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Job Strain and the Risk of Breast Cancer: A Nested Case-Control Study within the CARTaGENE Cohort

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Abstract

Background

Breast cancer is the most commonly diagnosed cancer among Canadian women. Although some occupational exposures have been associated with breast cancer risk, the role of psychosocial factors such as job strain remains unclear. We examined the association between job strain and breast cancer risk among women in Quebec.

Methods

A case-control study was nested within the CARTaGENE cohort, including 196 incident breast cancer cases diagnosed between 2009 and 2020 and 784 age-matched controls. Baseline job strain was assessed using an adapted 15-item Job Content Questionnaire covering psychological demands, decision latitude, and workplace social support. Job strain was defined using the quadrant-based approach by dichotomizing psychological demand and decision latitude scores at the median, producing four categories: job strain (high demand, low control), low strain (reference), active (high demand, high control), and passive (low demand, low control). Conditional logistic regression estimated incidence rate ratios (IRR) and 95% confidence intervals (95% CI).

Results

Compared with the low-strain category, job strain was inversely associated with breast cancer risk (IRR = 0.61; 95% CI 0.36–0.99), while the active (IRR = 0.83; 95% CI 0.54–1.25) and passive (IRR = 0.69; 95% CI 0.45–1.03) categories were not statistically significant. Comparing job strain with combined non-exposed categories, showed association (IRR = 0.73; 95% CI 0.46–1.11). No differences were observed across strata defined by education level. However, job strain was positively associated with breast cancer among women in the lowest income group (IRR = 2.37; 95% CI 1.15–4.86).

Conclusion

Our findings provide no substantial evidence that job strain is a risk factor for breast cancer over a 10-year follow-up period, although socioeconomic position may influence the association.

Background

Breast cancer is the second most common cancer worldwide, with a higher incidence rate found in high-income countries (1). In Canada, breast cancer is the most frequently diagnosed cancer among females (2), constituting over 13% of women's cancer-related deaths and thus, the second leading cause of cancer mortality across all age groups, following lung cancer (3). Although incidence and mortality rates have declined over recent decades, demographic aging and population growth continue to increase the absolute number of breast cancer diagnoses (3–5). Identifying modifiable risk factors therefore remains essential for informing primary prevention strategies.

Given the substantial time that individuals spend at work, occupational environments represent a meaningful context for potential carcinogenic exposures. While the health effects of physical and chemical hazards, such as radiation or industrial chemicals, have been investigated extensively, considerably less attention has been given to the psychosocial aspect of working conditions. Work-related stress is increasingly recognized as a relevant exposure, supported by growing evidence on the biological pathways activated during chronic stress, including neuroendocrine and immune responses that may influence long-term health outcomes (6,7).

One of the most widely used conceptual frameworks for characterizing psychosocial stressors at work is Karasek's job strain model (8). The model conceptualizes job strain as the combination of high psychological demands and low decision latitude, typically assessed with the Job Content Questionnaire (JCQ) (9–11). Job strain has been associated with several chronic conditions, including cardiovascular disease (12) and type 2 diabetes (13), but its role in cancer etiology remains uncertain.

Evidence regarding job strain and breast cancer specifically is limited and inconsistent. In a Swedish cohort of 36,332 women aged 30–50 years, Kuper et al. (14) reported that women exposed to job strain had an increased risk of breast cancer compared with those in low-strain jobs (HR = 1.40; 95% CI: 1.10–1.90) (14). In contrast, analyses from the Nurses' Health Study in the United States found no statistically significant association between job strain and breast cancer compared to low-strain jobs, including a study of 26,936 postmenopausal women aged 46–72 years (RR = 0.78; 95% CI: 0.52–1.16), and a study of 37,562 female registered nurses aged 30–55 years (RR = 0.87; 95% CI: 0.76–1.06) (15,16). Similarly, a meta-analysis of 12 European cohorts including 116,056 men and women aged 17–70 years and 5,765 incident cancer cases reported no association between job strain and overall cancer (HR = 0.97; 95% CI: 0.90–1.04) and breast cancer risk (HR = 0.97; 95% CI: 0.82–1.14) (17). These discrepancies may reflect differences in study design, exposure assessment, follow-up duration, and population characteristics.

To date, the association between job strain and breast cancer has not been examined in a Canadian population. Given differences in labor market structures, occupational distributions, and social policies across countries, evaluating this relationship within a Canadian cohort may provide additional insight. In this study, we investigated whether job strain, assessed at baseline using the JCQ, was associated with incident breast cancer among women aged 40–69 years residing in metropolitan regions of Quebec, Canada.

Methods

Study Population

The CARTaGENE (CaG) cohort is the largest ongoing prospective cohort with a biobank in Quebec, Canada (18). Between 2009 and 2010, CaG carried out its initial recruitment wave (Phase A), enrolling approximately 20,000 adults aged 40–69 years from Montreal, Quebec City, Sherbrooke, and Saguenay through stratified random sampling from provincial health insurance registries (18). At baseline, participants completed self-administered questionnaires which collected information on sociodemographic characteristics, lifestyle factors, and occupational information, including the JCQ. Data collection also included an interviewer-administered health questionnaire, standardized physical measurements, and biospecimen collection.

For the present analysis, we conducted a nested case-control study within Phase A of the CaG cohort. Incident breast cancer cases were identified through linkage of CaG participants with the Quebec Cancer Registry and the provincial health insurance administrative database [Régie de l'assurance maladie du Québec (RAMQ)] from cohort entry to 2020. These data sources provide virtually complete coverage of cancer diagnoses and healthcare encounters in the province, supporting near-complete ascertainment of incident breast cancer.

