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Shift work and breast cancer among women textile workers in Shanghai, China

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Abstract
Purpose Although night-shift work has been associated with elevated risk of breast cancer in numerous epidemiologic studies, evidence is not consistent. We conducted a nested case–cohort study to investigate a possible association between shift work including a night shift and risk of breast cancer within a large cohort of women textile workers in Shanghai, China.
Methods The study included 1,709 incident breast cancer cases and 4,780 non-cases. Data on historical shift work schedules were collected by categorized jobs from the factories, where the study subjects had worked, and then were linked to the complete work histories of each subject. No jobs in the factories involved exclusively night-shift work. Therefore, night shift was evaluated as part of a rotating shift work pattern. Hazard ratios and 95 % confidence intervals were calculated using Cox proportional hazards modeling adapted for the case–cohort design for years of night-shift work and the total number of nights worked. Additionally, analyses were repeated with exposures lagged by 10 and 20 years.
Results We observed no associations with either years of night-shift work or number of nights worked during the entire employment period, irrespective of lag intervals. Findings from the age-stratified analyses were very similar to those observed for the entire study population.
Conclusions The findings from this study provide no evidence to support the hypothesis that shift work increases breast cancer risk. The positive association between shift work and breast cancer observed in Western populations, but not observed in this and other studies of the Chinese population, suggests that the effect of shift work on breast cancer risk may be different in Asian and Caucasian women.

Keywords Breast cancer · Night-shift work · Shift work · Dose–response

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Background

Breast cancer is the most frequent non-skin cancer among women, and incidence is increasing worldwide [1]. Although intensive research has been conducted to improve the understanding of the biology of breast cancer, the etiology of breast cancer remains poorly explained.

The etiologic contributions of occupational risk factors have not been adequately studied, especially in view of the large numbers of women in the workforce worldwide with potentially hazardous exposures. A potential effect of shift work on cancer risk, presumably caused by disruption of circadian rhythms, has received increasing attention in recent years. In 2007, the International Agency for Research on Cancer (IARC) classified shift work that involves disruption of circadian rhythms, a probable cause of human cancer (group 2A), based on sufficient evidence from animal studies and limited evidence from epidemiological research, focused primarily on risk of breast cancer [2]. The IARC review considered eight epidemiological studies investigating the effects of shift work at night on breast cancer, of which five reported a moderate increased risk of breast cancer with shift work. The most convincing evidence came from two cohort studies [3, 4] and one nested case–control study [5], all conducted among US nurses, in which significantly increased risks of breast cancer were observed for long-term shift work (more than 20–30 years), although no effects were found for shorter durations of shift work in those studies. Since then, the results of a number of population-based case–control or cohort studies [6–8] have been published on the possible association between shift work and breast cancer risk. They were further included in three updated review and meta-analyses of shift work and breast cancer risk. [9–12] Based on 15 carefully selected and newly published studies, which included three studies on flight attendants and four studies on nurses [9], Kamdar et al. conducted a meta-analysis and found a weak association (21 % increased risk for workers with ever night-shift work and 4 % increased risk for workers worked on night shifts 8 years or longer) between night-shift work and the risk of breast cancer. The other two subsequent reports on review and meta-analysis of the same studies, excluding three studies on flight attendants and using an improved study assessment method, found a positive association between night work and the risk of breast cancer when data from the case–control studies were pooled, but no association in pooled cohort studies [10, 12]. In all three reports, the authors acknowledged the large heterogeneity between studies in study design, exposure assessment, and confounding adjustment. Most of the studies examined suffered from a low quality of exposure assessment, often based on self-report.

To date, the evidence from epidemiological studies for a causal association between night-shift work and breast cancer risk remains inconclusive. Apart from the published study by Pronk et al. [7], all epidemiologic studies on shift work and breast cancer had been conducted in predominantly Caucasian women.

We undertook the current study to determine whether shift work altered the risk of breast cancer in a large, well-characterized cohort of textile workers in China.

Materials and methods

Study population and case finding

The present study was an extension of a series of case–cohort studies of textile industry exposures to dusts, chemicals, and other physical agents in relation to risks of various cancers [13–17]. Briefly, the previous studies were based in a cohort of 267,400 workers from 503 textile factories in the Shanghai Textile Industry Bureau (STIB) who were recruited in 1989–1991 for a randomized trial of the effect of breast self-examination on breast cancer mortality [13, 18]. The cohort consisted of active and retired employees who were permanent residents of Shanghai born between 1 January 1925 and 31 December 1958. At enrollment into the trial, women were administered a baseline questionnaire that elicited information on demographic variables, lifestyle habits, and reproductive history.

Follow-up of the cohort has been described previously [13]. All women were followed for breast cancer incidence through July 2000 by frequent review of factory medical records, and from annual medical reports submitted by each factory clinic to a cancer and death registry maintained by the Station for the Prevention and Treatment of Cancer of STIB. Case identification was supplemented by manual reviews of records from the Shanghai Cancer Registry (SCR) and a computerized matching of the trial cohort to the SCR data. All incident breast cancer cases were verified by review of pathology reports or histologic review of tissue slides as part of the trial. A total of 1,763 breast cancer cases were identified and verified.

