausal status *				0.57	0.35, 0.93	.025	0.94	0.48, 1.83	.846			
Age (in 5 year increments)					0.87	0.75, 1.01	.062					
Lives alone					0.99	0.53, 1.84	.963					
Working for pay					0.99	0.59, 1.66	.980					
SCQ score					1.01	0.92, 1.12	.798					
Prior HRT					0.64	0.29, 1.38	.254					
Adjuvant chemotherapy during 12 months					1.38	0.82, 2.34	.228					
Radiation therapy during 12 months					1.50	0.76, 2.98	.241					
Reconstruction during 12 months					0.82	0.32, 2.09	.680					
Type of surgery: conservation (ref) vs mastectomy					1.60	0.72, 3.6	.251					
Irritability		41.7	29.7								Overall Model X ² =12.25; p=.269	
	Menopausal status			0.58	0.36, 0.94	.027	0.60	0.32, 1.15	.126			
	Age (in 5 year increments)						0.94	0.82, 1.07	.342			

SYMPTOM OCCURRENCE		LOGISTIC REGRESSION RESULTS									
Symptom	Occurrence rate %		Covariate	Unadjusted Model			Adjusted Model				
	PRE (n=115)	POST (n=212)		OR	CI	p-value	OR	CI	p-value		
Lost sexual interest	22.4	13.7	Lives alone	0.98	0.55, 1.75	.939	0.98	0.55, 1.75	.939		
			Working for pay	0.93	0.57, 1.51	.769	0.93	0.57, 1.51	.769		
			SCQ score	1.07	0.98, 1.17	.144	1.07	0.98, 1.17	.144		
			Prior HRT	1.13	0.58, 2.20	.714	1.13	0.58, 2.20	.714		
			Adjuvant chemotherapy during 12 months	0.90	0.54, 1.50	.684	0.90	0.54, 1.50	.684		
			Radiation therapy during 12 months	1.63	0.85, 3.10	.140	1.63	0.85, 3.10	.140		
			Reconstruction during 12 months	0.78	0.32, 1.91	.588	0.78	0.32, 1.91	.588		
			Type of surgery: conservation (ref) vs mastectomy	1.85	0.86, 4.00	.117	1.85	0.86, 4.00	.117		
			Overall Model			X ² =26.27; p=.003					
			Menopausal status [*]			0.54	0.30, 0.98	.039	1.18	0.53, 2.59	.687
Age (in 5 year increments)			0.77 0.64, 0.92 .005								
Lives alone			0.18 0.05, 0.60 .005								
Working for pay			0.92 0.49, 1.71 .784								
SCQ score			1.03 0.91, 1.16 .680								
Prior HRT			1.30 0.53, 3.2 .571								
Adjuvant chemotherapy during 12 months			0.99 0.52, 1.91 .987								
Radiation therapy during 12 months			0.69 0.31, 1.56 .377								
Reconstruction during 12 months			1.18 0.4, 3.51 .763								
Type of surgery: conservation (ref) or mastectomy			0.61 0.22, 1.72 .353								

Abbreviations: CI = confidence interval; HRT = hormone replacement therapy; OR = odds ratio; PRE = premenopausal; POST = postmenopausal; ref = reference group; SCQ = Self-administered Comorbidity Questionnaire; vs = versus

* reference group = premenopausal women

Table 4

Results of unadjusted and adjusted logistic regression analyses that evaluated for differences between premenopausal and postmenopausal women in symptom occurrence rates with interaction effects 12 months after breast cancer surgery