Eligibility Criteria

Among the 19,985 participants in the Phase A of the CaG cohort, all women were considered initially eligible for inclusion (n = 10,304). We first excluded participants with a prevalent cancer diagnosis at baseline, identified either through linkage with the Quebec Cancer Registry and the RAMQ administrative databases (n = 712) or through self-report in the baseline questionnaire (n = 454). Incident breast cancer cases were then identified through linkage with the Quebec Cancer Registry and the RAMQ from baseline until 2020, yielding 329 incident cases.

As job strain could only be assessed among CaG participants who were employed and who completed the JCQ, both cases and potential controls were required to be employed at baseline and to have completed the adapted JCQ. Individuals not meeting these criteria were excluded (n = 119 cases; n = 3,197 potential controls). We further excluded participants who did not answer at least half of the items (≥ 3 of 5) in both the psychological demand and decision latitude scales, consistent with recommended practice for JCQ-based scales (19), resulting in the exclusion of 14 additional cases and 1,217 potential controls. After these exclusions, 196 incident breast cancer cases remained eligible. For the analyses involving the social support scale (referred to as iso-strain, described later in the Exposure Measurement section), breast cancer cases who did not respond to any social support items were further excluded (n = 34). Controls were then selected from the remaining eligible participants using risk-set sampling at a ratio of four controls per case (n = 784 controls for 196 cases), with age matching applied within ± 5 years at the time of sampling (Fig. 1).

Exposure Measurement

The full version of the JCQ is a widely used and validated instrument for assessing psychosocial working conditions and was originally developed with 36 items covering multiple dimensions of the job strain model (10,20). As part of the CaG baseline questionnaire, an abbreviated questionnaire derived from the previously published JCQ was administered to assess job strain(18,21). This version included 15 items covering the three core dimensions of the job strain model: psychological demands (five items), decision latitude (five items, including three items assessing skill discretion and two assessing decision authority), and social support (five items). Psychological demands capture the intensity and pace of work, including workload, time pressure, and conflicting demands. Decision latitude reflects the degree of control workers have over how they perform their tasks and includes two components: skill discretion (opportunities to use and develop skills) and decision authority (freedom to make decisions about work activities). The social support scale, derived in the CaG baseline questionnaire from the previously published JCQ(10,21), measures perceived support from supervisors and coworkers in the workplace.

Each item was rated on a four-point Likert scale ranging from 1 (“strongly disagree”) to 4 (“strongly agree”). Scale (i.e. dimension) scores were computed by summing item responses and applying the weighting scheme proposed by Karasek to approximate the scale range used in the full JCQ (20,22). When participants did not complete all five items within a given scale, the scale score was reweighted proportionally to account for missing items, provided that at least half of the items were answered. After weighting, scale scores ranged from 12 to 48 (23). Previous validation studies of the JCQ have reported Cronbach’s alpha coefficients exceeding 0.65 for these scales, indicating moderate and acceptable internal consistency (24). In the present study, Cronbach’s alpha coefficients were higher than 0.65 for all scales with a coefficient of 0.76 for psychological demand and 0.67 for decision latitude, consistent with these findings.

Job strain can be defined using several approaches, including continuous and categorical representations (25–27). In the continuous approach, sometimes referred to as the quotient approach, job strain is calculated as the ratio of the psychological demand score by the decision latitude score, with higher values reflecting greater imbalance between job demands and job control that a person has. However, the most commonly used method is quadrant-based classification. This approach dichotomizes psychological demand and decision latitude scores at the median value of the study population (24). Cross-classification of these dichotomized scales produces four job types: high demand and low control (job strain), low demand and high control (low strain), high demand and high control (active), and low demand and low control (passive) (Fig. 2).

In the present study, job strain was analyzed using two reference groups. First, participants exposed to job strain were compared with those in the low-strain category, representing the most favorable psychosocial work environment. Second, job strain was compared with a broader non-exposed group combining the low strain, active, and passive categories. Additionally, to capture a higher level of psychosocial stress, we defined iso-strain as the combination of job strain and low workplace social support (i.e., high demand, low control, and low social support). For iso-strain analyses, the reference group included all other combinations of psychological demand, decision latitude, and social support.

Covariables

Potential confounders of the association between job strain and breast cancer were identified based on an extensive literature review and represented in a directed acyclic graph (DAG) (Appendix A). The DAG was used to determine the minimal sufficient adjustment set required to estimate the total effect of job strain on breast cancer. The resulting adjustment set included age, education, ethnicity, physical activity, socioeconomic status (SES), shift work, and occupational exposures. Missing values for all confounding variables were low (< 5% for all variables) and were therefore imputed using the median for continuous variables and the mode for categorical variables (29).

Participants’ highest level of education reported at baseline was categorized into three groups: high school or less, college, and university. In addition, self-reported ethnicity was grouped into six categories: White, Black, Latino, Asian, Arab, and other. Socioeconomic status was approximated using annual household income reported at baseline, which was categorized into three groups: low (≤$49,999), middle ($50,000-$74,999), and high (≥$75,000) (30,31). Physical activity was assessed using questions derived from the International Physical Activity Questionnaire (IPAQ), in which participants reported the number of minutes per

week spent in leisure-time, domestic, and work-related physical activities. These activities were assigned metabolic equivalent task (MET) values (32), and total physical activity was calculated as the sum of MET-hours per week across activities and treated as a continuous variable. Finally, shift work was categorized into three groups: day shifts, night or rotating shifts, and other.

