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Smoking and quality of life among female survivors of breast, colorectal and endometrial cancers in a prospective cohort study

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Abstract

Purpose—To examine the association of smoking and quality of life (QOL) among survivors of breast, colorectal, or endometrial cancers.

Methods—The study included women who joined the Iowa Women's Health Study in 1986 and were subsequently diagnosed with breast, colorectal, or endometrial cancers through 2004 (n=1920). Smoking status was reported at baseline and in 2004; QOL was assessed in 2004 using the Medical Outcomes Study Short Form-36. Multivariate-adjusted odds ratios were calculated to examine the associations of smoking status and poor QOL (score lower than one-half a standard deviation below the mean of the non-smokers).

Results—Compared with non-smokers, persistent smokers had higher likelihood of reporting poor Physical Functioning (odds ratio [OR] = 2.40, 95% confidence interval [CI] = 1.32–4.37), Mental Health (OR = 1.92, CI = 1.09–3.40), and Role Emotional (OR = 2.01, CI = 1.10–3.66), whereas former smokers had higher likelihood of reporting poor Physical Functioning (OR = 1.65, CI = 1.10–2.45), Mental Health (OR = 1.62, CI = 1.11–2.37), and General Health (OR = 1.51, CI = 1.03–2.21). A statistically significant trend toward higher likelihood of poor QOL was observed across smoking groups in Vitality, Physical Functioning, Mental Health, and Role Emotional. Further adjustment for physical activity resulted in attenuation of the odds ratios and p-values for trend.

Conclusion—Among women with breast, colorectal, or endometrial cancers, smokers were more likely than former or non-smokers to have poor QOL. Physical activity explained, in part, the association between smoking status and QOL in our study.

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Keywords

cancer survivors; smoking; quality of life; physical activity; SF-36

INTRODUCTION

Smoking is a risk factor for many types of cancer, including cancers of the lung, bladder, esophagus, stomach, kidney, cervix, pancreas, and head and neck.¹ In addition, many studies suggest that smoking may reduce the effectiveness of cancer therapies and increase the risk of developing a second primary cancer.² Evidence has also emerged that suggests smoking can affect the quality of life (QOL) of cancer patients. A cross-sectional study of head and neck cancer patients found that current smokers experienced significantly poorer physical functioning, general health perceptions, vitality, social functioning, and emotional functioning compared with nonsmokers.³ In prospective cohort studies, adverse effects on QOL were consistently noted in head and neck cancer patients who continued smoking after diagnosis.^{4,5} Among newly diagnosed lung cancer patients, persistent smokers reported significantly lower QOL compared with never smokers and moderately lower QOL compared with former smokers or those patients who quit between diagnosis and subsequent evaluation.⁶ These results are consistent with associations observed in the general population that show nonsmokers with the highest QOL followed by former and then current smokers.^{7–10}

One important shortcoming of the evidence of the negative impact of smoking on QOL among cancer survivors is that these data are derived from studies done in populations with smoking-related cancers including cancers of the lung and head and neck. Also these studies included relatively young population with short follow up after cancer diagnosis.^{3–5} Although survivors of breast, colorectal and endometrial cancers represents majority among females, relatively less is known about the association between smoking status and QOL in this population. The present study compared QOL among non-smokers, former smokers, and persistent smokers diagnosed with breast, colorectal, or endometrial cancers using data collected from participants in a large prospective cohort study of cancer incidence in postmenopausal women.

METHODS**Study population**

The Iowa Women's Health Study (IWHS) is a population-based, prospective cohort study launched in 1986 to examine whether diet, body fat distribution, or other potential risk factors were associated with cancer incidence in postmenopausal women. Detailed methods for the IWHS have been described previously.¹¹ In brief, a self-administered questionnaire was sent to 99,826 women, ages 55 to 69, randomly selected from the Iowa driver's license database in 1986. The questionnaire was completed by 41,836 women (42%), with five follow-up questionnaires sent in 1987, 1989, 1992, 1997, and 2004. Demographic and lifestyle information was collected including smoking status, prior health conditions, and anthropometrics; quality of life was measured in 2004. The vital status (living or deceased)

of non-responders to follow-up surveys was determined through the National Death Index. The IWHS was approved by the University of Minnesota's Institutional Review Board.

