A prospective study of job strain and risk of breast cancer

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A prospective study of job strain and risk of breast cancer

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Background There is conflicting evidence on whether stress is a risk factor for breast cancer. The present study examined prospectively the relationship between stress at work and risk of breast cancer.

Methods Participants comprised 26 936 postmenopausal women in the Nurses' Health Study ages 46–72 who were in paid employment, and who had no previous history of cancer. Multivariate-adjusted regression analysis was used to examine the relationship between job strain (measured by the Karasek Job Content Questionnaire in 1992) and risk of incident invasive and *in situ* breast cancer.

Results From 1992 through 1994, 219 women were diagnosed with breast cancer. No evidence was found for a relationship between job stress and risk of breast cancer. Compared with women in low strain jobs, the multivariate-adjusted relative risks of breast cancer were RR = 0.78 (95% CI : 0.52–1.16) for high-strain jobs; RR = 0.76 (95% CI : 0.49–1.17) for active jobs; and RR = 0.94 (95% CI : 0.67–1.34) for passive jobs. Although job strain was related to less breast cancer screening among women in highly demanding jobs, it was not associated with tumour size.

Conclusions Job stress was not related to an increase in the incidence of breast cancer in the present cohort of nurses.

Keywords Breast cancer, stress, work

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Breast cancer incidence has been rising in most developed countries.[1–3] These trends are contemporaneous with the growing participation of women in the labour force. Although several studies have examined the relationship between stress and breast cancer, few have reported on the relation between work stress and risk of breast cancer.

Evidence on the relationship between stress and breast cancer has been conflicting.[4–6] Most of the early studies were retrospective, raising the possibility of recall bias. More recent studies of breast cancer have attempted to measure stress immediately before a biopsy procedure.[7–9] Although such designs may be preferred to a retrospective approach, it is possible that the measured level of stress of patients who are interviewed immediately before a breast biopsy would be considerably biased by the stress from the impending procedure.

Findings from studies on stress and breast cancer have ranged from no association,[4,7,10] an inverse association,[11] to a positive association.[12] Greer and Morris[13] reported an association between suppressed anger and breast cancer diagnosis, while Schonfield[14] found greater life change scores among women with benign tumours compared to those with malignant tumours. These data taken together are at best inconclusive. In addition to inappropriate designs and methodological flaws as discussed by Fox;[15,16] the inherent complexities of measuring stress also present a major challenge.[17] Nonetheless, persistent reports of the link between perceived stress and breast cancer[6,8,9,18–21] suggest the value of conducting well-designed studies in this area.

Given the remarkable secular trends in women's participation in the workforce, a potentially important source of stress in women's daily lives is job strain. The Job Content Questionnaire developed by Karasek[22] is a widely used, self-reported measure of job stress that has been found to predict health outcomes ranging from diminished functional status to cardiovascular disease.[23–27] The present study examined the relationship between job strain, defined by the individual's evaluation of her job characteristics, and the incidence of invasive or *in situ* breast cancer. The data come from a large prospective study of working women.

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Materials and Methodology

Study population

The Nurses' Health Study began in 1976 when 121 700 US female registered nurses, age 30–55 years, were identified from the 1972 files of state boards of nursing and the American Nurses Association. Nurses completed a mailed questionnaire on known or suspected risk factors for cancer and coronary heart disease.[28,29] The population is followed every 2 years with a mailed questionnaire that updates information on exposures and health outcomes.

Population for analysis

A total of 75 453 women responded to a single mailing of the 1992 questionnaire (69% response) that included the Karasek Job Content Questionnaire. Of these, 10 824 women were premenopausal and a further 23 309 women did not provide responses to the Karasek Job Content Questionnaire as they were no longer in paid employment. We excluded from the analyses all women who had reported breast cancer or other cancer on any questionnaire up to 1992 (n = 3137). A further 11 247 women were excluded because of missing information on key covariates, such as body mass index (BMI), age at menarche, and educational attainment. The final study population comprised 26 936 employed women who provided complete information on all covariates of interest. These women were followed as part of the entire Nurses' Health Study cohort through the 1994 questionnaire. For non-respondents to the 1994 questionnaire, we attempted telephone contacts and identified deaths through next-of-kin as well as searches of the National Death Index.

Identification of cases of breast cancer

On each questionnaire, nurses were asked to report any diagnosis of breast cancer and the date of diagnosis. For each case of breast cancer reported, we requested permission to review the relevant hospital records and pathology reports to confirm the diagnosis. Past confirmation checks have revealed extremely high accuracy of self-reported breast cancer in this cohort (over 90%).[30] We therefore based our analysis on newly diagnosed invasive and *in situ* breast cancer cases occurring after the return of the 1992 questionnaire but before 1 June 1994 among postmenopausal women who had not previously reported having cancer.