Occupational exposures in the longest-held job held by participants were assessed via linkage with the Canadian Job Exposure Matrix (CANJEM), which provides estimates of exposure to 258 occupational agents (33). CANJEM assigns, for each occupation, a probability of exposure defined as the proportion of workers within that occupation who were exposed to a given agent during a specific time period. We elected to link CANJEM to the longest-held job versus the current job held by participants at baseline as we wanted to capture a more substantial period of occupational exposure over the working life. In contrast, job strain was only assessed using the baseline job reported at cohort enrollment, reflecting the participant's current psychosocial work environment at the time of exposure assessment. Longest-held jobs were coded according to the International Standard Classification of Occupations 1968 (ISCO-68) and linked to CANJEM at the most detailed level available (i.e., 5-digit ISCO) followed by broader resolutions (i.e., 3-digit or 2-digit) when linkage was not feasible. Overall, 80.4% of job codes were linked at the 5-digit ISCO level, while 15.7% and 3.9% were linked at the 3-digit and 2-digit levels, respectively. After linkage, the probability of exposure (0-100%) to all 258 physical and chemical agents for each participant's longest-held job was available. Based on classifications by the International Agency for Research on Cancer (IARC) and previous literature, we identified 43 agents in CANJEM that have been investigated as potential risk factors for breast cancer, including ionizing radiation, ethylene oxide, polychlorinated biphenyls, pesticides, polyaromatic hydrocarbons, organic solvents, cadmium, arsenic, and nickel. Occupational exposure was defined as a binary variable (exposed vs. not exposed) and classified as exposed when the estimated probability of exposure to any of these agents was ≥ 25% (34).

Statistical Analysis

Conditional logistic regression was used to estimate incidence rate ratios (IRR) and 95% confidence intervals (95% CI) for the association between job strain and breast cancer incidence. This approach accounted for the age matching applied during risk-set sampling and robust variance estimates were obtained using a sandwich estimator (35). We first fitted age-adjusted models, followed by minimally adjusted models that included confounders identified from the DAG.

Sensitivity Analysis

Moreover, several sensitivity analyses were conducted to evaluate the robustness of our findings. First, to assess potential non-differential exposure misclassification, we restricted the analysis to participants who answered all five items of the psychological demand and decision latitude scales, excluding individuals with partially completed scales (i.e., three or four responses). Second, given differences in breast cancer etiology and particularly in hormone receptor-positive breast cancer risk between premenopausal and postmenopausal women (36,37), we stratified the association between job strain and breast cancer according to presumed menopausal status at baseline. Presumed premenopausal women were defined as participants who reported being premenopausal at baseline and who were younger than 50 years at the time of case diagnosis or control sampling, based on the assumption that women below this age are unlikely to have reached menopause (38). Third, because job strain may be related to SES through occupational characteristics, we stratified analyses by education level (high school or less, college, university) and household annual income (≤$49,999, $50,000-$74,999, ≥$75,000). Finally, we repeated the main and stratified analyses using two alternative definitions of job strain. First, job strain was modeled as a continuous variable using the ratio of psychological demand to decision latitude (job control) scores, with effect estimates expressed per one-unit increase. Second, job strain was categorized into quartiles based on its distribution in the study population and modeled as a dichotomous variable comparing participants in the highest quartile to those in the lower three quartiles, representing individuals with the greatest imbalance between job demands and job control versus all others.

Results

General Characteristics of the Study Population

A total of 196 incident breast cancer cases in the CaG cohort diagnosed over a 10-year follow-up period were included in our study. The mean age at cancer diagnosis was 55.8 ± 6.1 years. Controls (n = 784), individually matched to cases based on age (± 5 years),

had a mean age of 56.2 ± 6.0 years at the time of sampling. Table 1 presents selected baseline characteristics of the study population. Overall, cases had a slightly higher proportion of individuals with university education and household income ≥ $75,000 compared with controls. Cases were also more likely to have a family history of breast cancer, to have used menopausal hormone therapy (MHT), to report slightly lower levels of physical activity, and to be categorized as obese compared with controls.

Table 1 Selected Characteristics of Participants at Baseline

Characteristics	Controls (n=784)	Cases (n=196)
Numerical Variables (Mean (SD))		
Age (Year)	56.21 (5.98)	55.76 (6.11)
Physical Activity (MET-Hours/Week)	45.90 (42.04)	44.07 (41.60)
Categorical Variables (n (%))		
Ethnicity		
White	700 (89.3)	181 (92.3)
Asian	11 (1.4)	3 (1.5)
Black African	16 (2.0)	2 (1.0)
Arab	17 (2.2)	4 (2.0)
Latino	13 (1.7)	3 (1.5)
Other	11 (1.4)	1 (0.5)
Missing	16 (2.0)	2 (1.0)
Household Annual Income		
$49,999 or less	204 (26.0)	43 (21.9)
$50,000 to $74,999	171 (21.8)	44 (22.4)
$75,000 and up	409 (47.2)	109 (51.0)
Missing	39 (5.0)	9 (4.6)
Education Level		
High School or less	154 (19.6)	41 (20.9)
College	285 (36.4)	57 (29.1)
University	345 (44.0)	66 (50.0)
Family History of Breast Cancer		
Yes	78 (9.9)	29 (14.8)
No	706 (90.1)	167 (85.2)
Menopausal Status at Baseline		
Postmenopausal	335 (42.7)	75 (38.3)
Premenopausal	445 (56.8)	118 (60.3)
Missing	4 (0.5)	3 (1.5)
Ever Use of Menopausal Hormone Therapy		
Yes	147 (18.8)	48 (24.5)
No	636 (81.1)	148 (75.5)
Missing	1 (0.1)	0 (0.0)
Smoking		
Never	335 (42.7)	87 (44.4)

