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The association between post-diagnosis health behaviors and long-term quality of life in survivors of ductal carcinoma in situ: a population-based longitudinal cohort study.

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Research involving human participants. The study was approved by the University of Wisconsin Health Sciences Institutional Review Board. All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

Informed consent. Informed consent was obtained from all individual participants included in the study.

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Abstract

Purpose.—Women diagnosed with ductal carcinoma *in situ* (DCIS) often experience adverse changes in health-related behaviors following diagnosis. The impact of health behaviors on long-term quality of life (QoL) in DCIS survivors has not been investigated.

Methods.—We examined the association of post-diagnosis body mass index (BMI), physical activity, alcohol, and smoking with QoL among 1,448 DCIS survivors aged 20–74 enrolled in the population-based Wisconsin *in Situ* Cohort from 1997–2006. Health behaviors and QoL were self-reported during biennial post-diagnosis interviews. Physical and mental QoL were measured using the validated SF-36 questionnaire. Generalized linear regression was used to determine the association between behaviors and QoL with adjustment for confounders. Lagged behavior variables were used to predict QoL during follow-up and avoid reverse causation.

Results.—Women reported 3,536 QoL observations over an average 7.9 years of follow-up. Women maintaining a healthy BMI had on average a significantly higher summary measure score of physical QoL than obese women (normal vs. obese: $\beta = 3.02$; 2.18, 3.85). Physical QoL scores were also elevated among those who were physically active (5+ hours/week vs. none: $\beta = 1.96$; 0.72, 3.20), those consuming at least 7 drinks/week of alcohol (vs. none: $\beta = 1.40$; 0.39, 2.41), and non-smokers (vs. current smokers: $\beta = 1.80$; 0.89, 2.71). Summary measures of mental QoL were significantly higher among women who were moderately physically active (up to 2 hours/week vs. none: $\beta = 1.11$; 0.30, 1.92) and non-smokers (vs. current smokers: $\beta = 1.49$; 0.45, 2.53).

Conclusions.—Our results demonstrate that maintaining healthy behaviors following DCIS treatment is associated with modest improvements in long-term QoL. These results inform interventions aimed at promoting healthy behaviors and optimizing QoL in DCIS survivors.

Keywords

breast cancer; ductal carcinoma in situ; health-related behaviors; health-related quality of life; epidemiology; exercise; body mass index; alcohol drinking; smoking

Background

Ductal carcinoma *in situ* (DCIS) is a non-invasive breast cancer diagnosis in which malignant cells are confined to the basement membrane of the breast ducts [1]. DCIS diagnoses have increased with the widespread use of screening mammography, and currently account for about 20% of all new breast cancer cases in the US [2]. Despite a very favorable prognosis [3, 4] and treatment options that typically exclude chemotherapy [5], women with DCIS have demonstrated short-term declines in quality of life (QoL) similar to women treated for invasive breast cancer [6, 7]. Little is known about long-term QoL in DCIS

survivors, although our recent analysis found that measures of mental QoL in DCIS patients significantly declined beginning at 5 years after diagnosis [8].

Given the increase in number of DCIS patients and the length of survival, understanding modifiable factors that could improve long-term QoL following diagnosis of DCIS is increasingly important. Research suggests that after a DCIS diagnosis, women tend to decrease physical activity levels or remain inactive, gain weight, and more than half of smokers continue smoking [9–12]. However, no studies have investigated the impact of these health behaviors on long-term QoL among DCIS survivors. Given the impact of a DCIS diagnosis and surgical, radiation, and endocrine treatments on both QoL and health behaviors, it is unclear whether the associations between health behaviors and QoL would be the same in DCIS survivors as those observed in the general population.

In invasive breast cancer populations, increased levels of physical activity have been associated with higher QoL [13–16]; whereas weight gain or overweight/obese status and current smoking have been associated with lower quality life [14, 15, 17]. To our knowledge no studies have investigated the impact of alcohol on quality of life among breast cancer survivors. Understanding lifestyle factors that affect QoL in DCIS survivors will inform behavior recommendations and interventions aimed at promoting healthy behaviors after DCIS diagnosis.

Physical activity, body mass index (BMI), alcohol consumption, and smoking are widely studied health behaviors that have previously been shown to be associated with quality of life in the general population [18–21]. The Wisconsin *in Situ* Cohort (WISC), a population-based cohort of DCIS survivors with up to 17 years of follow-up, includes longitudinal data on each of these factors. We sought to estimate the association of these health behaviors with higher physical and mental QoL in this population.