Measurement of exposure variables

Job Content Questionnaire

Work stress was measured by the Karasek Job Content Questionnaire.[22] It is a self-administered instrument developed from the Quality of Employment Surveys—nationally representative data bases for job characteristics in the US. The 27-item version of the questionnaire measures seven dimensions of work (Appendix 1) and was administered in 1992 to measure job conditions among the study participants.

The instrument measures both the psychological workload ('demands') and the level of 'control' (combined measure of job decision authority and skill discretion) to manage the workload. The Job Content Questionnaire provides four job-strain categories based on combinations of the demand and control dimensions of the job. The demand/control model predicts adverse consequences when high psychological demands are combined with a low level of control over task content (high-strain jobs).

The psychometric properties of the questionnaire have been reported in detail elsewhere.[22] The test-retest reliability using occupation as the unit of analysis provides a correlation above 0.9 for all aspects of the scale including decision latitude, skill discretion, decision authority, psychological demands, and social support. The Cronbach's alpha coefficients (the average internal correlations between the different questions that make up the scales) are reasonably high for these dimensions, ranging from 0.59 for psychological demands to 0.83 for social support. The internal scale reliability of the psychological workload measure based on national data was 0.61 for women in a sample of US occupations. The Job Content Questionnaire also differentiates between occupations according to level of control. The job control dimension correlates well with worker trait data on the Dictionary of Occupational Titles (DOT)[31] and a high degree of correlation has been reported between objective and self-report measures of job control suggesting the convergent validity of the instrument. The psychological job demand scores, although highly reproducible, discriminate less well between occupations. However, low correlations with stress outside the work place suggest that it is unlikely that strain from other spheres of life contributes to the job stress rating.[22] The measure of social support assesses support from both supervisors and co-workers. The total work-based support measure has a reliability of 0.81 for women.[22] The demands and control subscales are split along the median values of responses to create a 2×2 matrix of job conditions. Jobs that are high in demands and low in control ('high strain' jobs) are posited to have the most deleterious health effects.[22] The remaining three categories of jobs defined by the demands/control matrix are: high demands/high control ('active' jobs); low demands/high control ('low strain' jobs);and low demands/low control ('passive' jobs). Following previous research,[23–27] low strain jobs constituted the reference group for comparison against all other job types. An extension of the demands/control matrix further posits that jobs characterized by high demands, low control, and low social support at work ('iso-strain' jobs) are associated with poor health outcomes.[32] McAbee[33] also identified organizational social support as a buffering agent against occupational stress and burnout.

Other covariates

Age, alcohol consumption (ethanol g/week), physical activity, and BMI (kg/m^2) were included as continuous variables. Mailed, self-administered questionnaires to measure alcohol consumption are reproducible, valid and have a 0.84 correlation with diet records.[34] Recreational physical activity, obtained from the 1992 questionnaire, was assessed from a highly reproducible, validated questionnaire[35] that asked about the frequency of women's engagement in eight common activities during the past year. The score is measured in metabolic-equivalent hours (MET-hours) per week. One MET-hour is equivalent to the energy expenditure during one hour of rest. For example, walking at an average pace for one hour is estimated to consume about 3.0 MET units, while jogging or bicycling is estimated to consume about 7.0 MET units. Family history of breast cancer and personal history of benign breast disease were analysed as dichotomous variables (yes/no).

Postmenopausal hormone use was categorized as never user of postmenopausal hormone, past user, and current user. Other categorical variables included age at menarche (at 8–11 years, 12, 13, 14, and 15–21 years); type of menopause (natural, or surgical—further categorized as both ovaries removed, one ovary removed, or neither ovary removed); a combined variable for parity and age at first birth (nulliparous, 1–2 births *and* age at first birth <25 years, 1–2 births *and* age at first birth 25–34 years, 1–2 births *and* age at first birth >35 years, 3+ births *and* age at first birth <25 years… 3+ births *and* age at first birth >35 years); and age at menopause (<47 years, 47–50, ⩾51).

Additionally, we controlled for the women's educational attainment (registered nursing degree only, bachelors degree, masters degree, doctoral degree), as well as their occupational type (inpatient/emergency room nurse, outpatient nurse, operating room nurse, nurse education, nurse administrator, multiple nursing occupations, other nursing type, and non-nursing occupation).

