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The relative importance of specific risk factors for insomnia in women treated for early-stage breast cancer

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Abstract

Background—Many individual risk factors for insomnia have been identified for women with a history of breast cancer. We assessed the relative importance of a wide range of risk factors for insomnia in this population.

Methods—Two thousand six hundred and forty-five women ≤ 4 years post-treatment for Stage I (≥ 1 cm)–IIIA breast cancer provided data on cancer-related variables, personal characteristics, health behaviors, physical health/symptoms, psychosocial variables, and the Women's Health Initiative–Insomnia Rating Scale (WHI-IRS; scores ≥ 9 indicate clinically significant insomnia).

Results—Thirty-nine per cent had elevated WHI-IRS scores. In binary logistic regression, the variance in high/low insomnia group status accounted for by each risk factor category was: cancer-specific variables, 0.4% (n.s.); personal characteristics, 0.9% (n.s.); health behaviors, 0.6% (n.s.); physical health/symptoms, 13.4% ($p < 0.001$); and, psychosocial factors, 11.4% ($p < 0.001$). Insomnia was associated with worse depressive (OR = 1.32) and vasomotor symptoms (particularly night sweats) (OR = 1.57).

Conclusion—Various cancer-specific, demographic, health behavior, physical health, and psychosocial factors have been previously reported as risk factors for insomnia in breast cancer. In our study (which was powered for simultaneous examination of a variety of variables), cancer-specific, health behavior, and other patient variables were not significant risk factors when in the presence of physical health and psychosocial variables. Only worse depressive and vasomotor symptoms were meaningful predictors.

Keywords

breast cancer; insomnia; depression; mood; vasomotor symptoms; night sweats; hot flashes; quality of life

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Introduction

Insomnia is a heterogeneous complaint reflecting poor sleep quality and/or lack of restful sleep that causes distress and impairment in daily functioning. The sleep quality component may include delayed sleep onset and sleep maintenance difficulties (frequent awakenings, waking early, difficulty resuming sleep). Insomnia affects approximately 20% of adults in the general population and is more common in cancer patients [1] (prevalence estimates in cancer range from 23–61% [2-5]) and may be particularly common in women who have undergone treatment

for breast cancer [6,7]. For example, a recent report found that $\frac{1}{2}$ of women who had completed treatment for breast cancer reported non-specific sleep problems [3,7], 19% met criteria for insomnia syndrome which was chronic in 95% of cases [3,7], and 23–44% reported insomnia 2–6 years after receiving their breast cancer diagnosis [8,9]. Despite its elevated prevalence and potential impact on quality of life (QOL) [4,7,10,11] insomnia in cancer has only recently begun to receive attention and little is known about risk factors for insomnia in this population [4].

Various risk factors for insomnia have been identified in the general population. These include demographic and personal characteristics (e.g. being female [12], older age [13-16], lower education/socioeconomic status [17-19], being divorced/single [20], obesity [21,22]), unhealthy behaviors (e.g. low physical activity [15,23,24], alcohol intake [25,26], smoking [27-31]), poor physical health [32,33] and physical symptoms (e.g. pain [23,34-37], vasomotor symptoms [38-43]), and poor psychosocial functioning (e.g. poor social functioning [44,45], life stress [15,46-49], depression/depressive symptoms [19,23,50], and personality traits such as anger/hostility [51]).

Insomnia in breast cancer has been linked with various risk factors, including cancer-specific variables (e.g. stage [3,52], treatment [3,11]), physical health/symptoms (e.g. physical health [10,14,53], pain [52,53], vasomotor symptoms [8,54], GU symptoms [11]), fatigue [53,55, 56], light exposure [57], and other variables identified as linked with insomnia in the general population (e.g. being widowed/separated [3], lower education [52], poor social support [52], depression/psychological distress [52,53]). A recent survey of breast cancer patients found that 58% reported that cancer caused or exacerbated their sleep problems [3]. In a study of 15 breast cancer survivors compared with healthy women matched on age, race/ethnicity and menopausal status, global sleep scores were linked with depression and fatigue but not frequency of hot flashes [55]. However, results have been inconsistent. For example, other studies either did not observe links between cancer-specific variables and insomnia in breast cancer or found relationships opposite to those reported above (e.g. initial treatment [11], social support [52], education [3]).