Methods

Study Population

Details of the Wisconsin *in Situ* Cohort (WISC) have been described previously [9]. In short, the cohort enrolled women with a first primary non-invasive breast cancer diagnosis, as reported to the mandatory Wisconsin Cancer Reporting System during 1997–2006. The current study includes women diagnosed with ductal carcinoma (ICD-O [22] codes 8201, 8230, 8500, 8501, 8503, 8507, 8521–8523, and 8543). Women were female residents of Wisconsin aged 20–74 at the time of diagnosis. Women were excluded from the cohort if their date of diagnosis was not known, if they had no listed telephone number, or if they were not able to participate in a telephone interview. Of the eligible cases, 78% enrolled in the study, including 1925 DCIS cases [9]. The study was approved by the University of Wisconsin Health Sciences Institutional Review Board and informed consent was obtained from all individual participants included in the study.

All participants completed a baseline telephone interview at enrollment, which occurred at an average of 1.3 years following the date of diagnosis. Starting in 2003, follow-up interviews were conducted biennially and are currently on-going (Figure 1). Study

participants were eligible for re-contact if at least two years have passed since the previous interview. As the enrollment and follow-up contact periods were overlapping, not all women were eligible for each cycle of the follow-up interviews. Follow-up interviews were administered by telephone until 2010, when a mailed survey was introduced. Of the subjects eligible for the first follow-up, 79% participated; of those eligible for the second follow-up, 85% participated; of those eligible for a third follow-up, 73% participated; and of those eligible for a fourth follow-up, 73% participated. The current study includes data collected in the baseline interview plus up to four follow-up interviews (through 2013) for each woman.

Assessment of Health Behaviors

The specific questionnaire items used to ascertain health behaviors are provided as Supplementary Material. At the baseline interview participants self-reported their current weight and recalled their weight at one year prior to diagnosis and height at age 18. Current weight was updated at each subsequent data collection. BMI at each data collection period was calculated using self-reported height and weight.

Physical activity was recalled for one year pre-diagnosis at the baseline interview using a validated questionnaire patterned after the Nurses' Health Study [23]. Subjects reported the number of months per year and hours per week spent in the following recreational physical activity categories: running, jogging, bicycling, swimming, aerobics/dance, racquet sports, walking/hiking, and other strenuous activity. At each following re-contact, respondents were asked to name physical activities in which they regularly participated, and reported the number of months per year and hours per week spent participating in each activity.. For consistency with prior WISC studies [24–27], regular participation was defined as activities performed for at least 30 minutes per week and for at least 3 months per year. A composite variable was created to reflect the average hours per week spent in regular physical activity participation over the past year for each data collection period.

Alcohol intake was recalled for one year pre-diagnosis at the baseline interview and updated at each subsequent data collection. Subjects reported the number of cans or bottles of beer, glasses of wine, and drinks of hard liquor consumed per day, week, or month. A variable was created to summarize the total number of drinks per week at each data collection period.

Smoking was assessed at baseline by asking subjects to report whether they had smoked over 100 cigarettes in their lifetime. Subjects who met this criteria were asked whether they had been smoking at one year prior to diagnosis and whether they were current smokers. Current smoking status was updated at each follow-up data collection.

Any response items which participants refused to answer during the telephone survey or left blank on the mailed survey were coded as missing. Missingness for behavior variables during follow-up ranged from 0.1–3.0% on the telephone survey and from 0.8–22.8% on the mailed survey (see Supplemental Material for missingness rates by health behavior and assessment period).

Assessment of Quality of Life

Quality of life was assessed using the validated Medical Outcomes Study Short Form 36 Health Status Survey (SF-36) [28]. Subjects responded to 36 questions regarding physical and mental health. A standard scoring procedure was used to convert these responses into summary scores for eight domains of mental and physical health [29]. The domain scores were further summarized into mental component summary (MCS) and physical component summary (PCS) scores. Higher scores on the PCS and MCS reflect better physical and mental QoL, respectively. These scores were normalized to results from a standard population that is representative of US population norms in regards to age, household size, and income [30]. The standardized scores were then transformed to a mean of 50 and standard deviation of 10 to make valid comparisons between scales and to US population norms. Differences of 3–5 points on the mental and physical component SF-36 summary scores are widely considered clinically significant [29, 31–33].