Former Smoker	323 (41.2)	80 (40.8)
Current Smoker	125 (15.9)	29 (14.8)
Missing	1 (0.1)	0 (0.0)
Alcohol Consumption		
Never	51 (6.5)	12 (6.1)
Once a Week or less	543 (69.3)	133 (67.9)
2 to 5 Times per Week	159 (20.3)	45 (23.0)
Almost Every Day	30 (3.8)	6 (3.1)
Missing	1 (0.1)	0 (0.0)
Body Mass Index		
Underweight	8 (1.0)	2 (1.0)
Normal	347 (44.3)	78 (39.8)
Overweight	255 (32.5)	64 (32.7)
Obese	168 (21.4)	52 (26.5)
Missing	6 (0.8)	0 (0.0)
Shift Work		
Day	660 (84.2)	164 (83.7)
Night and Rotating	36 (4.6)	8 (4.1)
Other	86 (10.9)	24 (12.2)
Missing	2 (0.3)	0 (0.0)
Occupational Exposure[a]		
Yes	199 (25.4)	35 (17.9)
No	585 (74.6)	160 (81.6)
Missing	0 (0.0)	1 (0.5)

[a] Including ionizing radiation, ethylene oxide, polychlorinated biphenyls, pesticides, polyaromatic hydrocarbons, organic solvents, and certain metal compounds

The Scores of the JCQ Scales

The distributions of the JCQ subscale scores, stratified by case-control status, are presented in Table 2. The scores ranged from a minimum of 12 to a maximum of 48 for each scale. On average, cases had lower psychological demand scores and higher decision latitude and social support scores compared with controls.

Table 2

Distribution of the Job Content Questionnaire (JCQ) Scales in Case and Control Groups

JCQ Scale	Total Population				Controls				Cases			
	n	Mean	Median	SD	n	Mean	Median	SD	n	Mean	Median	SD
Decision Latitude	980	35.60	36	6.05	784	35.49	36	6.01	196	36.19	36	6.20
Psychological Demands	980	30	30	6.47	784	30.12	30	6.36	196	29.60	29	6.88
Social Support	946	37.60	38.40	5.63	784	37.58	38.40	5.61	162	37.92	38.40	5.78

Main Results

Table 3 presents the IRRs for the risk of breast cancer associated with job strain considering different parameterizations. Age-adjusted models yielded results similar to those obtained in minimally adjusted models. In minimally adjusted models, exposure to job strain compared with the low-strain category was inversely associated with breast cancer risk (IRR = 0.61; 95% CI 0.36–0.99). While exposure to job strain compared with the non-exposed categories was not associated with breast cancer risk (IRR = 0.73; 95% CI 0.46–1.11). Additionally, exposure to iso-strain was associated with a lower risk of breast cancer in age-adjusted models (IRR = 0.58; 95% CI 0.31–0.98), although the association did not reach statistical significance in minimally adjusted models (IRR = 0.59; 95% CI 0.32–1.03).

Table 3

Age-Adjusted and Minimally Adjusted Incidence Rate Ratio (IRR) of Breast Cancer Associated with Exposure to Job Strain and Iso-Strain

Job Strain	**Controls (n = 784) n (%)**	**Cases (n = 196) n (%)**	**Age-Adjusted IRR (95% CI)**	**Minimally Adjusted[a] IRR (95% CI)**
Median-Based Quadrant				
Low strain (Low Demand/High Decision Latitude)	213 (27.2)	68 (34.7)	1.00 (Ref)	1.00 (Ref)
Passive (Low Demand/Low Decision Latitude)	233 (29.7)	51 (26.0)	0.69 (0.45–1.03)	0.72 (0.47–1.11)
Active (High Demand/High Decision Latitude)	182 (23.2)	48 (24.5)	0.83 (0.54–1.25)	0.83 (0.54–1.26)
Job Strain (High Demand/Low Decision Latitude)	156 (19.9)	29 (14.8)	0.58 (0.36–0.93)	0.61 (0.36–0.99)
Median-Based Quadrant, Dichotomous				
Non-Exposed (All Other Combinations)	628 (80.1)	167 (85.2)	1.00 (Ref)	1.00 (Ref)
Exposed (High Demand/Low Decision Latitude)	156 (19.9)	29 (14.8)	0.70 (0.45–1.06)	0.73 (0.46–1.11)
Iso-Strain	**Controls (n = 784) n (%)**	**Cases (n = 162) n (%)**	**Age-Adjusted IRR (95% CI)**	**Minimally Adjusted[a] IRR (95% CI)**
Median-Based Dichotomous				
Non-Exposed (All Other Combinations)	666 (84.9)	147 (90.7)	1.00 (Ref)	1.00 (Ref)
Exposed (High Demand/Low Decision Latitude/Low Social Support)	118 (15.1)	15 (9.3)	0.58 (0.31–0.98)	0.59 (0.32–1.03)

[a] Adjusted for age at diagnosis, ethnicity (White, Asian, Black African, Arab, Latino and Other), education level (high school or less, college, university), income level ($49,999 or less, $50,000-$74,999, $75,000 and up), physical activity (MET-hours/week), shift work (day, night and rotating, other), and occupational exposures (yes/no)

Sensitivity Analyses

Tables 4 and 5 present the results of sensitivity analyses examining the association between job strain and breast cancer across different analytic restrictions and subgroups. As shown in Table 4, restricting the analysis to participants with at least four completed items in both the psychological demand and decision latitude scales yielded an IRR of 0.67 (95% CI 0.41–1.06) for job strain compared with the non-exposed category in minimally adjusted models. Similarly, restricting the analysis to participants with complete JCQ data resulted in an attenuated estimate (IRR = 0.72; 95% CI 0.43–1.15) for job strain compared with the non-exposed category.