Most of the above studies did not have sufficient statistical power to evaluate the relative importance of a broad array of potential risk factors. Thus, it remains unclear if any of the identified risk factors might prove more or less important when evaluated in the presence of a wider range of variables. Gaining a better understanding of the relative importance of risk factors for insomnia in breast cancer is essential for the assessment, identification and treatment of survivors of this disease. The purpose of this study was to determine: (1) how breast cancer survivors with/without insomnia differ on a wide range of cancer-related and other variables; and (2) the relative importance of each of these variables as risk factors for insomnia when considered in the presence of other variables in multivariate statistical models.

Methods

Participants

Participants were from the Women's Healthy Eating and Living (WHEL) Study randomized trial of a dietary intervention on breast cancer recurrence/survival [58]: 3088 women (≤ 4 years post-completion of initial treatment for Stage I (≥ 1 cm)–IIIA disease). Recruitment occurred at seven clinical sites in California, Oregon, Arizona, Texas; recruitment strategies included letters to women on tumor registries, referrals from oncologists and community outreach programs, and local advertisements. The study was conducted in accordance with ethical standards for research involving human participants and was approved by the Institutional Review Boards at each participating site. Participants provided informed consent before enrolling.

Assessment

The WHEL Study intervention was designed using social cognitive theory [58] which guided selection of assessment instruments. Because of the opportunity the study provided, domains beyond those specific to dietary change and breast cancer outcomes were included. Participants completed the Thoughts and Feelings and Personal Habits Questionnaires adapted from the Women's Health Initiative (WHI) [59]. The current analyses use baseline data for 2645 women having complete data. To select variables to include in these analyses, we employed a biopsychosocial framework, which considers how illness, treatment, and other factors influence the patient's experience [60].

Sleep assessment

We used the 10-item WHI-Sleep Disturbance Scale (WHI-SDS; see Table 1 for items and scoring); higher scores indicate more frequent complaints in the past 4 weeks. Eight items assess sleep complaints and two assess overall sleep quality and duration. The WHI-SDS has shown evidence of internal consistency reliability (Cronbach's $\alpha = 0.68$ in our data set). An overall insomnia score for the 5-item WHI Insomnia Rating Scale (WHI-IRS) can be calculated as the average of scores for trouble falling asleep, waking several times, waking early, trouble resuming sleep, and overall sleep quality [61]. Scores ≥ 9 indicate clinically significant insomnia; between group differences of 0.50 SD are meaningful [62]. While other cut-points on the WHI-IRS can be used, Levine *et al.* recommend a score of 9 to minimize false-positives while maintaining acceptable sensitivity [62]. The WHI-IRS was validated in 66 269 postmenopausal women [61] and a clinical trial involving 850 postmenopausal women [40]. The WHI-IRS has a stable factor structure [61]; excellent internal consistency (Cronbach's $\alpha = 0.79$ in our data set and in the validation study [62]) and test–retest ($r = 0.84$ for 8–14 days) reliability [62]; and, validity [41,62].

Cancer-specific variables

Objective cancer-specific variables (verified via records review by clinical site staff) include diagnosis date and stage, mode(s) of initial treatment, and tamoxifen use.

Personal characteristics

Demographic information was obtained by interview. Body mass index (BMI; weight [kg]/height [m^2]) was calculated using weight/height measurements from clinic visits.

Health behaviors

Current smoking was self-reported. Physical activity was assessed by questionnaire and converted into metabolic equivalents (METs) [63]. Total energy expenditure was obtained by weighting time/week by METs: mild activity/walking ≤ 3 miles/h = 1.5 METs; moderate

activity/walking > 3 miles/h = 4.0 METs; vigorous activity = 8.0 METs. Dietary intake was obtained via repeated dietary recalls [58,64]. A composite score was developed to gauge adherence to NCI cancer prevention daily dietary recommendations [65] (1-point each: $\leq 30\%$ energy from fat; ≥ 20 g/day fiber; ≥ 5 servings fruit and vegetables/day). Scores were summed: 0 (met none) to 3 (met all). Alcohol intake (g/day) was calculated from conversion tables.