Statistical analysis

The main outcome, invasive or *in situ* breast cancer, were incident cases of cancer occurring between 1992 and 1994. The main independent variable was the four types of job conditions, which were entered as dummy variables with the 'low strain' category as the reference. The following additional independent variables were included as covariates in the analyses: age; behavioural factors (alcohol consumption, exercise level, postmenopausal hormone use, and BMI); biological factors (family history of breast cancer, age at menarche, personal history of benign breast disease, parity and age at first birth, type of menopause, and age at menopause); and socioeconomic factors (educational attainment and nursing occupation type). To address issues of stress outside the work environment, we ran separate analyses including a variable for the amount of stress involved in providing care to sick or elderly relatives.

We repeated all the analyses restricting the case set to 182 women with invasive breast cancer to determine whether job strain was associated with a more advanced stage of disease. We also examined whether there was a relationship between level of stress and stage at diagnosis as determined by the presence of positive lymph nodes (yes/no) and the size of the tumour (⩽2 cm versus ⩾2.1 cm).

Finally, we examined the potential influence of social integration on the relationship between job strain and breast cancer by including in the final model a measure of (a) work support, and (b) social networks.[36] The presence or absence of worksite support was incorporated into the existing demand-control job type matrix, replacing the previous four categories with eight.

Results

During the 2-year follow-up we identified 219 cases of invasive and *in situ* breast cancer among women who had been employed within the last 2 years. Approximately one-quarter of our total sample of employed women (n = 6535) reported being in high-strain jobs characterized by high demand and low control. One-third reported being in jobs that were low in demand and also low in control (passive work) (n = 9494), and approximately two-fifths of all women were in each of the other two types of jobs (low strain, and active work) (Table 1). Women in jobs with a high level of control (active jobs and low strain jobs) had higher educational attainment compared to women in jobs with low levels of control (high strain and passive jobs). Women in active and high strain jobs were more likely to be working as inpatient, emergency room, and operating room nurses, whereas women in low strain jobs were more likely to be working as nurse educators, administrators and outpatient nurses. Few other differences were apparent, other than the following: women in low strain and active jobs engaged in more physical activity compared to women in high strain and passive jobs. Women in active and passive jobs reported higher alcohol intake compared to women in low strain and high strain jobs (Table 1).

Compared with the risk for women in low strain jobs, the age-adjusted relative risk (RR) of breast cancer was not elevated for women in high strain jobs (RR = 0.78, 95% CI : 0.52–1.16), or for the other two job categories (Table 2). After adjustment for a range of potential confounding variables, the RR remained virtually unchanged. Restricting the analyses to women with invasive breast cancer (n = 182) did not alter the lack of association between job strain and this disease. Compared with women in low strain jobs, women in high strain jobs were not at increased risk of invasive breast cancer (RR = 0.71, 95% CI : 0.45–1.12). We repeated the multivariate analyses by adding a variable for stress in the home environment, as assessed by responses to an item on the 1992 questionnaire: 'How stressful would you say it is to provide regular care to: your children, grandchildren, disabled or ill spouse, or disabled or ill parent?' Responses included: not applicable, not at all, a little bit, moderately, and extremely. There was no association between home stress and the risk of breast cancer (e.g. multivariate RR = 0.99, 95% CI : 0.52–1.91 comparing women reporting extreme caregiving stress to no stress). Nor did control for stress in the home environment affect the null association between job conditions and breast cancer risk (multivariate RR for high strain job = 0.81, 95% CI : 0.53–1.22).

We next examined the possible influence of stage of disease in the relationship between job strain and breast cancer by examining the relationships between strain and the incidence of breast cancer (1) with positive node, (2) with negative node, (3) with tumour size ⩽2 cm, and (4) with tumour size >2 cm. Among the 219 women diagnosed with breast cancer, 55 had medical records confirming the spread of tumour to lymph nodes at the time of diagnosis. Compared with women in low strain jobs, women in other job types did not have an increased age-adjusted RR for node positive breast cancer, although the 95% CI were wide due to the small number of cases. After inclusion of all other covariates in the model, the RR remained virtually unchanged. The risk of breast cancer for women in high strain jobs compared to low strain jobs was 0.83 (95% CI : 0.54–1.27). Analyses were also performed stratified by tumour size at diagnosis (<2 cm, or ⩾2 cm). Irrespective of tumour size, there was again no significant increase in the RR for breast cancer among women in any of the job types.