Table 4

Age-Adjusted and Minimally Adjusted Incidence Rate Ratio (IRR) of Breast Cancer Associated with Exposure to Job Strain in Participants with at Least 4 Answered Questions of the Psychological Demand and Decision Latitude Scales, and in Participants with 5 Answered Questions of the Psychological Demand and Decision Latitude Scales

	Job Strain (Median-Based Dichotomous)[a]	Controls n (%)	Cases n (%)	Age-Adjusted IRR (95% CI)	Minimally Adjusted[b] IRR (95% CI)
		(n = 735)	**(n = 183)**		
At Least 4 Questions Being Answered in Each Scale	Non-Exposed	592 (81.0)	158 (86.3)	1.00 (Ref)	1.00 (Ref)
	Exposed	143 (19.0)	25 (13.7)	0.66 (0.41–1.02)	0.67 (0.41–1.06)
		(n = 665)	**(n = 162)**		
All 5 Questions Being Answered in Each Scale	Non-Exposed	533 (80.2)	138 (85.2)	1.00 (Ref)	1.00 (Ref)
	Exposed	132 (19.8)	24 (14.8)	0.70 (0.43–1.11)	0.72 (0.43–1.15)

[a] Exposed = High Demand/Low Decision Latitude; Non-Exposed = All Other Combinations

[b] Adjusted for age at diagnosis, ethnicity (White, Asian, Black African, Arab, Latino and Other), education level (high school or less, college, university), income level ($49,999 or less, $50,000-$74,999, $75,000 and up), physical activity (MET-hours/week), shift work (day, night and rotating, other), and occupational exposures (yes/no)

Table 5
Age-Adjusted and Minimally Adjusted Incidence Rate Ratio (IRR) of Breast Cancer Associated with Exposure to Job Strain By Presumed Menopausal Status, Education, and Income Level Strata

		Job Strain (Median-Based Dichotomous)[a]	Controls (n = 784) n (%)	Cases (n = 196) n (%)	Age-Adjusted IRR (95% CI)	Minimally Adjusted[b] IRR (95% CI)
Presumed Menopausal Status	Premenopausal	Non-Exposed	81 (75.7)	24 (92.3)	1.00 (Ref)	1.00 (Ref)
		Exposed	26 (24.3)	2 (7.7)	0.26 (0.04–0.96)	0.31 (0.04–1.24)
	Postmenopausal	Non-Exposed	547 (80.8)	143 (84.1)	1.00 (Ref)	1.00 (Ref)
		Exposed	130 (19.2)	27 (15.9)	0.79 (0.50–1.23)	0.84 (0.52–1.33)
Education Level Strata	High School and less	Non-Exposed	118 (76.6)	31 (75.6)	1.00 (Ref)	1.00 (Ref)
		Exposed	36 (23.4)	10 (24.4)	1.06 (0.45–2.31)	1.03 (0.42–2.35)
	College	Non-Exposed	214 (75.1)	47 (82.5)	1.00 (Ref)	1.00 (Ref)
		Exposed	71 (24.9)	10 (17.5)	0.64 (0.29–1.29)	0.56 (0.25–1.16)
	University	Non-Exposed	296 (85.8)	89 (90.8)	1.00 (Ref)	1.00 (Ref)
		Exposed	49 (14.2)	9 (9.2)	0.61 (0.27–1.24)	0.58 (0.25–1.20)
Income Level Strata	$49,999 and less	Non-Exposed	154 (75.5)	25 (58.1)	1.00 (Ref)	1.00 (Ref)
		Exposed	50 (24.5)	18 (41.9)	2.22 (1.10–4.39)	2.37 (1.15–4.86)
	$50,000-$74,999	Non-Exposed	134 (78.4)	40 (90.9)	1.00 (Ref)	1.00 (Ref)
		Exposed	37 (21.6)	4 (9.1)	0.36 (0.10–0.97)	0.41 (0.11–1.14)
	$75,000 and up	Non-Exposed	340 (83.1)	102 (93.6)	1.00 (Ref)	1.00 (Ref)
		Exposed	69 (16.9)	7 (6.4)	0.34 (0.14–0.71)	0.33 (0.13–0.71)

[a] Exposed = High Demand/Low Decision Latitude; Non-Exposed = All Other Combinations

[b] Adjusted for age at diagnosis, ethnicity (White, Asian, Black African, Arab, Latino and Other), education level (high school or less, college, university), income level ($49,999 or less, $50,000-$74,999, $75,000 and up), physical activity (MET-hours/week), shift work (day, night and rotating, other), and occupational exposures (yes/no)

As shown in Table 5, when analyses were stratified by presumed menopausal status, no statistically significant association was observed in either group. However, estimates were closer to the null when analyses were restricted to presumed postmenopausal women (IRR = 0.84; 95% CI 0.52–1.33) compared with presumed premenopausal women (IRR = 0.31; 95% CI 0.04–1.24) in minimally adjusted models. Stratifying by education level revealed no association between job strain and breast cancer in any group: high school or less (IRR = 1.03; 95% CI 0.42–2.35), college (IRR = 0.56; 95% CI 0.25–1.16), or university (IRR = 0.58; 95% CI 0.25–1.20), although estimates were further from the null in the latter two groups. When stratifying by household income, exposure to job strain was positively associated with breast cancer among women in the lowest income group (IRR = 2.37; 95% CI 1.15–4.86), showed no clear association in the middle-income group (IRR = 0.41; 95% CI 0.11–1.14), and was inversely associated with breast cancer in the highest income group (IRR = 0.33; 95% CI 0.13–0.71) in minimally adjusted models.