Covariate assessment

Education level, income, surgical treatment type (ipsilateral or bilateral mastectomy, breast conserving surgery with or without radiation), and post-treatment endocrine therapy use (tamoxifen, raloxifene, or aromatase inhibitors) were assessed at baseline and not updated at subsequent data collections. These covariates were therefore considered static in our analysis. For dynamic characteristics, age at interview, menopausal status, postmenopausal hormone therapy use, number of comorbidities, and health insurance status were updated at each data collection and were therefore treated as time-varying in our analysis. Number of comorbidities was calculated based on diagnoses included in the Charlson Comorbidity Index [34].

Statistical analysis

All statistical analyses were performed using SAS version 9.4. To examine the association of post-diagnosis health behaviors on QoL, we used data from the four post-diagnosis data collection periods. A total of 315 women did not contribute QoL information at any follow-up data collections beyond enrollment and were therefore excluded from the study. An additional 162 women reported a second breast cancer diagnosis during the study period and were also excluded, since the diagnosis and treatment of second events may affect both health behaviors and QoL. These exclusions resulted in 1,448 DCIS cases who contributed 3,536 observations (mean 2.4, range 1–4 observations per woman). Women excluded from the study did not differ substantially from the remaining women with regards to baseline characteristics.

The analytic dataset was composed of up to four follow-up measures per woman, with health behaviors and QoL reported simultaneously at each observation. Missing values of health behaviors and covariates were estimated using multiple imputation with ten iterations [35]. The imputation models were performed separately for each of the four follow-up assessment periods using the PROC MI procedure in SAS. The models included the BMI, physical activity, alcohol, smoking, and quality of life variables collected at that data period, in addition to the health behavior, demographic, risk factor, and treatment variables collected at the baseline interview. Demographic and risk factor variables included age, education,

insurance status, marital status, income, number of comorbidities, history of mammography, and family history of breast cancer. Treatment variables includes type of surgery and use of endocrine therapy.

We used cross-lagged linear regression models to estimate the associations between each health behavior and subsequent mental and physical QoL [36]. This approach takes full advantage of the multiple measurements of both the predictor and outcome variables of interest, and accounts for reciprocal causation in which QoL may influence future health behavior (e.g., women with poor physical QoL may be unable to engage in physical activity). QoL at each observation was modeled as a function of health behavior status from the previous observation (the cross-lagged association of interest) as well as QoL at the previous observation (the autoregressive association which represents the stability of the construct from one measurement to the next). Controlling for the autoregressive associations in this manner effecting minimizes bias by ruling out the possibility that a cross-lagged effect is due only to the fact that the predictor and outcome variable were correlated at the preceding time point [36, 37]. As a result, QoL was predicted in our models by earlier health behaviors, independent of the association between those behaviors and earlier QoL. The analysis incorporated repeated measures to account for within-woman correlations. All longitudinal analyses were adjusted for static and time-varying covariates as described above, as well as for remaining health behaviors assessed at the previous observation (e.g., the association between BMI and QoL was adjusted for physical activity, alcohol intake, and smoking status). Surgical treatment type, post-treatment endocrine therapy use, and postmenopausal hormone use did not have an impact on the association between health behaviors and QoL in any model, and were therefore omitted from the final models. We tested for interaction with time since diagnosis using cross-product terms to determine if the effect of health behavior on QoL differed over time.

All statistical tests, including tests of cross-product interaction terms, were considered significant at a p value of 0.05 or less.

Results

A total of 1,488 women with DCIS were included in the study. At baseline, a majority of women reported some education beyond high school (58%), were free of comorbidities (68%), and were covered by private (59%) and/or government (31%) insurance (Table 1). Most women were healthy weight (44%, BMI 18.5–24.9 kg/m²), reported some physical activity (74%), and consumed some alcohol (83%). Over 85% of women were non-smokers at baseline.

We observed that women who were overweight (BMI 25.0–29.9 kg/m²) or obese (BMI 30+ kg/m²) during post-diagnosis reported lower physical QoL at the following data collection compared to their healthy weight counterparts (BMI 18.5–24.9 kg/m²) (Table 2, Figure 2a). No significant difference in mental QoL was observed by BMI category (Table 2, Figure 2b). Women reporting any level of physical activity had subsequent higher physical QoL compared to sedentary women (Table 2, Figure 3a). In addition, women reporting moderate levels of physical activity (up to 5 hours/week) had subsequent higher mental QoL than

sedentary counterparts; however this association did not hold for women reporting more than 5 hours/week of physical activity (Table 2, Figure 3b). Women consuming at least 7 drinks per week reported higher levels of physical QoL at the following data collection, but no other associations with alcohol consumption were observed (Table 2, Figure 4a, b). Finally, compared to non-smokers, current smokers reported significantly lower levels of both physical and mental QoL (Table 2, Figure 5a, b).