Incident cancers diagnosed within the IWHS cohort were ascertained between 1986 and 2004 by linkage to the State Health Registry of Iowa, which participates in the National Cancer Institute's Surveillance, Epidemiology, and End Results (SEER) program. After excluding 1,511 women who reported a cancer diagnosis at baseline, 40,325 women were prospectively followed for cancer occurrence. A total of 4,328 women developed incident breast, colorectal, or endometrial cancer (the three cancer types eligible for this study) from 1986 to 2004. For the purpose of this analysis, women with one of these three cancers were classified as respondents if they completed the questionnaire in 2004 (n=1,949), as deceased participants if they died prior to 2004 (n=1,389), and as non-respondents if they failed to return the 2004 questionnaire (n=796) or did not complete the QOL section of the 2004 questionnaire (n= 193) or if their 2004 questionnaire was completed by proxy (n=1).

The questionnaires sent to participants in 1986 and 2004 included the question, "Do you smoke cigarettes now?" Of the 1,949 respondents, 1,928 women answered this question in both 1986 and 2004. Based on their response, participants were classified as non-smokers if they answered "no" in both 1986 and 2004 (n=1,720), former smokers if they answered "yes" in 1986 but "no" in 2004 (n= 141), or persistent smokers if they answered "yes" in both 1986 and 2004 (n=59). Eight women reported no smoking in 1986 but smoking in 2004; however, due to the small sample size, these women were excluded from this study. Thus, 1,920 women were eligible respondents for the present study. Data on the usual number of cigarettes smoked was not available.

QOL

The Medical Outcomes Study Short Form-36 Version 2 (SF-36) was included in the 2004 follow-up questionnaire to measure QOL of the IWHS cohort.^{12, 13} SF-36 is a reliable and valid instrument for global assessment of quality of life. It measures QOL in the past four weeks on eight scales: General Health, Physical Functioning, Role Physical, Bodily Pain, Vitality, Mental Health, Role Emotional, and Social Functioning. Each individual scale was standardized to age-specific 1998 population norms by using z-score standardization and norm-based transformation of each scale's z-score using established algorithms.¹⁴ A mean of 50 represents the population average for a given scale, with each point below or above the mean indicating 1/10th of a standard deviation. Higher scores indicate better QOL in all scales.

Cancer diagnosis and treatment

Primary cancer type, diagnosis date, histology, stage, and first course of treatment were obtained from SEER. Cancer stage was classified into four categories: in situ, local, regional, distant. The proportion of women receiving surgery, radiation therapy, or chemotherapy was also calculated.

Demographics, health, and lifestyle characteristics

Potential confounding factors in the relationship between smoking status and QOL were obtained from the baseline questionnaire in 1986 and/or the 2004 questionnaire. Age and education were collected at baseline. Participants were also compared for how they rated their overall health at baseline. Participants reported their current height and weight at baseline and in 2004. Body mass index for each time point was calculated as weight (kilograms) divided by height (meters) squared; categories were defined as normal ($< 24.9 \text{ kg/m}^2$), overweight (25.0 to 29.9 kg/m^2), and obese ($\geq 30 \text{ kg/m}^2$).¹⁵ Physical activity level was also obtained at baseline and at follow-up in 2004. Women were assigned a “high” physical activity level score if they participated in vigorous activity (such as jogging, racquet sports, swimming, aerobics, strenuous sports) two or more times per week or participated in moderate activity (such as bowling, golf, light sports or physical exercise, gardening, taking long walks) more than four times per week. Women were assigned a “medium” physical activity level score if they participated in vigorous activity once a week or participated in moderate activity one to four times per week. All remaining women were assigned a “low” physical activity level score. At baseline and at each follow-up, women reported medical history, including diabetes mellitus, hypertension, fracture, stroke, heart disease, rheumatoid arthritis, or Parkinson’s disease. Women were classified as having one of these conditions based upon the first report of the health condition at any data collection point. The cumulative number of comorbid conditions reported on all questionnaires was calculated for each participant.

Data Analysis and Statistical Methods

To examine non-response bias, eligible respondents, deceased participants, and non-respondents were compared for demographics, lifestyle characteristics, comorbid conditions, and cancer-related characteristics. To identify potential confounders, similar comparisons were performed among eligible respondents according to smoking status – that is, non-smokers, former smokers, and persistent smokers.