Two methods were utilized to construct a comparison group. The 3,139 breast cancer-free women who had been randomly selected from the cohort using an age stratification scheme for a series of occupational studies were utilized in the current study [15]. Some of the breast cancer cases had been previously included in two nested case–control studies of nutritional factors and induced abortion [19, 20]. The 1,697 controls for those studies were selected from the cohort members such that their age distribution approximated that of the breast cancer cases. These controls were added to the comparison group. Thus, the total number of women in the comparison group in this study is 3,139 + 1,697 = 4,836.

One hundred ten subjects (54 breast cancer cases and 56 non-case subjects) were excluded due to missing either the baseline questionnaire or work history information, leaving

1,709 breast cancer cases and 4,780 non-case subjects for the risk estimate analyses.

Exposure assessment

Work history

Information on all textile industry jobs that were held by each study subject since the date of first employment in the STIB was collected by trained field workers from review of factory personnel records (80 %), interviews of factory supervisors (12 %), and in-person interviews of women or their relatives (8 %). For each job that a woman held, the field workers recorded the dates of employment, workshop, and job tasks.

Shift work

Each STIB factory had its own history of shift work that was mandated by government policy. Shift work policies changed over time, with changes having been relatively uniform across factories within the same sector (cotton, wool, etc.). Therefore, data on shift work were collected by major manufacturing processes (e.g., fiber processing, spinning, dyeing) from all factories.

Trained study interviewers obtained a historical shift work profile for all but three factories where cases and non-cases had worked, based on interviews of factory management personnel. Shift work patterns in those three factories (two textile machinery manufacturing and one fabric bleaching and printing factory), in which 11 subjects ever worked, were estimated from other factories of the same sectors. No jobs in the STIB factories involved exclusively night-shift work. Therefore, we only considered night shift as part of a rotating shift pattern. Whether a job involved a rotation schedule, shift rotation cycle, daily rotation schedule (start time and end time of each shift), and changes of shift policy over time were recorded.

The factory-level shift work information was linked to each study subject's work history data. Each job was first classified into never/ever involved a rotating night-shift work. Night shift was defined as continuous working between 2400 and 0500 h. The number of total nights worked per month was computed for jobs involving a night shift. For example, a woman worked as an operator in the spinning process in Cotton Mill No. 1 between 1975 and 1980. The shift work information from the factory indicates that machine operators in the spinning process worked on a three-shift rotation schedule from 1970 to 1985: 2 days on morning shifts (0600–1400), 2 days on swing shift (1400–2200), 2 days on night shift (2200–0600), then 2 days off-work before starting the rotation cycle again. Therefore, each rotation cycle took 8 days. The total number of nights for the woman worked per month would be 7.5 nights [2 nights $\times$ (30 days/8 days)]. Total nights the woman worked on the job are 7.5 nights $\times$ 12 months $\times$ 5 years.

In addition, the associations of breast cancer with night work exposure were examined by lagging exposure times by 10 or 20 years before the diagnosis of breast cancer to take into account a possible latency period of the effect of exposure to night work on breast cancer risk.

The study was approved by the Institutional Review Boards of the Fred Hutchinson Cancer Research Center, the University of Washington, and the Station for Prevention and Treatment of Cancer of STIB, in accordance with an assurance filed with the Office for Human Research Protections (OHRP) of the US Department of Health and Human Services.

Statistical analysis

For the analysis addressing associations between night-shift work and breast cancer, we conducted Cox proportional hazards modeling, adapted for the age-stratified case–cohort design, to calculate relative risk estimates [hazard ratios (HRs) and 95 % confidence intervals (CIs)] for breast cancer associated with various measures of night-shift work. Robust variance estimates were used to compute standard errors of hazard ratios. The risk period was defined as time since entry into the cohort until the date of breast cancer diagnosis, death, or end of follow-up on 31 July 2000, whichever came first. Because workers' durations of shift work changed during the risk period, we organized the analytic dataset into risk sets to accommodate the time-dependent exposure, using the computational methods developed by Langholz and Jiao [21]. For each risk set, cumulative exposure to night-shift work was calculated first as the duration of years worked on rotating shift work including a night shift, then as cumulative number of nights worked, for the cases and non-cases up to the cases' failure times. Cumulative exposure during the entire work history was categorized into five groups: unexposed and four quartiles of exposure, with the cutoff points defined by the distribution of cumulative exposure among the cases. Dose–response trends were tested by the statistical significance of the coefficient for linear trend on the median values of the quartile groups among exposed subjects only.

Analyses were also conducted in which exposures were lagged by 10 and 20 years to take into account disease latency. We repeated the analyses in a subgroup of all women to examine the effects of a more frequent shift rotation: two morning–two swing–two night clockwise rotating cycle on risk of breast cancer.