Psychosocial functioning

The RAND36 measures aspects of health relevant to functional status and well-being [66] and is valid/reliable ($\alpha = 0.75\text{--}0.91$) in breast cancer [67-69]. Self-reported responses yield four physical and four mental subscales (scored 0–100: higher scores = better health). Subscales are summarized into physical and mental health factors [66]. Other scales include MOS Social Support (9 items; $\alpha = 0.93$) [70]; social strain (four items from national surveys; $\alpha = 0.71$ [71]); life events (11 Alameda Co. Study items [72]); Life Orientation Test-Rev optimism (six items; $\alpha = 0.79$ [73]), Negative Emotional Expressiveness Questionnaire (NEE; seven items; $\alpha = 0.64$ [74]), Cook–Medley Cynicism (13 items; $\alpha = 0.74$ [75]).

The 8-item Center for Epidemiologic Studies-Depression screen (CESDsf) was developed to identify people likely to have a mood disorder. We have used this scale in prior reports on depressive symptoms [76] and QOL [10] in breast cancer, and it was recently used to assess depression in studies of hormone replacement therapy and QOL [77] and depression vs postmenopausal cardiovascular sequelae [78]. Items can be summed to yield a total score. When using a logarithmic scoring system, scores exceeding 0.06 suggest clinically significant insomnia [79]. CESDsf reliability ($\alpha = 0.73$) and validity [76] have been supported in women with a history of breast cancer.

Physical health/symptoms

The RAND36 physical health factor was included as a measure of overall physical health. A 34-item self-report inventory assessed symptom occurrence/severity: 0 (none) to 3 (severe) [80]. Factor analysis yielded a 5-factor solution (overall $\alpha = 0.79$): pain ($\alpha = 0.74$); gastrointestinal (GI; $\alpha = 0.63$); vasomotor ($\alpha = 0.82$); genitourinary (GU; $\alpha = 0.51$); psychological ($\alpha = 0.75$) [10]. Because the psychological factor is redundant with the CESDsf, it was not used.

Statistical analysis

Potential predictors were chosen from WHEL Study variables using a biopsychosocial framework to identify risk factors in the breast cancer literature and the general insomnia literature. Data were analyzed using SPSS 14.0 (Chicago, IL) software. Chi-squared and *t*-tests were used to compare high vs low insomnia groups on risk factors. Binary logistic regression (Nagelkerke's R^2 to gauge model fit [81]), with WHI-IRS group (> 9 vs ≤ 9) as the outcome variable, was used to determine the *relative* importance of risk factors. Significance was set at $p \leq 0.01$ to avoid observing meaningless differences. Using a stepwise approach with forced entry, variables were entered in categorical blocks: Step 1, cancer-specific variables; Step 2, personal characteristics; Step 3, health behaviors; Step 4, physical health/symptoms; Step 5, psychosocial variables.

Results

Participant characteristics

Detailed characteristics of this sample were presented elsewhere [76]. To summarize, participants averaged 53 years of age (range = 28–74), were highly educated, 71% were married. Mean BMI was 27.4 kg/m² and the women were racially/ethnically representative of

the general breast cancer population (85% white non-Hispanic, 5% Hispanic, 4% African-American, 4% Asian/Pacific Islander). Over $\frac{1}{3}$ were diagnosed with Stage I (≥ 1 cm), 56% with Stage II and 5% with Stage IIIA disease. The sample was uniformly distributed regarding time since diagnosis (23% ≤ 1 year; 33% 1–2 years; 24% 2–3 years; 20% 3–4 years); 60% were using tamoxifen. Only 5% currently smoked. Participants averaged 841 METs of physical activity/week. Regarding alcohol intake, 16% reported none, 71% averaged ≤ 1 drink/day, 9% averaged 1–2 drinks/day, 4% averaged > 2 drinks/day. In terms of insomnia, the women averaged 7.6 ± 4.7 on the WHI-IRS, which is 15% higher than the mean of 6.6 ± 4.5 for 66 269 postmenopausal women from the WHI Study [61].