Two approaches were employed to examine the association between smoking status and QOL. First, age-adjusted mean scores for each SF-36 scale across smoking groups were calculated using generalized linear regression. A p-value of less than 0.05 was used to determine the statistical significance of differences across the age-adjusted mean scores. This approach has been used in most QOL studies using SF-36. However, the difference in mean scores across smoking groups may not provide clinically meaningful information. Therefore we used the second approach reporting the percent of individuals with poor QOL which was defined as scores that fell more than one-half a standard deviation below the mean of the non-smokers since clinicians are mostly interested in identifying patients with poor QOL. One-half a standard deviation is chosen based on systematic review by Norman who concluded that $\frac{1}{2}$ SD appears to be clinically meaningful difference in QOL assessment.¹⁶ Then the odds ratio was calculated for poor QOL in each SF-36 scale among former smokers and persistent smokers compared to non-smokers. Odds ratios and 95% confidence intervals for this analysis were obtained using logistic regression.

Potential confounders, including baseline general health perception, education, cancer type, cancer stage, surgery, radiation therapy, chemotherapy, length of survival, the number of comorbid conditions, BMI, and physical activity, were individually examined for whether they meaningfully changed the age-adjusted mean scores of any SF-36 scale. Only BMI and physical activity, as measured in 2004, changed the score more than 5% in absolute value in any scale. Multivariate-adjusted odds ratios were calculated adjusted for age at baseline, stage of cancer, number of comorbid conditions and BMI (2004). Because of changes to the odds ratios when physical activity (2004) was added to the multivariate model, results are presented separately from those adjusted for age, stage, comorbidity and BMI. Finally, a linear trend test of odds ratios across smoking status was performed.

RESULTS

Participant characteristics

Descriptive characteristics of deceased participants, non-respondents, and eligible respondents are listed in Table 1. At baseline, eligible respondents were generally younger, more educated, less obese, never smokers, and healthier as measured by general health perception and incidence of chronic disease and fractures as compared to deceased participants or non-respondents. In addition, eligible respondents were more physically active at baseline compared to deceased participants, as well as being more likely to have had their cancer diagnosed at an earlier stage (in situ or local). Deceased participants were more frequently diagnosed with colorectal cancer and less frequently diagnosed with breast cancer compared to eligible respondents or non-respondents. Non-respondents and eligible respondents did not differ significantly in terms of the type of cancer, stage at diagnosis, or therapy received.

Non-smokers were slightly older than former or persistent smokers. (Table 2) The percentage of obese non-smokers was higher than former or persistent smokers at baseline. Although this percentage remained relatively unchanged from baseline to 2004, the percentage of obese former smokers increased and surpassed that of non-smokers by 2004. In contrast, the number of obese persistent smokers decreased by 2004. Low physical activity was common among all groups, especially persistent smokers, both at baseline and in 2004. Although non-smokers and former smokers were more likely than persistent smokers to have diabetes, hypertension, heart disease, and/or fracture, these differences were not statistically significant. However, the difference in stroke among the groups was statistically significant ($p < 0.05$), with stroke being more common among persistent smokers than former or non-smokers. Breast cancer was the most common diagnosis in both smoking groups followed by colorectal and endometrial cancer. Persistent smokers were more likely to have localized cancer compared to former smokers. Most participants received surgical treatment for their cancers; however, the proportion was lowest among persistent smokers. No difference was found in education level, general health perception at baseline, or survival since cancer diagnosis among the three groups.

QOL

The QOL of non-smokers was comparable to or slightly higher than that of former and persistent smokers as assessed by age-adjusted mean scores for each SF-36 QOL scale (Figure 1). Non-smokers had higher mean scores than former smokers for the Vitality, Physical Functioning, Mental Health, Social Functioning, and General Health scales, while they had higher mean scores than persistent smokers for the Physical Functioning, Mental Health, Role Emotional, and Social Functioning scales. Mean scores did not differ statistically between former and persistent smokers on any SF-36 scale.