No interactions with time since diagnosis were observed in any of the longitudinal analyses ($p > 0.10$ for all interactions).

Discussion

We observed that BMI, physical activity, alcohol intake, and smoking influenced long term QoL among DCIS survivors. Specifically, physical QoL was higher among women with BMI within the normal range compared to overweight or obese women, among active women compared to sedentary women, among women consuming at least 7 alcoholic drinks per week compared to non-drinkers, and among non-smokers compared to current smokers. Mental QoL was higher among moderately active women compared to sedentary women, and among non-smokers compared to current smokers. Overall, the observed differences in QoL according to health behaviors were modest compared to the widely accepted threshold of 3–5 points for clinically significant differences.

Many of our results are consistent with findings among survivors of invasive breast cancer, as well as among women in the general population. Lower physical QoL has been reported for obese breast cancer survivors compared to normal weight counterparts [38, 39]; Similarly, in the general population, it has been found that obesity is associated with decreased physical QoL, with a dose-response relationship at increasing BMI [19]. Previous studies have suggested that obesity impacts physical QoL more than mental QoL [40], since the greatest effects of overweight and obese status are typically on physical domains such as vitality, pain, and functional limitations [41]. In the general population, Ul-Haq et al. found that mental QoL was significantly lower among those with class III obesity (BMI ≥ 40 kg/m²), compared to those with normal BMI (19.0–24.9 kg/m²), while there was no difference in mental QoL between those with class I/II obesity (BMI 30.0–39.9 kg/m²) compared to those with a normal BMI [19].

Physical activity is known to improve body composition, balance, ability to lift objects, endurance, and flexibility [42] and has been associated with higher physical QoL among invasive breast cancer survivors [39, 40, 43]. Furthermore, positive associations between physical activity and mental QoL have been attributed to the effect of exercise on improved body image, self-esteem, memory capacity, and executive functioning [44, 45]. These positive effects are also found among women in the general population, with both physical and mental QoL found to be higher among women achieving greater levels of physical activity, compared to those who are sedentary [18]. Finally, the negative effects of smoking on both physical and mental QoL have been clearly demonstrated among survivors of invasive breast cancer [17, 46, 47] and in the general population [48, 49].

Previous literature among invasive breast cancer survivors have reported mixed findings regarding the association between physical activity levels and mental QoL, with some reporting positive associations [14, 39, 43] and others reporting no association [40, 50]. In our study of women with DCIS we found that moderate physical activity was associated with elevated mental QoL, but there was not a dose-response pattern at higher levels of activity.. The relatively small number of women in the highest activity category limited the precision of our estimate.

We are not aware of prior studies alcohol use in relation to quality of life among breast cancer survivors. We found that physical QoL was significantly higher among women with DCIS who reported at least 7 alcoholic drinks/week. Alcohol consumption is contraindicated with numerous medications [51]. Women who are able to regularly consume alcohol may be those not taking medication and may therefore exhibit higher physical QoL. We adjusted for numerous comorbidities that are associated with medication use, but residual confounding remains possible. It is possible that moderate alcohol consumption could promote physical QoL through its cardioprotective effects [52, 53], though alcohol is also associated with elevated risks for several cancers and other diseases [54]. Our findings on physical QoL and alcohol intake were consistent with data from the Nurses' Health Study, which found that women in the general population who consumed about one alcoholic drink daily (7 alcoholic drinks/week) had higher physical quality of life compared to less frequent drinkers [55].

Previous analysis in the WISC cohort has shown that surgical treatment type and use of post-treatment endocrine therapy (tamoxifen, raloxifene or aromatase inhibitors) do not have significant effects on long-term QoL among DCIS survivors [8]. Our results indicate that both positive and negative health behaviors may impact both physical and mental QoL in this population. The clinical significance of these effects may be considered modest given that they generally consist of 1–3 points on the 100-point scale for the SF-36 physical and mental component summary measures of QoL. Notably, however, the degree of change considered clinically significant varies across disease groups and individual patients [56, 57]. To our knowledge no studies have evaluated the minimum important differences in SF-36 scores among DCIS survivors specifically. Women who value modest improvements in health related quality of life may benefit from efforts to promote the adoption or maintenance of healthy behavior habits at the point of DCIS diagnosis. Furthermore, evidence suggests that DCIS survivors are more likely to die from cardiovascular disease or other causes than from breast cancer [3]. Obesity, sedentary behavior, excessive alcohol, and smoking are all established risk factors for cardiovascular disease [58–60]. Consequently, the explicit promotion of healthy behaviors following DCIS diagnosis and treatment could have broader impact beyond improved QoL to improving overall mortality among DCIS survivors [3].