Finally, we examined the influence of two measures of social support on the relationship between job strain and the incidence of breast cancer in two settings—social support in the work place as well as in other domains of life. Using the high control/low demand/high support job type as the reference

Table 1 Age-adjusted distributions of behavioural and biological factors according to Karasek's job characteristics among 26 936 women working in 1992, Nurses' Health Study

Subject characteristics Job type	Low demand/ high control (Low strain)	Low demand/ low control (Passive)	High demand/ low control (High strain)	High demand/ high control (Active)
No. of subjects	5538	9494	6535	5369
(Percentage)	(20.6%)	(35.2%)	(24.3%)	(19.9%)
Family history of breast cancer (%)	10.5	11.4	11.3	11.1
Menarche (<age 13 years, %)	48.5	50.4	50.4	48.9
Benign breast disease (%)	44.8	44.9	46.9	47.8
Natural type of menopause (%)	59.4	60.8	58.1	58.3
Nulliparous (%)	6.3	6.6	6.7	6.7
Parous and age at first birth <25 years (%)	56.7	55.9	55.6	57.0
Parous and age at first birth 25–29 years (%)	29.8	29.9	30.5	28.9
Parous and age at first birth 30–34 years (%)	5.9	6.3	5.6	5.8
Parous and age at first birth 35+ years (%)	1.3	1.5	1.8	1.4
Mean physical activity (MET[a]hours/wk)	19.3	17.4	17.9	20.6
Mean alcohol intake (g/wk)	30.5	33.5	30.8	35.6
⩾51 years at menopause (%)	28.3	28.4	27.1	27.7
Current use of post-menopausal hormones (%)	47.5	44.7	47.7	47.8
Mean body mass index (kg/m^2)	26.3	26.2	26.2	26.1
Educational attainment				
Registered nurse (%)	54.0	72.3	73.9	56.8
Bachelors degree (%)	25.8	20.1	19.0	24.0
Masters degree (%)	17.9	7.1	6.5	16.4
Doctoral degree (%)	2.2	0.5	0.6	2.8
Nursing occupation type				
Inpatient/emergency room (%)	5.8	8.9	19.0	11.6
Operating room (%)	1.2	1.7	5.1	3.4
Outpatient (%)	11.1	9.8	7.9	7.9
Nursing education (%)	7.4	2.9	2.4	5.8
Nursing administration (%)	11.0	4.7	5.2	15.3
Other nursing type (%)	32.6	41.5	36.5	28.8
Multiple nursing job (%)	3.3	1.7	2.3	4.9
Non-nursing occupation (%)	27.5	28.7	21.6	22.3

[a] MET as defined in text.

category, we found no substantial difference in RR of breast cancer related to any job types. Similar results were obtained from an examination of the social networks in domains outside of work, where the RR of breast cancer associated with job types remained virtually unchanged after we included social networks in the model. In addition, level of social integration was itself unrelated to risk of breast cancer.

Discussion

In this 2-year prospective study we found no association between job stress as measured by the Job Content Questionnaire and incidence of invasive or *in situ* breast cancer. No specific job type was associated with increased risk of breast cancer. Previous studies have suggested that high strain jobs are associated with deleterious health consequences, including cardiovascular disease.[23–27] To the extent that job strain can be considered a form of stress, the present results do not lend support to the notion that breast cancer is caused by stress. The upper bounds of the CI for the observed multivariate-adjusted RR for job types do not exceed 1.36, ruling out a substantial association between job strain and breast cancer.

In a recent commentary, Burke and Goodkin[17] listed what they considered to be important elements of a fair test to examine the role of life stresses in the development of cancer. They identified the importance of: a prospective study design; an examination of one specific cancer; the study of psychosocial risk factors that have been shown to be relevant to the aetiology of the particular type of cancer; and the consideration of the interaction between the environmental stressors and the individual's responses. Hilakivi-Clarke *et al.*[18] in an earlier review of the role of lifestyle factors in the onset and progression of breast cancer, also stressed the importance of examining the interaction among stress, personality, and availability of psychosocial support.

The present study prospectively examined the incidence of breast cancer in relation to women's reports of their work environment, using a well-established measure of job strain.

Table 2 Relative risks (RR) and 95% CI regressions for job strain groups and (a) *in situ* and invasive breast cancer and (b) invasive among employed women, 1992–1994

	Invasive and *in situ*				**Invasive**		
Job strain groups	Cases	Non-cases	Age-adjusted RR (95% CI)	Multivariate RR* (95% CI)	Cases	Non-cases	Multivariate RR* (95% CI)
Low demand/high control (Low strain)	48	5489	1.00	1.00	43	5485	1.00
Low demand/low control (Passive)	83	9411	0.94	0.98	69	9403	0.91
			(0.67–1.34)	(0.68–1.40)			(0.62–1.34)
High demand/high control (Active)	39	5331	0.76	0.78	30	5327	0.72
			(0.49–1.17)	(0.51–1.20)			(0.45–1.15)
High demand/low control (High strain)	49	6486	0.78	0.81	40	6481	0.71
			(0.52–1.16)	(0.54–1.22)			(0.45–1.12)
Total cases and non-cases	219	26 717			182	26 696	