Non-smokers were least likely to have poor QOL followed by former smokers and persistent smokers for six of the eight SF-36 scales (Table 3). Only General Health and Role Physical did not correspond to this pattern by smoking status. Compared to non-smokers, persistent smokers were at increased risk of poor QOL in Physical Functioning, Mental Health, and Role Emotional whereas former smokers were at increased risk in Physical Functioning, Mental Health, and General Health. A statistically significant trend toward higher likelihood of poor QOL was observed across smoking groups in Vitality, Physical Functioning, Mental Health, and Role Emotional. Further adjustment for physical activity resulted in considerable attenuation of the odds ratios and p-values for trend.

DISCUSSION

Among postmenopausal women who developed non-smoking related cancers of breast, colorectal and endometrial origin while participating in a prospective cohort since 1986 the present study found that persistent or former smokers were more likely to have poor QOL after cancer diagnosis. These results are consistent with studies in the general population⁷⁻¹⁰ and studies in survivors of smoking-related cancers.³⁻⁶ In the general population, current smokers were twice as likely to report poor physical and mental health compared to non-smokers⁹, and former smokers scored lower than non-smokers in Physical Functioning and General Health.¹⁰ In a study of head and neck cancer survivors, persistent smokers had poorer role function and cognitive function compared to never smokers, while former smokers scored between never smokers and current smokers.⁵

The beneficial effect of smoking cessation on QOL has been shown in the general population⁸ as well as in head and neck cancer patients.⁴ Although comparisons between smoking groups did not always yield statistically significant differences in QOL in the present study, a significant trend toward worse QOL was observed for former and persistent smokers compared to non-smokers. That former smokers had somewhat better QOL than persistent smokers suggests that smoking cessation could improve QOL among survivors of non-smoking related cancers. The lack of a statistically significant difference in QOL scores between former and persistent smokers could be due to the relatively small number of subjects. Another explanation is that former smokers may have quit smoking after development of an illness, such as heart attack or stroke, which in turn lowered their QOL scores, thereby leading to an underestimation of the difference in QOL between former and persistent smokers.

The likelihood of poor QOL in former and persistent smokers relative to non-smokers may have been underestimated for two reasons. First, eligible respondents were more likely to be never smokers than deceased participants or non-respondents to the 2004 questionnaire. Because these latter two groups were excluded from the analysis, survivorship bias could have affected the results if, as seems highly possible, eligible respondents who smoked and survived to complete the 2004 questionnaire were healthier and as a consequence reported better QOL than women excluded from the analysis. This conclusion is supported by the lower proportion of women with more than three comorbid conditions among persistent smokers compared to non-smokers. Second, approximately 23% of women classified as non-smokers at baseline had smoked prior to study entry. These women may have quit smoking due to health conditions that could contribute to poorer QOL. In addition, women were classified as former smokers without regard to the time they last smoked. Although smoking status was assessed at each follow-up, this information represents only an approximation of the length of smoking cessation because the questionnaires were administered infrequently, at irregular intervals, and did not record the date last smoked.

Physical activity is usually not taken into account in studies evaluating the impact of smoking on QOL. In this study, adjustment for physical activity greatly attenuated the difference in QOL among smoking groups relative to non-smokers. This finding suggests that low physical activity among persistent and former smokers was one of the main reasons for poor QOL. A recent systematic review on smoking and physical activity showed that 60% of studies reported physical activity to be less likely among smokers relative to non-smokers.¹⁷ The most common explanation for this inverse relationship is that positive or negative behaviors tend to cluster together, thus, smokers were more likely to engage in risky behaviors.¹⁸ This clustering has also been observed among cancer survivors.¹⁹ Another possibility is that the ability to engage in physical activity may be impaired by reduced physical capacities in smokers, especially with respect to pulmonary function.²⁰ An alternative explanation can be found in what is known about the relationship between physical activity, depression and smoking. Physical activity and depression have been inversely associated in some studies, potentially because physical activity increases the release of norepinephrine, which in turn is associated with decreased rates of depression.^{21–22} In contrast, smoking and depression are often found to be positively related.²³ Therefore, it is possible that lower levels of physical activity may lead to increased levels of depression and, consequently, smoking.²⁴ However, since previous studies show a positive association between physical activity and QOL among cancer survivors¹⁹ and even in elderly populations,²⁵ it seems more plausible that physical activity is in the causal pathway leading to poor QOL among smokers.