LOGISTIC REGRESSION RESULTS									
Symptom	Covariates	Unadjusted Model			Adjusted Model				
		OR	CI	p-value	OR	CI	p-value		
Logistic Regression Results for Total Sample									
Hot flashes PRE = 58.3% POST = 45.3%	Overall Model X ² =59.53; p<.001								
	Menopausal status*	0.56	0.35, 0.89	.015	5681.12	136.43, 236576.94	<.001		
	Age (in 5 year increments)						1.00, 1.92	.050	
	Lives alone						0.51, 1.65	.770	
	Working for pay						0.39, 1.07	.089	
	SCQ score						0.97, 1.17	.188	
	Prior HRT						1.10, 4.36	.026	
	Adjuvant chemotherapy during 12 months						0.66, 1.87	.692	
	Radiation therapy during 12 months						0.59, 2.10	.739	
	Reconstruction during 12 months						0.63, 3.68	.352	
	Type of surgery: conservation (ref) vs mastectomy						0.44, 2.10	.921	
	Age × menopausal status						0.29, 0.61	.000	
	Adjusted Regression of Hot Flashes Occurrence on Age, Stratified by Menopausal Status								
Premenopausal						1.43	0.99, 2.06	.055	
Postmenopausal						0.56	0.46, 0.69	<.001	
Overall Model X ² =41.70; p<.001									
Night Sweats PRE = 44.3% POST = 32.5%	Menopausal status*	0.59	0.37, 0.94	.026	1132.50	29.38, 43655.1	<.001		
	Age (in 5 year increments)						1.30	0.94, 1.80	.117
	Lives alone						1.05	0.57, 1.92	.872
	Working for pay						0.97	0.59, 1.59	.892
	SCQ score						1.04	0.95, 1.15	.397

LOGISTIC REGRESSION RESULTS							
Symptom	Covariates	Unadjusted Model			Adjusted Model		
		OR	CI	p-value	OR	CI	p-value
Depression PRE = 34.5% POST = 24.5%	Prior HRT				2.35	1.18, 4.67	.015
	Adjuvant chemotherapy during 12 months				1.04	0.62, 1.75	.872
	Radiation therapy during 12 months				0.85	0.45, 1.62	.632
	Reconstruction during 12 months				0.91	0.38, 2.20	.837
	Type of surgery: conservation (ref) vs mastectomy				1.28	0.58, 2.82	.536
	Age × menopausal status				0.49	0.34, 0.71	<.001
	Adjusted Regression of Night Sweats Occurrence on Age, Stratified by Menopausal Status						
	Premenopausal				1.31	0.92, 1.88	.140
	Postmenopausal				0.63	0.52, 0.76	<.001
	Overall Model X ² =30.92; p=.001						
	Daytime sweats PRE = 39.7% POST = 26.9%	Menopausal status*	0.60	0.37, 0.99	.047	338.93	6.92, 16611.16
Age (in 5 year increments)					1.41	0.98, 2.02	.061
Lives alone					0.89	0.47, 1.71	.733
Working for pay					1.02	0.60, 1.73	.937
SCQ score					1.18	1.07, 1.30	.001
Prior HRT					0.83	0.39, 1.76	.620
Adjuvant chemotherapy during 12 months					1.04	0.60, 1.79	.889
Radiation therapy during 12 months					0.82	0.42, 1.61	.571
Reconstruction during 12 months					1.19	0.47, 2.98	.717
Type of surgery: conservation (ref) vs mastectomy					1.16	0.51, 2.64	.725
Age × menopausal status					0.54	0.36, 0.80	.002
Adjusted Regression of Depression Occurrence on Age, Stratified by Menopausal Status							
Premenopausal				1.50	1.00, 2.25	.048	
Postmenopausal				0.77	0.64, 0.92	.003	
Overall Model X ² =34.535; p=.011							
Menopausal status*	0.53	0.33, 0.87	.011	137.20	3.53, 5329.31	.008	