Supplementary Results

We conducted additional analyses using two alternative representations of job strain: a quartile-based dichotomous variable and a continuous variable based on the job strain score. These analyses were performed for both the main models and the models stratified by menopausal status, education level, and household income (Supplementary Tables 1–3). Results for both parameterizations were consistent with the main findings, showing no statistically significant association between job strain and breast cancer in minimally adjusted models when job strain was categorized using quartiles, comparing participants in the highest quartile (Q4) to those in the lower quartiles (Q1-Q3) (IRR = 0.71; 95% CI 0.42–1.15) or treated as a continuous exposure (IRR = 0.62 per one-point increase in the job strain score; 95% CI 0.30–1.15).

In stratified analyses using continuous and quartile-based job strain parameterizations, findings were generally consistent with the main results across strata defined by presumed menopausal status. Across education levels, job strain was associated with a lower breast cancer risk when analyzed as a quartile-based dichotomous variable (IRR = 0.39; 95% CI 0.13–0.97). Similarly, in the high-income stratum, job strain was inversely associated with breast cancer when analyzed using the quartile-based dichotomous variable (IRR = 0.26; 95% CI 0.07–0.68). Although results from the stratified analyses by income and education using alternative parameterizations of job strain were not entirely consistent with the main findings, differences in effect estimates were observed across strata defined by education and household income.

Discussion

In this nested case-control study, we investigated the relationship between job strain and the risk of breast cancer in the CaG cohort. Our findings suggest that exposure to job strain compared to the non-exposed category (low strain, active and passive groups combined) was not significantly associated with breast cancer risk, although the marginal significance observed when comparing job strain to low strain may suggest a potential inverse relationship. Additionally, exposure to the combination of job strain and low social support (iso-strain) was not associated with breast cancer risk. As noted, point estimates rarely exceeded 1.0, which supports the absence of a positive association.

Our findings align with two previous prospective studies on job strain and the risk of breast cancer conducted within the US Nurses' Health Study. Achat et al. reported that there was no association between exposure to job strain, compared to low strain, and breast cancer risk in postmenopausal females during a two-year follow-up (RR = 0.78; 95% CI 0.52–1.16) (15). Subsequently, Schernhammer et al. (16) investigated the association in both premenopausal and postmenopausal women in the same cohort over an eight-year follow-up and reported similar findings (RR = 0.87; 95% CI 0.73–1.04), although in their analysis, job strain was used as a mean score considering both data collected at baseline and during follow-up (16).

Similarly, Heikkilä et al. demonstrated that exposure to job strain, compared to non-exposed individuals, did not influence the risk of breast cancer in a pooled study of 12 European cohorts, including more than 1000 incident breast cancer cases (RR = 0.97; 95% CI 0.82–1.14) (Heikkilä et al., 2013). Additionally, in a Danish female nurse cohort, Vesterlund et al. (39) used a brief, three-item questionnaire to measure job strain twice, with a six-year interval between assessments, and being exposed to job strain in both assessments was defined as prolonged job strain. Their findings indicated that there was no association between exposure to prolonged job strain and the risk of hormone-related cancers, including breast cancer (RR = 0.82; 95% CI 0.60–1.20) (39). Nevertheless, their results could not be directly interpreted here as they did not examine breast cancer risk separately from other hormone-related cancers. In contrast, Kuper et al. (14) showed that exposure to job strain, compared to low strain, significantly increased the risk of breast cancer in a Swedish women cohort during a 12-year follow-up (RR = 1.40; 95% CI 1.10–1.90) (14).

In sensitivity analyses, restricting the analysis to participants with complete or near-complete responses to the JCQ scales did not markedly change the results. Similarly, when stratifying by presumed menopausal status and education, no association was observed between job strain exposure and breast cancer risk across the different strata compared with the non-exposed category.

However, differences emerged when analyses were stratified by household income. Within the lowest income stratum (≤$49,999), exposure to job strain was positively associated with breast cancer in both age-adjusted and minimally adjusted models. In contrast, job strain was inversely associated with breast cancer in the highest income stratum (≥$75,000). These differences across SES strata may suggest potential effect modification by SES on the association between job strain and breast cancer. In other words, the disadvantaged populations might experience and be affected by job strain differently than those from higher socioeconomic groups. One possible explanation is that individuals in different socioeconomic groups may experience and respond to work-related stressors differently. Although income does not directly reflect decision latitude, which is captured by the

control dimension of the job strain model, it may represent an external reward associated with occupational position. Experimental and physiological studies suggest that rewarding stimuli can modify stress responses, with engagement in rewarding or secure activities potentially attenuating physiological stress reactions (40,41). In this context, socioeconomic position may shape how individuals experience and respond to work-related stressors. Higher socioeconomic status may be associated with greater access to financial security and other material or psychosocial resources that could mitigate the impact of stressful working conditions. Conversely, individuals in lower socioeconomic groups may experience additional stressors beyond the workplace. Financial insecurity has been shown to increase exposure to psychological stress and may interact with occupational stressors (42). Limited material or psychosocial resources may also reduce the ability to cope with stressful working conditions, which could contribute to the differing patterns observed across income strata.

Regardless of the parameterization method, neither the quartile-based dichotomous job strain nor the continuous job strain score showed a significant association with breast cancer in minimally adjusted models. This reinforces the robustness of the main results, suggesting that job strain, as measured in this study, may not be a primary risk factor for breast cancer. When further stratified by menopausal status, job strain remained nonsignificant in both premenopausal and postmenopausal women. Similarly, no association was observed among participants with lower or middle education and income levels. However, a significant inverse association emerged in both higher education and higher income groups when job strain was analyzed as a quartile-based dichotomous variable. This pattern aligns with our main findings and supports the hypothesis that higher SES may buffer the physiological effects of job strain and mitigate its potential health impact.