Bivariate comparisons

Table 1 compares high vs low WHI-IRS groups on the 10 WHI-SDS sleep items. More than 1/3 (39%) reported insomnia (scores ≥ 9 ; ‘insomnia group’); those with insomnia used medication or alcohol more than twice as often for sleep. While the insomnia group had a 17% higher mean napping score, only a trend was observed for differences in propensity to fall asleep during quiet activities. The insomnia group was 4 times as likely to experience delayed sleep onset (difficulty falling asleep) and 2–4 times as likely to experience sleep maintenance insomnia (waking several times, waking early). The insomnia group reported mean sleep quality in the restless-to-average range; the non-insomnia group mean was average-to-sound. The insomnia group reported 8% greater sleep duration than the non-insomnia group.

Table 2 compares high vs low WHI-IRS groups on each risk factor. The groups did not differ significantly on any cancer-specific variable, although a trend was observed for the insomnia group to have a more recent diagnosis of breast cancer. For personal characteristics, only education differed by group: the insomnia group had less education. For health behaviors, the insomnia group was more sedentary and a trend was observed for the insomnia group to report dietary patterns that did not follow NCI guidelines. The insomnia group was significantly worse on all physical health/symptoms variables. The groups differed significantly on all psychosocial variables except negative emotional expressiveness. The insomnia group reported less social support, more social strain, more ambivalence over expressing negative emotions, more hostility, and more stressful events. The insomnia group reported more depressive symptoms, with a mean score exceeding the 0.06 cut-point for clinical significance.

Binary logistic regression

Using WHI-IRS group (> 9 vs ≤ 9) as the outcome variable, we used binary logistic regression to determine the relative importance of the categories of risk factors (Table 3). In Step 1, cancer-specific variables as a whole did not significantly explain variance in insomnia group status ($R^2 = 0.004$; $p = 0.292$); however, more time since diagnosis was a significant individual protective factor (Wald = 6.591; OR = 0.904, $p = 0.010$).

In Step 2, patient characteristics taken together were not significant predictors of variance in insomnia group status (overall $R^2 = 0.013$; $p = 0.027$; $\Delta R^2 = 0.009$; $p = 0.013$). However, higher education (Wald = 6.932; OR = 0.725; $p = 0.008$) joined greater time since diagnosis (Wald = 7.471; OR = 0.896; $p = 0.006$) as significant protective factors.

In Step 3, health behaviors as a whole did not explain a significant amount of variance in insomnia group status (overall $R^2 = 0.019$; $p = 0.008$; $\Delta R^2 = 0.006$; $p = 0.050$); however, the model overall was significant at this point. In terms of individual variables, more exercise (Wald = 8.164; OR = 1.365; $p = 0.004$) and greater time since diagnosis (Wald = 7.555; OR = 0.895, $p = 0.006$) were significant individual protective factors; education was no longer significant.

In Step 4, physical health/symptoms explained significant variance in insomnia group status (overall $R^2 = 0.153$; $p < 0.001$; $\Delta R^2 = 0.134$; $p < 0.001$). Vasomotor (Wald = 104.223; OR = 1.686; $p < 0.001$), gastrointestinal (Wald = 10.953; OR = 1.409, $p = 0.001$), and pain (Wald = 10.318; OR = 1.338; $p = 0.001$) symptoms were significant individual risk factors; better physical health (Wald = 27.052, OR = 0.985; $p < 0.001$) was protective.

In Step 5, psychosocial variables explained a significant amount of variance in insomnia group status (overall $R^2 = 0.267$; $p < 0.001$; $\Delta R^2 = 0.114$, $p < 0.001$). More depressive (Wald = 174.526, OR = 1.317, $p < 0.001$) and vasomotor symptoms (Wald = 68.415, OR = 1.565, $p < 0.001$) were the only significant individual risk factors.

To determine which vasomotor symptom was driving this relationship, we reran the binary logistic regression using night sweats and hot flashes separately instead of the vasomotor factor. Night sweats (Wald = 19.221, OR 1.328, $p < 0.001$) were more significant than hot flashes (Wald = 6.304, OR = 1.179, $p = 0.012$).