LOGISTIC REGRESSION RESULTS								
Symptom	Covariates	Unadjusted Model			Adjusted Model			
		OR	CI	p-value	OR	CI	p-value	
Joint pain or stiffness PRE = 40.0% POST = 51.9%	Age (in 5 year increments)				1.30	0.93, 1.83	.121	
	Lives alone				0.78	0.42, 1.47	.446	
	Working for pay				0.91	0.54, 1.51	.705	
	SCQ score				1.08	0.98, 1.19	.122	
	Prior HRT				2.92	1.46, 5.83	.002	
	Adjuvant chemotherapy during 12 months				0.98	0.57, 1.66	.931	
	Radiation therapy during 12 months				1.21	0.61, 2.39	.581	
	Reconstruction during 12 months				0.62	0.24, 1.56	.308	
	Type of surgery: conservation (ref) vs mastectomy				2.18	0.97, 4.93	.060	
	Age × menopausal status				0.57	0.39, 0.83	.004	
	Adjusted Regression of Daytime Sweats Occurrence on Age, Stratified by Menopausal Status							
		Premenopausal				1.27	0.89, 1.81	.190
		Postmenopausal				0.74	0.63, 0.89	.001
	Overall Model X ² =23.66; p=.014							
	Menopausal status*	1.62	1.02, 2.57	.043	387.32	6.64, 22601.80	.004	
	Age (in 5 year increments)				1.88	1.26, 2.79	.002	
	Lives alone				0.97	0.56, 1.68	.906	
	Working for pay				0.89	0.55, 1.42	.614	
	SCQ score				1.07	0.98, 1.17	.133	
	Prior HRT				1.00	0.54, 1.86	.993	
	Adjuvant chemotherapy during 12 months				1.40	0.85, 2.32	.188	
	Radiation therapy during 12 months				0.63	0.34, 1.17	.145	
	Reconstruction during 12 months				1.31	0.54, 3.16	.551	
	Type of surgery: conservation (ref) vs mastectomy				0.61	0.28, 1.31	.206	
	Age × menopausal status				0.54	0.36, 0.83	.004	
Adjusted Regression of Joint Pain Occurrence on Age, Stratified by Menopausal Status								

LOGISTIC REGRESSION RESULTS							
Symptom	Covariates	Unadjusted Model			Adjusted Model		
		OR	CI	p-value	OR	CI	p-value
Wake during the night PRE = 61.7% POST = 63.7%	Premenopausal				2.07	1.33, 3.23	.001
	Postmenopausal				1.00	0.86, 1.15	.947
					Overall Model X ² =23.12; p=.017		
	Menopausal status *	1.08	0.67, 1.73	.764	149.89	4.59, 4893.95	.005
	Age (in 5 year increments)				1.25	0.91, 1.72	.170
	Lives alone				0.92	0.52, 1.63	.779
	Working for pay				0.64	0.39, 1.05	.079
	SCQ score				1.10	1.00, 1.21	.058
	Prior HRT				1.29	0.67, 2.48	.447
	Adjuvant chemotherapy during 12 months				0.90	0.53, 1.51	.678
	Radiation therapy during 12 months				1.06	0.57, 1.97	.855
	Reconstruction during 12 months				2.53	0.99, 6.47	.052
	Type of surgery: conservation (ref) vs mastectomy				0.70	0.32, 1.54	.380
	Age × menopausal status				0.62	0.44, 0.88	.008
	Adjusted Regression of Wake During the Night Occurrence on Age, Stratified by Menopausal Status						
	Premenopausal				1.29	0.92, 1.80	.142
	Postmenopausal				0.76	0.64, 0.90	.001
					Overall Model X ² =29.37; p=.002		
Numbness or tingling PRE = 27.8% POST = 29.7%	Menopausal status *	1.12	0.67, 1.86	.673	174.64	3.33, 9171.79	.011
	Age (in 5 year increments)				1.29	0.89, 1.87	.185
	Lives alone				1.52	0.83, 2.79	.174
	Working for pay				0.74	0.44, 1.24	.253
	SCQ score				1.08	0.98, 1.18	.143
	Prior HRT				1.05	0.52, 2.12	.900
	Adjuvant chemotherapy during 12 months				2.47	1.45, 4.20	.001
	Radiation therapy during 12 months				0.82	0.42, 1.60	.562