Our study has several limitations. Despite the opportunity to prospectively identify cancer cases and smoking status, we collected QOL data at only one point in time. Although QOL can change during the course of cancer survivorship,²⁶ the mean time since diagnosis was similar across smoking groups, suggesting that QOL was not affected by variation in the acute or long-term effects of a cancer diagnosis in the study population. Second, QOL and lifestyle factors were collected with the self-administered questionnaires which may subject to positivity bias. Another limitation of the study is that the amount of smoking was not assessed. Thus, the possibility that persistent smokers were among the lightest or heaviest

smokers in the cohort cannot be excluded. The former is more likely as evidenced by the lower prevalence of comorbid conditions among persistent smokers. However, important comorbidity data was also missing, especially data on the incidence of chronic obstructive pulmonary disease, emphysema, and depression. Thus, some differences in QOL by smoking status could be due to the presence of unaccounted comorbid conditions. Finally, the reason for and timing of smoking cessation was not available.

In conclusion, this study found that postmenopausal women with non-smoking related cancers reported poorer QOL if they were persistent or former smokers than if they had never smoked during the observation period. Indeed, the trend toward worse QOL with increasing level of active smoking suggests that continued smoking after cancer diagnosis may lead to poorer QOL in survivors of non-smoking related cancers. Also we found that physical activity may be the mechanism by which smoking leads to poorer QOL among smokers. Knowing this, oncologists may consider a cancer diagnosis to be a teachable moment for promoting health behavior change.^{27–29}

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Figure 1. Age-adjusted SF-36 scores according to smoking status

* p<0.05 compared to non-smokers

Abbreviations: SF-36, Medical Outcomes Study Short Form-36; Phys, Physical; func, functioning; Hlth, Health; Emot, Emotional; Soc, Social; Gen, General

Table 1

Selected characteristics of women diagnosed with breast, colorectal or endometrial cancer in the Iowa Women's Health Study according to response to the 2004 follow-up questionnaire

	At 2004 follow-up					
	Deceased Participants (n=1,389)		Non-respondents ¹ (n=1,019)		Eligible Respondents (n=1,920)	
	n	%	n	%	n	%
Baseline characteristics, 1986						
Age 65 years	595	42.8	334	32.8	410	21.4
Post secondary education	519	37.5	376	37.0	851	44.4
General health, excellent	253	18.5	237	23.6	566	29.8
Body mass index 30kg/m ²	458	33.0	286	28.1	494	25.7
Cigarette smoking, never	863	63.2	648	65.9	1333	69.4
Physical activity, low	719	52.8	450	45.6	888	46.8
Diabetes	162	11.7	48	4.7	73	3.8
Hypertension	606	43.6	405	39.7	679	35.4
Heart disease	63	4.5	22	2.2	34	1.8
Heart attack	151	10.9	75	7.4	122	6.4
Fracture	189	13.6	142	13.9	234	12.2
Comorbidity index ² 2	272	19.6	134	13.2	212	11.0
Cancer characteristics, 1986–2004						
Type of Cancer						
Breast	669	48.2	651	63.9	1216	63.3
Colorectal	544	39.2	248	24.3	464	24.2
Endometrial	176	12.7	120	11.8	240	12.5
Stage at diagnosis						
In situ	64	4.7	102	10.1	234	12.3
Local	550	40.5	663	65.9	1250	65.7
Regional	463	34.1	230	22.9	403	21.2
Distant	280	20.6	11	1.1	16	0.8
Cancer Therapy Received						

	At 2004 follow-up					
	Deceased Participants (n=1,389)		Non-respondents ¹ (n=1,019)		Eligible Respondents (n=1,920)	
	n	%	n	%	n	%
Surgery	1272	91.6	995	97.6	1907	99.3
Chemotherapy	335	24.1	168	16.5	347	18.1
Radiation therapy	281	20.2	246	24.1	448	23.3

¹ Twenty nine ineligible respondents were excluded because smoking data was not available (n=21) or the women did not smoke in 1986 but did in 2004 (n=8).

² Comorbidity index is the sum of self-reported illness including diabetes, hypertension, heart disease, heart attack, and fracture.