Discussion

Insomnia is a common comorbidity in cancer patients that may occur with greater frequency and/or severity in breast cancer than other cancers [6,7]. While several studies have documented correlates of insomnia in breast cancer, we are unaware of any with sufficient power to compare, simultaneously, the relative importance of a broad range of individual risk factors. Here, we examined cancer-specific variables, patient characteristics, health behaviors, physical health/symptoms, and psychosocial variables in multivariate analysis to determine their relative importance in explaining risk for clinically significant insomnia in women with a history of breast cancer. By considering such a wide range of risk factors in multivariate analyses, this study helps to clarify the relative importance of risk factors for insomnia in these women. Many of the risk factors previously identified as important *vis-a-vis* insomnia in this population appear to be rather unimportant when considered in the presence of a broader range of variables.

When comparing means for each individual risk factor separately between the high/low insomnia groups, greater insomnia was linked with lower education, less physical activity, worse physical health/symptoms, and worse psychosocial functioning, with a trend observed for less time since diagnosis. This replicates some of the findings from prior studies reported in the literature.

What is perhaps most novel and interesting in this study is how the importance of various risk factors changes dramatically when considered simultaneously with a wide range of predictors in bivariate logistic regression analysis. Considered as a single group, the cancer-specific variables were not significant predictors of insomnia group status; however, more years since diagnosis was a significant individual protective factor. When personal characteristics entered the model, as a group they also did not explained a significant amount of variance; however, at that point in the analysis, more years since diagnosis and more education were significant individual protective factors. When health behaviors entered, the model as a whole explained a small (1.9%) but significant amount of variance in insomnia group status, but the unique contribution due to the group of health behavior variables was not significant. However, less physical activity emerged as a significant individual risk factor and more time since diagnosis remained a significant individual protective factor.

It was only after physical health/symptom variables entered that the model explained a meaningful amount (15.3%) of variance in insomnia group status. While more vasomotor symptoms, poorer physical health, more GI symptoms and pain emerged as significant individual risk factors, none of the cancer-specific, personal characteristic, or health behavior

variables were significant individual predictors. This suggests that physical health/symptoms explain the variance in insomnia group status previously attributed to time since diagnosis and physical activity.

Finally, the psychosocial variables explained an additional 11.4% of variance in insomnia group status. Of the previously identified individual risk/protective factors, only vasomotor symptoms remained significant; *post hoc* analysis revealed this was driven more by night sweats than by hot flashes. However, depressive symptoms emerged as the strongest risk factor. This suggests mood may explain the variance in insomnia group status previously attributed to GI, GU and pain symptoms.

Links between mood and insomnia are well-documented and insomnia is a diagnostic criterion for mood disorders; thus, it is not surprising that depressive symptoms emerged as a significant risk factor for insomnia in this population. In addition, while the literature on risk factors for insomnia in breast cancer remains relatively new [4], there are data suggesting the importance of vasomotor symptoms vis-a-vis insomnia in studies of breast cancer [8,54] and menopausal women in general [38-43]. Vasomotor symptoms are well-established sequelae of the climacteric, whether natural or treatment induced.

Most notably, these findings underscore the importance of assessing and analyzing a wide range of variables when attempting to identify risk factors for insomnia. Factors commonly associated with poorer outcomes in cancer (e.g. worse or more recent illness, more extensive treatment, older age, obesity, socioeconomic status, unhealthy behaviors) do not appear to be helpful in identifying women with a history of breast cancer who are at increased risk for insomnia. Rather, clinically significant depression, particularly in the presence of vasomotor symptoms (especially night sweats) of even mild-to-moderate severity, should trigger further evaluation of sleep in this population.