There are several limitations to our study. First, job strain was assessed based on a single measurement of participants' primary job held at baseline. Consequently, information on the duration of exposure or previous occupational histories was not available. Individuals who had experienced prolonged job strain in earlier employment but subsequently moved to lower-strain positions would be classified as non-exposed in this study. Conversely, participants who had recently entered high-strain jobs might have been classified as exposed despite relatively short exposure durations, which may be less relevant for a disease with a long latency period such as breast cancer. Further, the operationalization of job strain may have introduced additional sources of measurement error. In this study, job strain was defined using the median-based quadrant approach, which classifies individuals according to whether their psychological demand and decision latitude scores fall above or below the sample-specific medians. Although this approach is widely used in occupational epidemiology, it may introduce exposure misclassification, particularly for individuals whose scores fall close to the median thresholds. In addition, dichotomizing continuous scale scores may lead to a loss of information and reduced statistical power, and the resulting classification can depend on the specific cut-points used (43).

Second, the measurement properties of the exposure instrument should also be considered. CaG employed an adapted 15-item version of the JCQ rather than the original 36-item instrument. Although abbreviated versions of the JCQ are frequently used in large population-based studies, the internal consistency of the scales may differ across populations (10,24,44).

Third, uncontrolled confounding may still be present despite adjustment for the minimal sufficient set of covariates. For instance, although annual household income is commonly used as a proxy for SES, it may not fully capture the broader social and structural dimensions encompassed by SES (45). In addition, residual confounding may remain even among the variables included in the models. As an example, occupational exposures were assessed using CANJEM, which, like other job exposure matrices, assigns exposure estimates at the occupational level rather than the individual level. Consequently, participants holding the same job code receive identical exposure estimates, which may introduce non-differential exposure misclassification. Furthermore, for 19.6% of participants, occupational information was available only at the 2-digit or 3-digit ISCO level, resulting in broader occupational categories and potentially less precise exposure estimates.

Finally, theoretical models such as the job strain model may not fully capture individual variation in the perception and management of workplace stressors. Workers in the same occupational environment may adopt different coping strategies when facing stressful conditions (42). These strategies may include adjusting levels of job involvement, reducing effort, or creating cognitive or emotional distance from work demands (46). As a result, the same work environment may be perceived as stressful by some individuals but not by others, potentially influencing the physiological stress response (47). Moreover, the job strain model does not explicitly incorporate aspects of work related to reward or reciprocity, which are central components of the effort-reward imbalance model (46). According to this model, stressful experiences arise particularly under conditions of high effort combined with low reward, including financial compensation, esteem, or job security. As also observed in our results, the lack of these

extrinsic rewards in the lower SES levels may explain the opposing pattern across income strata in the association between job strain and breast cancer.

Nevertheless, this study contributes to the limited body of research examining the association between job strain and breast cancer risk. We also explored whether the association between job strain and breast cancer differed across socioeconomic strata defined by education and household income, an aspect that has been less frequently examined in this literature. Furthermore, the CaG cohort benefits from its linkage to CANJEM, which allowed us to control for participants' occupational exposures as a confounding variable. To our knowledge, this marks the first time such an adjustment for the occupational environment has been included in research on psychological aspects of work, enhancing the robustness of our findings.

Conclusion

In conclusion, our findings do not provide any evidence that job strain, assessed ~ 10 years before diagnosis, is a significant risk factor for breast cancer. However, a positive association emerged among individuals in the lowest income group, suggesting that socioeconomic status may influence the relationship. Future research on work-related stress could explore alternative measures that more accurately reflect the interaction between personal and occupational characteristics. They should also investigate the complex interplay between work-related stress, socioeconomic factors, and other chronic stressors in cancer development.

Abbreviations

CaG - CARTaGENE Cohort

CANJEM - Canadian Job Exposure Matrix

CI - Confidence Interval

DAG - Directed Acyclic Graph

HR - Hazard Ratio

IARC - International Agency for Research on Cancer

IPAQ - International Physical Activity Questionnaire

IRR - Incidence Rate Ratio

ISCO-68 - International Standard Classification of Occupations 1968

JCQ Job - Content Questionnaire

MET - Metabolic Equivalent Task

MHT Menopausal Hormone Therapy

RAMQ - Régie de l'assurance maladie du Québec

RR - Relative Risk

SES - Socioeconomic Status

Declarations

Ethics approval and consent to participate

Participants provided written informed consent to participate in the CARTaGENE cohort. The present study was approved by the CHUM Research Ethics Committee (approval no. 23.285). The CHUM Research Ethics Committee adheres to the principles and

operating requirements of the Tri-Council Policy Statement: Ethical Conduct for Research Involving Humans (TCPS 2) and the International Council for Harmonisation Good Clinical Practice (ICH-GCP) guidelines, under designation by the Québec Ministry of Health and Social Services (MSSS).

Consent for publication

Not applicable.

Availability of data and materials

The data that support the findings of this study are available from CARTaGENE but restrictions apply to the availability of these data, which were used under license for the current study, and so are not publicly available. Data are however available from the authors upon reasonable request and with permission of CARTaGENE.

Competing interests

The authors declare that they have no competing interests.