Our study is strengthened by the large cohort of DCIS survivors with four periods of follow-up data collection over up to 17 years. Some limitations of our design should be noted. The simultaneous collection of behavior and QoL information at each data collection cannot protect against potential reverse causation; however, we ensured the temporal relationship between behavior and QoL in our analysis by using behavior reported at the previous data collection to predict current QoL [36, 37]. Our investigation is also limited by reliance on

self-reported health behaviors. To conform with social acceptability, women may be more likely to report lower levels of BMI [61] and alcohol intake [62], and higher levels of physical activity [63]. This misclassification would make it more difficult to observe significant associations between health behaviors and QoL. In addition, the SF-36 survey was not designed specifically for breast cancer populations. In studies among invasive breast cancer survivors, both floor and ceiling effects were observed in certain domains of the SF-36 [64, 65]. These could have limited our ability to detect more subtle differences in QoL by health behavior. Although we adjusted for factors associated with health behavior and QoL including comorbidities and socioeconomic indicators, it is possible that confounding by unmeasured factors impacted our results. Finally, the WISC is composed primarily of women of European descent, and we were therefore not able to investigate differences in QoL by race or ethnicity.

Conclusions

Prior studies have demonstrated that compared to controls from the general population, women diagnosed with DCIS experience adverse changes in health-related behaviors and health-related QoL [6–11]. To our knowledge, our current study provides the first evidence for the association between health behaviors and long term QoL among DCIS survivors. We found that negative health behaviors (overweight/obese status, sedentary behavior, smoking) were associated with lower physical and/or mental QoL, while positive health behaviors (physical activity, non-smoking) were associated with higher physical and/or mental QoL. While the associations of health behaviors with long term QoL among DCIS survivors appears to be modest, they exceed the impact of treatment regimens [8], and these health behaviors may also confer added benefits of lower cardiovascular disease risk [58–60]. Given that specific negative health behavior changes have been observed following treatment for DCIS, our findings provide important information for women and clinicians to consider during DCIS management and survivorship care.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Abbreviations

BMI	body mass index
DCIS	ductal carcinoma in situ
QoL	quality of life

WISC

Wisconsin In Situ Cohort

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Figure 1.
Recruitment and follow-up timeline for DCIS cases in the Wisconsin In Situ Cohort (WISC), 1997–2013.

Figure 2. Longitudinal association of post-diagnosis quality of life (A: physical component score; B: mental component score) in relation to body mass index among 1,488 women with DCIS in the Wisconsin In Situ Cohort, 1997–2013. Adjusted for quality of life at previous interview, age at interview, menopausal status, number of comorbidities, education, income, insurance status, and remaining behaviors.

Figure 3.

Longitudinal association of post-diagnosis quality of life (A: physical component score; B: mental component score) in relation to physical activity among 1,488 women with DCIS in the Wisconsin In Situ Cohort, 1997–2013. Adjusted for quality of life at previous interview, age at interview, menopausal status, number of comorbidities, education, income, insurance status, and remaining behaviors.

Figure 4.

Longitudinal association of post-diagnosis quality of life (A: physical component score; B: mental component score) in relation to alcohol intake among 1,488 women with DCIS in the Wisconsin In Situ Cohort, 1997–2013. Adjusted for quality of life at previous interview, age at interview, menopausal status, number of comorbidities, education, income, insurance status, and remaining behaviors.

Figure 5. Longitudinal association of post-diagnosis quality of life (A: physical component score; B: mental component score) in relation to smoking status among 1,488 women with DCIS in the Wisconsin In Situ Cohort, 1997–2013. Adjusted for previous quality of life at previous interview, age at interview, menopausal status, number of comorbidities, education, income, insurance status, and remaining behaviors.

Table 1:

Selected baseline characteristics of the study population (N=1,448), Wisconsin In Situ Cohort, 1997-2013.