Limitations

This study has certain limitations. Participants were predominantly non-Hispanic white, well-educated, married women from the western/southwestern US who volunteered for a study of the effect of diet modification on breast cancer recurrence/survival. Thus, these women may have attitudes in general and about health behaviors in particular that may not be fully representative of all women treated for early-stage breast cancer. These findings may not generalize to all women from racial/ethnic minority or other groups having different attitudes, access to health care, health knowledge and social support. However, race/ethnicity and health behaviors were not significantly associated with insomnia status in these analyses. In addition, because this sample consisted of women who had early-stage disease (Stage I (≥ 1 cm)–IIIA), results may not generalize to women with ductal carcinoma *in situ* or more advanced disease.

This study relied on self-report of most of the non-cancer-specific variables, including insomnia. Self-report is subject to response bias. However, we previously reported that Marlowe–Crowne Social Desirability Scale scores were not meaningfully associated with any of the self-report scales [10]. The final model only explained about 27% of variance. Variables such as anxiety and cancer-related worry/fear as well as history of insomnia and use of sleep aids were not assessed and could account for additional variance in insomnia symptoms. Cancer-related (e.g. Tamoxifen use) and other variables might also interact to influence risk for insomnia; and relationships between cancer-related variables and insomnia could be mediated by other risk factors. In future studies, such other factors or relationships among predictors should be considered. Regarding insomnia, it has been observed that self-report scales do not correlate as strongly as might be expected with objective sleep assessment. However, insomnia is ultimately a subjective experience and objectively measured sleep does not always correlate with outcomes as well as subjective report of sleep. Data are cross-

sectional; therefore, direction of causation of relationships between variables cannot be determined.

Conclusion

These findings suggest the importance of sufficient power and multivariate analysis of a breadth of constructs to more fully understand insomnia and, possibly, reconcile disparate observations in the literature. We previously reported that cancer-specific variables were unimportant in understanding which women treated for breast cancer would experience clinically significant depression. In that report, it was recommended that healthcare professionals consider contextual variables, not simply disease-specific factors, to identify women at risk for distress. These new findings suggest a similar approach in dealing with insomnia. The treatment team cannot assume that having more extensive disease or treatment, or being more recently diagnosed, portends probable insomnia. Conversely, one cannot suppose that a more encapsulated tumor and localized treatment, or greater time since diagnosis, ensure a survivorship replete with sound sleep. As recently stated in the NIH State-of-the-Science conference on insomnia, insomnia is a co-morbid condition and should be treated concurrently with other disorders present [82]. Disease, as well as its context, must be considered to optimize the care of the patient. And for certain important outcomes (e.g. insomnia, depression), factors that are not cancer-specific appear to be most salient.

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Table 1Women's Health Initiative Sleep Disturbance Scale by Insomnia Group (mean $\pm$ SD; independent samples *t*-tests)

	WHI-IRS<9 (<i>n</i> = 1607)	WHI-IRS $\geq$ 9 (<i>n</i> = 1039)	<i>p</i> -Value
1. Did you take any kind of medication or alcohol at bedtime to help you sleep?	0.48 $\pm$ 1.09	1.10 $\pm$ 1.52	< 0.001
2. Did you fall asleep during quiet activities like reading, watching TV, or riding in a car?	1.54 $\pm$ 1.30	1.66 $\pm$ 1.35	0.026
3. Did you nap during the day?	0.89 $\pm$ 1.09	1.04 $\pm$ 1.15	< 0.001
4. Did you have trouble falling asleep?	0.47 $\pm$ 0.79	1.82 $\pm$ 1.37	< 0.001
5. Did you wake up several times at night?	1.66 $\pm$ 1.38	3.35 $\pm$ 0.81	< 0.001
6. Did you wake up earlier than you planned to?	0.55 $\pm$ 0.81	2.36 $\pm$ 1.22	< 0.001
7. Did you have trouble getting back to sleep after you woke up too early?	0.38 $\pm$ 0.65	2.25 $\pm$ 1.19	< 0.001
8. Did you snore?	0.82 $\pm$ 1.41	0.88 $\pm$ 1.46	0.308
9. Overall, how was your typical night's sleep during the past 4 weeks?	1.38 $\pm$ 0.83	2.62 $\pm$ 0.73	< 0.001
10. About how many hours of sleep did you get on a typical night in the last 4 weeks?	7.76 $\pm$ 0.95	8.35 $\pm$ 1.03	< 0.001
WHI Insomnia Rating Scale (scores $\geq$ 9 indicate clinically significant insomnia)	4.45 $\pm$ 2.41	12.40 $\pm$ 2.91	< 0.001

Scoring key:

Items 1–8: 0 ('No, not in past 4 weeks'), 1 ('Yes, less than once a week'), 2 ('Yes, 1 or 2 times a week'), 3 ('Yes, 3 or 4 times a week'), or 4 ('Yes, 5 or more times a week').