Table 2

Selected characteristics of women with breast, colorectal or endometrial cancer by smoking status, Iowa Women's Health Study

Characteristics	% of Women			P-value
	Non-smokers (n=1,720)	Former smokers (n=141)	Persistent smokers (n=59)	
Age at baseline, years				<0.05 [†]
Mean	61.2	59.9	59.7	
SE	0.1	0.3	0.5	
Post secondary education, %	44.8	41.1	39.0	0.82
General health in 1986, % Excellent	29.6	35.0	23.7	0.27
BMI 30kg/m ² , %				
Baseline,	26.9	12.2	15.6	<0.05
2004	26.4	29.0	7.0	<0.05
% Low physical activity				
Baseline	45.0	59.3	67.8	<0.05
2004	50.5	64.3	71.9	<0.05
3+ comorbid conditions, %	32.5	32.6	27.2	0.72
Type of comorbidity, %				
Diabetes mellitus	17.3	15.6	8.5	0.19
Hypertension	66.0	56.0	69.5	0.05
Heart disease	27.2	33.3	20.3	0.13
Stroke	6.6	9.2	15.3	<0.05
Fracture	39.1	38.3	28.8	0.64
Cancer type, %				0.40
Breast	63.1	66.0	64.4	
Colorectal	24.4	24.1	16.9	
Endometrial	12.5	9.9	18.7	
Years since cancer diagnosis				NS
Mean	8.4	8.2	8.3	
SE	0.1	0.4	0.7	
Cancer stage, %				<0.05
In situ	12.8	8.6	5.3	
Local	65.1	67.3	79.0	
Regional/Distant	22.0	23.7	15.8	
Cancer treatment, %				
Surgery	99.5	97.9	96.6	<0.05
Radiation treatment	23.5	23.4	18.6	0.69
Chemotherapy	18.4	17.0	11.9	0.42

SE=standard error; NS=not significant

[†] between non-smokers and former smokers as well as non-smokers and persistent smokers

Table 3

Odds ratios of poor QOL^{*} according to smoking status among women with breast, colorectal, or endometrial cancer, Iowa Women's Health Study

SF-36 scales	Non-smokers (n=1,720)			Former smokers (n=141)			Persistent smokers (n=59)			
	% ¹	Ref		% ¹	OR ²	95% CI	% ¹	OR ²	95% CI	P-value ³
Vitality	27.3	1.0		31.9	1.32	0.89–1.96	33.9	1.72	0.94–3.15	0.03
PA adjusted		1.0			1.14	0.76–1.71		1.21	0.64–2.28	0.42
Physical Functioning	29.6	1.0		35.5	1.65	1.10–2.45	39.0	2.40	1.32–4.37	0.0003
PA adjusted		1.0			1.38	0.91–2.09		1.45	0.76–2.75	0.08
Role Physical	47.4	1.0		49.7	1.29	0.89–1.86	45.8	1.21	0.68–2.15	0.20
PA adjusted		1.0			1.12	0.77–1.65		0.82	0.45–1.50	0.89
Mental Health	24.8	1.0		34.0	1.62	1.11–2.37	40.7	1.92	1.09–3.40	0.002
PA adjusted		1.0			1.47	1.00–2.16		1.36	0.74–2.47	0.06
Role Emotional	24.2	1.0		27.7	1.34	0.89–2.01	35.6	2.01	1.10–3.66	0.01
PA adjusted		1.0			1.19	0.78–1.80		1.35	0.72–2.55	0.24
Social Functioning	26.1	1.0		29.1	1.27	0.85–1.89	33.9	1.62	0.89–2.95	0.06
PA adjusted		1.0			1.11	0.73–1.67		1.05	0.55–1.99	0.69
Bodily Pain	30.4	1.0		33.3	1.21	0.82–1.79	37.3	1.60	0.89–2.87	0.07
PA adjusted		1.0			1.06	0.71–1.58		1.16	0.63–2.14	0.59
General Health	29.7	1.0		39.0	1.51	1.03–2.21	33.9	1.13	0.62–2.09	0.12
PA adjusted		1.0			1.32	0.89–1.95		0.76	0.40–1.45	0.88

PA=physical activity; OR=odds ratio; CI= confidence interval

^{*} Poor QOL defined as women with QOL scores $\frac{1}{2}$ SD below the mean for women in the non-smoking group.

¹ proportion of women who had poor QOL

² All odds ratios, 95% confidence intervals, and p-values for trend adjusted for age, stage of cancer, number of comorbid conditions and BMI (2004); estimates also adjusted for physical activity (2004) as indicated.

³ p-values for trend comparing former and persistent smokers to non-smokers