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Authors' contributions

EG conceptualized the study, developed the methodology, conducted the formal analysis, and drafted the original manuscript. BN contributed to the conceptualization and methodology of the study, provided supervision, and critically reviewed and edited the manuscript. VH contributed to the conceptualization and methodology of the study, provided supervision, and critically reviewed and edited the manuscript. LP-SP and JF contributed to the methodology and critically reviewed and edited the manuscript. KM contributed to the methodology, validation of the analyses, and critically reviewed and edited the manuscript. All authors read and approved the final manuscript.

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Figures

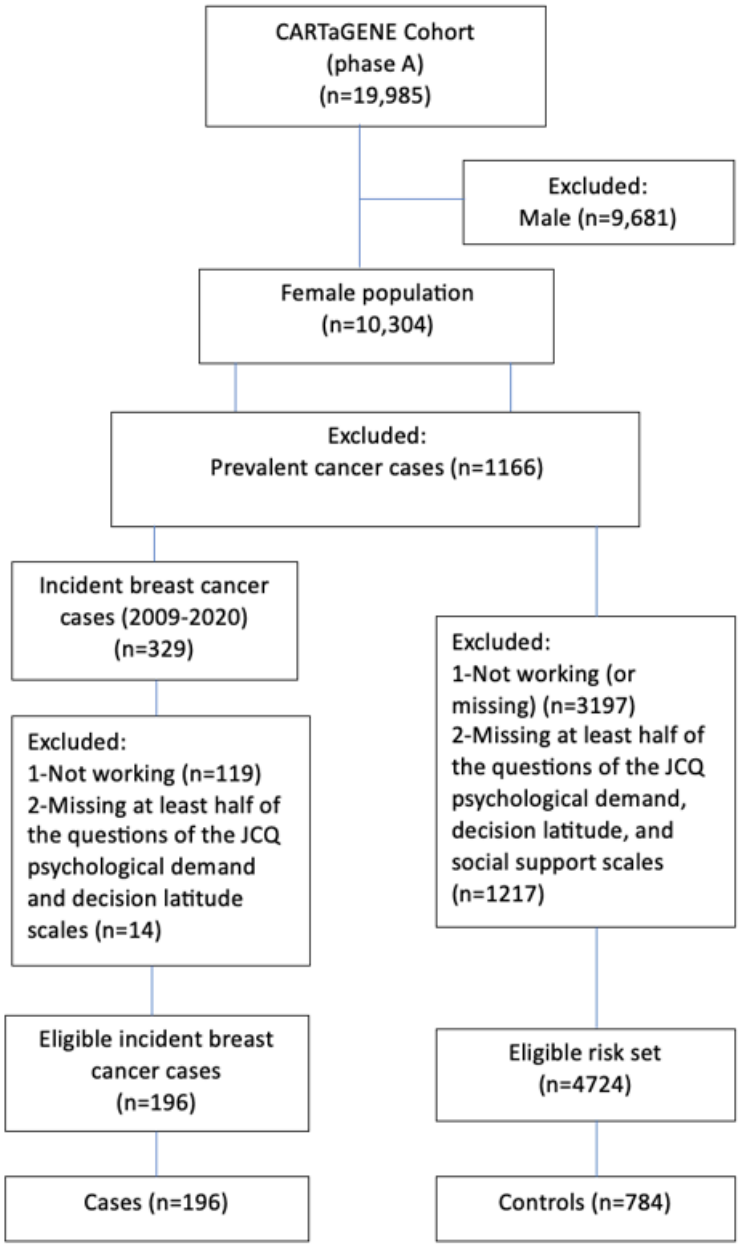


Figure 1

The Eligibility Criteria Flowchart Illustrating the Participant Selection Process and Exclusion Criteria Applied

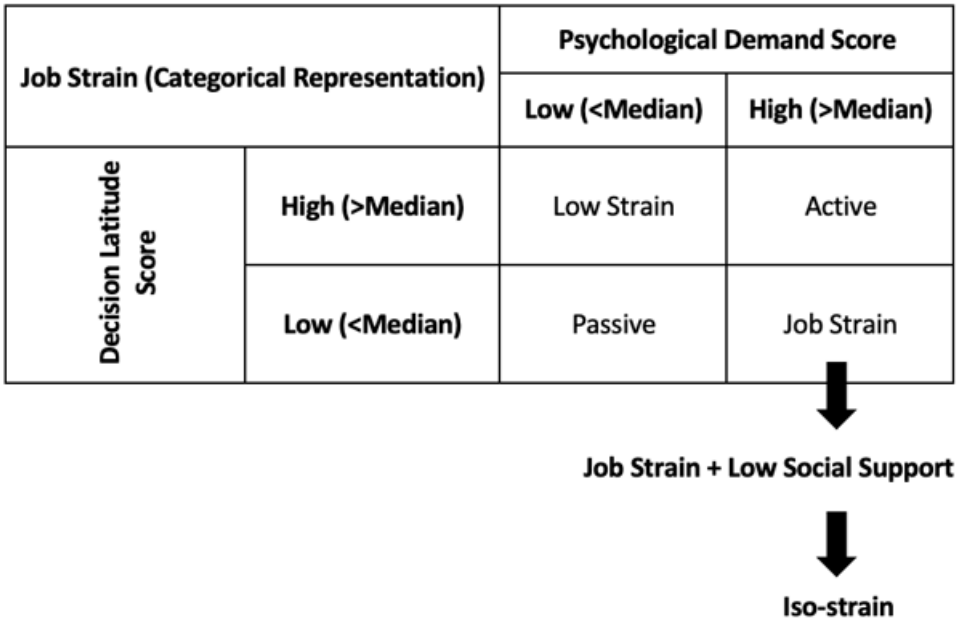


Figure 2

Combinations Formed by Psychological Demand, Decision Latitude, and Social Support Adapted from Rezvani et al. (28)

Supplementary Files

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