Item 9: 0 ('Very sound or restful'), 1 ('Sound or restful'), 2 ('Average quality'), 3 ('Restless'), or 4 ('Very restless').

Item 10: 5 h or less, 6, 7, 8, 9, 10 h or more.

Table 2
Comparison of characteristics at study entry by insomnia category

		WHI-IRS < 9 (N=1607)	WHI-IRS > 9 (N = 1039)	p-Value ^a
Cancer-specific variables				
Treatment	Surgery+radiation	319 (20%)	199 (19%)	0.947
	Surgery+chemo	439 (27%)	281 (27%)	
	Surgery+both	669 (42%)	444 (43%)	
	Surgery only	180 (11%)	115 (11%)	
Tamoxifen use	Current	958 (60%)	631 (61%)	0.501
	Former	111 (7%)	80 (8%)	
	Never	538 (34%)	328 (32%)	
Cancer stage	I (≥ 1 cm)	623 (39%)	410 (40%)	0.818
	II	905 (56%)	583 (56%)	
	IIIA	79 (5%)	46 (4%)	
Time since diagnosis (years)	< 1	369 (23%)	246 (24%)	0.053
	1–1.9	484 (30%)	352 (34%)	
	2–2.9	401 (25%)	253 (24%)	
	3–4	353 (22%)	188 (18%)	
Personal characteristics				
Age (years)	< 50	586 (37%)	385 (37%)	0.241
	50–59.9	616 (38%)	421 (41%)	
	≥ 60	405 (25%)	233 (22%)	
Married	Yes	1129 (70%)	745 (72%)	0.423
	No	478 (30%)	294 (28%)	
Race/ethnicity	White, non-Hispanic	1374 (86%)	885 (85%)	0.740
	Hispanic	77 (5%)	62 (6%)	
	African-American, non-Hispanic	61 (4%)	37 (4%)	
	Asian	51 (3%)	30 (3%)	
	Pacific Islander	14 (0.9%)	6 (0.6%)	
	American Indian	1 (0.1%)	2 (0.2%)	
	Mixed Race	17(1%)	12 (1%)	
	Other	2 (0.7%)	5 (0.5%)	
Education	≤ High school diploma	176 (11%)	147 (14%)	0.007
	Post-high school	532 (33%)	368 (35%)	
	College degree	497 (31%)	267 (26%)	
	Post-graduate	402 (25%)	257 (25%)	
Body mass index (weight in kg/ height in meters ²)	≤ 24.9	682 (42%)	416 (40%)	0.161
	25–29.9	516 (32%)	324 (31%)	
	≥ 30	409 (26%)	299 (29%)	
Health behaviors				
Physical activity (average metabolic equivalents/week)	<300	430 (27%)	344 (33%)	0.001
	300–999.9	577 (36%)	366 (35%)	
	≥ 1000	600 (37%)	329 (32%)	
Alcohol intake (average grams/ day)	0	264 (16%)	159 (15%)	0.842
(14g = 1 drink)	0.01–14	1136 (71%)	751 (72%)	
	14.1–28	143 (9%)	89 (9%)	
	> 28	64 (4%)	40 (4%)	
Current smoking	No	1534 (96%)	993 (96%)	0.889
	Yes	73 (5%)	46 (4%)	
Number of National Cancer Institute dietary guidelines met ^b	0 or 1	572 (36%)	418 (40%)	0.051
	2	495 (31%)	303 (29%)	
	3	540 (34%)	318 (31%)	
Physical health/symptoms				
Overall physical health	RAND36 Physical Health	78.95	69.90	< 0.001
Physical symptoms ^c	Pain symptoms factor	0.73	0.99	< 0.001
	Vasomotor symptoms factor	0.86	1.33	< 0.001
	Genitourinary symptoms factor	0.19	0.23	0.002
	Gastrointestinal symptoms factor	0.23	0.37	< 0.001
Psychosocial functioning				
Social support	MOS total social support ^d	38.44	37.00	< 0.001
Social strain	Social strain scale	6.61	7.38	< 0.001
Optimism	Life Orientation Test	18.04	16.99	< 0.001
Emotional expressiveness	Negative emotional expressiveness (NEE) scale	2.91	2.90	0.657
	Ambivalence over NEE	2.88	3.07	< 0.001
Hostility	Cook-Medley Cynicism/hostility	2.79	3.25	< 0.001
Life events		1.69	2.04	< 0.001
Energy/Fatigue	RAND36 Energy/Fatigue	63.06	52.56	< 0.001