	N (%) ^a
Age at Diagnosis (years)	
20-44	176 (12.3)
45-54	541 (36.8)
55-64	459 (32.0)
65-74	272 (18.9)
Education	
< High school diploma	58 (4.0)
High school diploma	557 (38.0)
Some college	392 (27.3)
College degree	441 (30.7)
Comorbidity Status	
None	997 (68.6)
One	308 (21.5)
Two	114 (7.9)
Three or More	29 (2.0)
Income	
Up to \$15,000	74 (5.2)
\$15,001 - \$50,000	611 (41.7)
\$50,001 - \$100,000	595 (41.4)
\$100,000+	168 (11.7)
Health insurance status	
No insurance	111 (7.7)
HMO/employer	862 (59.2)
Medicare, or Medicare plus supplement	427 (29.7)
Medicaid	12 (0.8)
Other	36 (2.5)
Surgical Treatment	
Mastectomy (ipsilateral or bilateral)	605 (41.7)
BCS without radiation	120 (8.6)
BCS with radiation	689 (47.3)
Biopsy only	34 (2.4)
Post-Treatment Endocrine Therapy Use	
No	846 (58.1)
Yes	602 (41.9)
BMI (kg/m ²)	
< 18.5	11 (0.8)
18.5 - 24.9	637 (43.5)
25.0 - 29.9	480 (33.4)
30.0+	320 (22.3)

	N (%) ^a
Physical activity (hours/week) ^b	
No activity	377 (26.3)
0.1 – 2.0	290 (20.2)
2.1 – 5.0	421 (28.4)
5.1+	360 (25.1)
Alcohol intake (drinks/week) ^b	
Non-drinker	238 (16.6)
0.1 – 2.0	693 (47.4)
2.1 – 7.0	341 (23.8)
7.1+	176 (12.3)
Smoking status	
Non-smoker	1241 (85.6)
Current smoker	207 (14.4)

HMO, Health Maintenance Organization; BCS, Breast Conserving Surgery; BMI, Body Mass Index

^aMissing values estimated using multiple imputation; category frequencies based on the mode of the ten imputations.

^bPhysical activity and alcohol intake recalled at one year pre-diagnosis

Table 2:

Longitudinal association between behavior and quality of life (QoL) following DCIS diagnosis, Wisconsin In Situ Cohort, 1997-2013 (N=1488 women).

	Physical Component Summary				Mental Component Summary			
	N ^a	Adjusted mean score ^b	β^b	95% confidence interval	Adjusted mean score ^b	β^b	95% confidence interval	
BMI (kg/m ²)								
<18.5	24	45.67	-0.99	(-4.07, 2.09)	52.19	0.49	(-2.46, 3.44)	
18.5 – 24.9	1365	46.66	Ref		51.70	Ref		
25.0 – 29.9	1188	45.32	-1.34	(-2.13, -0.55)	52.22	0.52	(-0.16, 1.20)	
30.0+	959	43.64	-3.02	(-3.85, -2.18)	51.87	0.17	(-0.58, 0.93)	
Physical activity (hours/week)								
None	1551	45.26	Ref		51.50	Ref		
0.1 - 2.0	524	46.32	1.06	(0.25, 1.88)	52.62	1.11	(0.30, 1.92)	
2.1 - 5.0	869	46.25	0.99	(0.19, 1.80)	52.33	0.82	(0.05, 1.60)	
5.1+	592	47.22	1.96	(0.72, 3.20)	51.80	0.30	(-0.92, 1.51)	
Alcohol intake (drinks/week)								
None	632	45.22	Ref		51.79	Ref		
0.1 - 2.0	1745	45.84	0.62	(-0.13, 1.36)	52.00	0.21	(-0.59, 1.00)	
2.1 - 7.0	770	45.88	0.66	(-0.19, 1.50)	52.28	0.49	(-0.42, 1.40)	
7.1+	389	46.62	1.40	(0.39, 2.41)	51.73	-0.06	(-1.16, 0.99)	
Smoking status								
Non-smoker	3255	46.42	Ref		52.53	Ref		
Current smoker	281	44.62	-1.80	(-2.71, -0.89)	51.03	-1.49	(-2.53, -0.45)	

^aNumber of quality of life observations according to behavior exposure status at the first post-diagnosis data collection

^bMean score and regression coefficient from model adjusting for: lagged QoL, age at interview, menopausal status, number of comorbidities, education, income, insurance status, and remaining behaviors