[a] Adjusted for age, family history of breast cancer, age at menarche (at 8–11 years, 12, 13, 14, or 15–21 years); type of menopause (natural, or surgical—further categorized as both ovaries removed, one ovary removed, or neither ovary removed); a combined variable for parity and age at first birth (nulliparous, 1–2 births *and* age at first birth <25 years, 1–2 births *and* age at first birth 25–34 years, 1–2 births *and* age at first birth >35 years, 3+ births *and* age at first birth <25 years… 3+ births *and* age at first birth >35 years); age at menopause (<47 years, 47–50, ⩾51); personal history of benign breast disease; physical activity (MET-hours per week); post-menopausal hormone use (current user of hormones, past user, never user); body mass index; educational attainment (registered nurse, bachelors, masters, doctoral degree); and type of nursing occupation (inpatient/emergency room, operating room, outpatient, nursing education, administration, multiple jobs, other nursing type, non-nursing occupation).

Our lack of information on personality factors prevented us from examining interactions between stress and personality. In addition to personality, the potential detrimental effects of stress can be mediated or buffered by the availability of social support. When we examined the influence of social support in the work place as well as the women's overall social network, however, we found no evidence of either a main effect of social ties on breast cancer risk, or a buffering effect of social ties on the effects of job stress.

The lack of an association between job strain and breast cancer may be related to the type of stress investigated or to additional factors unique to this cohort. With regard to the latter, our null findings may be reflective of insufficient heterogeneity within each of the demand/control quadrants despite the overall distribution among the quadrants. Although job conditions were distributed in predictable ways among nursing occupational types (e.g. the highest prevalence of high strain conditions among inpatient, emergency room, and operating room nurses), we lacked information on the specific nursing-related jobs for 30 to 40% of the cohort.

We were concerned that the lack of a relationship between job strain and breast cancer may reflect an association between job type and screening behaviour, of which the latter is related to the incidence of breast cancer. Of the women who were employed between 1990 and 1992, the number of women screened was 7787 (72.1%) in the passive job group, 4653 (73.9%) in the low strain job, 5336 (71.8%) in the high strain job, and 4456 (73.0%) in the active job group. Compared with women in low strain jobs, women in high demand jobs, regardless of the level of control, were less likely to be screened between 1992 and 1994 (high demand/high control OR = 0.90, 95% CI : 0.83–0.98; high demand/low control job OR = 0.88, 95% CI : 0.82–0.96). It seems plausible that a demanding job minimizes time and other resources necessary for preventive activities. Despite this apparent lower rate of screening among women in jobs high in demand, we did not observe any relation between job strain and diagnosis of larger tumours.

The validity of these null findings depends in part on the possible pathways between stressor and breast cancer as well as the length of the latent period—the interval from induction to clinical detection, which has been hypothesized to be ⩾5 years.[37,38] A long latent period would suggest that job strain occurring during the previous 2 to 3 years might not predict incidence. A limitation of this study is that we did not collect information on the duration of employment under different job conditions. On the other hand, job conditions assessed in this cohort in 1992 and 1996 demonstrate a moderate degree of stability, with correlation coefficients for job control and job demands of 0.60 and 0.54, respectively.

Conclusion

On the basis of a prospective 2-year study, using a well-documented measure of job-related stress, we found no evidence for an increased risk of breast cancer related to job strain. Job strain is an important component of the larger psychosocial environment experienced by working women. Further studies are needed to examine other specific work-site factors with longer duration of follow-up, as well as the interaction between personality and the home and work environments that may modify the individual's experience of stress, and hence, their risk of disease.

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Appendix

The seven dimensions of work from the Job Content Questionnaire

1. Psychological workload (five items: working fast, working very hard, excessive amount of work, enough time to get the job done, free from competing demands)
2. Job decision authority (three items: make decisions on my own, very little freedom to decide how to do work, a lot of say on what happens on job)
3. Skill discretion (six items: learn new things, repetitive work, creative, high level of skill, do a variety of different things on the job, opportunity to develop own special abilities)
4. Supervisor support (four items: supervisor is concerned about welfare, pays attention, helpful, gets people to work together)
5. Co-worker support (four items: competent co-workers, take a personal interest, friendly, helpful)
6. Job security (three items: security good, work steady, likelihood lose job in next 2 years)
7. Physical exertion (one item: lots of physical effort)