		WHI-IRS < 9 (N=1607)	WHI-IRS > 9 (N = 1039)	p-Value ^a
Depressive symptoms	Center for Epidemiologic Studies- Depression short form	0.03	0.09	< 0.001

^a χ^2 for categorical variables; *t*-tests for continuous variables.

^b 1 point each for $\leq 30\%$ of energy from fat, ≥ 20 g/day fiber, ≥ 5 servings/day fruit/vegetables (all daily).

^c Based on factor analysis of 34-item symptom checklist.

^d MOS, Medical Outcomes Study.

Table 3
Results of binary logistic regression analysis: risk factors vs WHI-IRS^a group

	Nagelkerke's R ² Total	Categories	Variables	Step 1 (OR)	Step 2 (OR)	Step 3 (OR)	Step 4 (OR)	Step 5 (OR)
<i>Block 1</i>	0.004 (n.s.)	Cancer-specific variables	Treatment	n.s.	n.s.	n.s.	n.s.	n.s.
			Current Tamoxifen use	n.s.	n.s.	n.s.	n.s.	n.s.
			Cancer stage	n.s.	n.s.	n.s.	n.s.	n.s.
			Years since diagnosis	0.904 ^{**}	0.896 ^{**}	0.895 ^{**}	n.s.	n.s.
<i>Block 2</i>	0.013 (n.s.)	Personal characteristics	Age		n.s.	n.s.	n.s.	n.s.
			Body mass index		n.s.	n.s.	n.s.	n.s.
			Married (no/yes)		n.s.	n.s.	n.s.	n.s.
			Ethnicity		n.s.	n.s.	n.s.	n.s.
			Education:					
			≤ high school		Reference	n.s.	n.s.	n.s.
			> high school		0.725 ^{**}	n.s.	n.s.	n.s.
<i>Block 3</i>	0.019 ^{**}	Health behaviors	Physical activity:					
			<300 METS			1.365 ^{**}	n.s.	n.s.
			300–999 METS			n.s.	n.s.	n.s.
			> 1000 METS			Reference	n.s.	n.s.
			Alcohol intake			n.s.	n.s.	n.s.
			Smoking			n.s.	n.s.	n.s.
			Diet composition			n.s.	n.s.	n.s.
<i>Block 4</i>	0.153 ^{***}	Physical health/ symptoms						
			RAND36 physical health				0.985 ^{***}	n.s.
			Pain symptoms				1.338 ^{***}	n.s.
			Vasomotor symptoms				1.686 ^{***}	1.565 ^{***}
			Genitourinary symptoms				n.s.	n.s.
			Gastrointestinal symptoms				1.409 ^{***}	n.s.
			Social support				n.s.	n.s.
<i>Block 5</i>	0.267 ^{***}	Psychosocial variables						
			Social strain					n.s.
			Optimism					n.s.
			Negative emotional expressiveness (NEE)					n.s.
			Ambivalence over NEE					n.s.
			Hostility					n.s.
			Life events					n.s.
			Energy/fatigue					n.s.
			Depressive symptoms					1.317 ^{***}

p < 0.001,

**
p < 0.010.

^a WHI-IRS, Women's Health Initiative Insomnia Rating Scale; binary outcome variable (scores < 9 vs ≥ 9).