LOGISTIC REGRESSION RESULTS							
Symptom	Covariates	Unadjusted Model			Adjusted Model		
		OR	CI	p-value	OR	CI	p-value
	Reconstruction during 12 months				1.06	0.42, 2.67	.905
	Type of surgery: conservation (ref) vs mastectomy				1.16	0.52, 2.60	.710
	Age × menopausal status				0.62	0.41, 0.92	.019
	Adjusted Regression of Numbness or Tingling Occurrence on Age, Stratified by Menopausal Status						
	Premenopausal				1.32	0.88, 1.98	.176
	Postmenopausal				0.79	0.66, 0.93	.006

Abbreviations: CI = confidence interval; HRT = hormone replacement therapy; OR = odds ratio; PRE = premenopausal; POST = postmenopausal; ref = reference group; SCQ = Self-administered Comorbidity Questionnaire; vs = versus

* reference group = premenopausal women

Table 5

Results of unadjusted and adjusted linear regression analyses that evaluated for differences in symptom severity and distress scores between premenopausal and postmenopausal women 12 months after surgery

SYMPTOM		LINEAR REGRESSION RESULTS								
Symptom	Severity Score (0–10) Mean (SD)	Covariate	Unadjusted Model				Adjusted Model			
	Premen		Postmen	B	CI	p-value	B	CI	p-value	
SYMPTOM SEVERITY										
Fatigue	4.7 (2.6)	3.8 (2.4)	Overall Model F=2.11; R ² =.12; p=.027							
			Menopausal status *	-0.73	-1.51, 0.06	.071	-1.00	-1.98, -0.01	.048	
			Age (in 5 year increments)					-0.15	-0.36, 0.06	.163
			Lives alone					0.36	-0.55, 1.27	.437
			Working for pay					-0.58	-1.35, 0.19	.140
			SCQ score					0.19	0.05, 0.34	.008
			Prior HRT					0.29	-0.74, 1.31	.580
			Any adjuvant chemotherapy in past 12 months					0.40	-0.42, 1.23	.336
			Any adjuvant radiation therapy in past 12 months					0.50	-0.43, 1.44	.290
			Any breast reconstructions months in past 12 months					-0.24	-1.58, 1.11	.729
			Type of surgery: lumpectomy (ref) vs mastectomy					-0.30	-1.47, 0.88	.616
Impatience	3.8 (2.3)	2.7 (1.8)	Overall Model F=2.22; R ² =.17; p=.022							
			Menopausal status *	-1.15	-1.88, -0.42	.002	-0.89	-1.80, 0.02	.055	
			Age (in 5 year increments)					-0.12	-0.30, 0.07	.227
			Lives alone					-0.31	-1.20, 0.58	.486
			Working for pay					-0.18	-0.92, 0.56	.639
			SCQ score					0.14	-0.01, 0.29	.061
			Prior HRT					-0.12	-1.16, 0.92	.816
			Any adjuvant chemotherapy in past 12 months					0.66	-0.11, 1.43	.091
			Any adjuvant radiation therapy in past 12 months					0.20	-0.74, 1.14	.678
			Any breast reconstructions months in past 12 months					0.66	-0.63, 1.95	.313

SYMPTOM		LINEAR REGRESSION RESULTS							
Symptom	Severity Score (0–10) Mean (SD)	Covariate		Unadjusted Model			Adjusted Model		
	Premen	Postmen	B	CI	p-value	B	CI	p-value	
			Type of surgery: lumpectomy (ref) vs mastectomy						
						-0.65		-2.05, 0.75	.36 0

Abbreviations: B = Beta coefficient; CI = confidence interval; HRT = hormone replacement therapy; Premen = premenopausal; Postmen = postmenopausal; ref = reference group; SCQ = Self-administered Comorbidity Questionnaire; vs = versus

* reference group = premenopausal women