Reproductive history including the number of live births (grouped as 1, 2, 3, 4, >5), lifetime duration of breast

Table 1 Characteristics of the cases and non-cases among woman textile workers in Shanghai, China

	Cases (n = 1,709)		Non-cases (n = 4,780)	
	n	%	n	%
Birth year				
1925–1929	266	(15.56)	1,090	(22.57)
1930–1934	371	(21.71)	1,158	(23.98)
1935–1939	173	(10.12)	523	(10.83)
1940–1944	113	(6.61)	251	(5.20)
1945–1949	252	(14.75)	453	(9.38)
1950–1954	335	(19.60)	625	(12.94)
1955–1958	199	(11.64)	730	(15.11)
Age at beginning of follow-up (years)				
30–40	568	(33.24)	1,396	(29.21)
>40–50	341	(19.95)	664	(13.89)
>50–60	556	(32.53)	1,721	(36.00)
>60–66	244	(14.28)	999	(20.90)
Duration of follow-up (years)				
Mean (SD)	5.19	(2.92)	10.9	(1.35)
Work history				
Years of employment in STIB				
≤20	524	(30.66)	1,354	(27.91)
>20–30	766	(44.82)	2,183	(45.67)
>30–40	414	(24.22)	1,236	(25.86)
>40	5	(0.29)	27	(0.56)
Average number of jobs held				
1	761	(44.53)	2,536	(53.05)
2	635	(37.16)	1,555	(32.53)
3	224	(13.11)	474	(9.92)
4+	67	(5.20)	33	(4.50)
Shift work				
No	968	(56.64)	2,341	(48.97)
Yes	741	(43.36)	2,439	(51.03)
Years doing shift work				
1–≤10	21	(2.83)	62	(2.54)
10–≤15	57	(7.69)	158	(6.48)
15–≤20	135	(18.22)	404	(16.56)
More than 20	528	(71.26)	1,815	(74.42)

feeding (grouped as never, <6, 7–12, 13–24, 25–36, 37–48, >49 months), and alcohol use (as yes/no) collected at baseline was examined as potential confounding factors. Prevalence of smoking was less than 10 % in the cohort, and is not an established risk factor for breast cancer, and therefore was not examined as a potential confounding factor.

Although we did not have data on age at menopause, we examined possible effect modification by repeating the risk estimates as described separately for women <50 and ≥50 years old.

Table 2 Risk of breast cancer in relation to years worked on rotating night shift among textile workers in the Shanghai textile industry (1,709 cases and 4,780 non-cases)

Cumulative exposure (years)	Cases	HR[a]	95 % CI
Entire employment period[b]			
0	557	1.00	(ref)
>0–12.8	286	0.99	(0.83, 1.17)
>12.8–19.92	290	0.97	(0.82, 1.15)
>19.92–27.67	289	0.90	(0.76, 1.06)
>27.67	287	0.88	(0.74, 1.05)
p value for trend*			0.095
10-year lag			
0	577	1.00	(ref)
>0–12.8	431	0.98	(0.84, 1.15)
>12.8–19.92	266	0.99	(0.83, 1.17)
>19.92–27.67	200	0.81	(0.67, 0.98)
>27.67	235	0.91	(0.75, 1.10)
p value for trend			0.060
20-year lag			
0	725	1.00	(ref)
>0–12.8	516	1.03	(0.89, 1.20)
>12.8–19.92	180	0.90	(0.74, 1.10)
>19.92–27.67	179	0.90	(0.74, 1.11)
>27.67	109	0.88	(0.68, 1.14)
p value for trend			0.035

[a] Hazard ratios (HR) and 95 % confidence interval (CI) adjusted for age at the beginning of follow-up (as a continuous variable)

[b] Exposure was categorized based on the distribution of the entire employment period of the exposed cases

* Trend tests were restricted to the exposed subjects. Cutpoints were determined based on the median values of each quartile

Magnetic field (MF) exposures, which have been investigated previously [22], are thought to share similar mechanisms of melatonin suppression and hormonal dysregulation. Joint effects of shift work and MF exposures were evaluated by stratifying subjects into four groups based on two levels of each exposure (cutpoints are 6.24 μT-years for MF exposure and 27.5 years for shift work duration).

All statistical analyses were performed in SAS, version 9.1 (SAS Institute Inc., Cary, North Carolina).

Results

Characteristics of study subjects

The average age at diagnosis for 1,709 cases was 53.4 years old. Breast cancer cases tended to be slightly younger than the comparison group (Table 1). All women entered the follow-up period between ages 30 and 66 years.

Table 3 Risk of breast cancer in relation to years worked on rotating night shift for two groups of women divided by age

Cumulative exposure (years)	Cases	HR[a]	95 % CI
Women < 50 years old (732 cases)			
Entire employment period[b]			
0	273	1.00	(ref)
>0–11.0	114	0.87	(0.67, 1.12)
>11.0–16.8	118	0.94	(0.73, 1.22)
>16.8–21.54	112	1.06	(0.81, 1.37)
>21.54	115	0.94	(0.72, 1.22)
p value for trend*			0.453
10-year lag			
0	292	1.00	(ref)
>0–11.0	239	0.89	(0.73, 1.10)
>11.0–16.8	125	1.02	(0.80, 1.31)
>16.8–21.54	69	1.07	(0.78, 1.46)
>21.54	7	0.88	(0.39, 1.99)
p value for trend			0.344
20-year lag			
0	437	1.00	(ref)
>0–11.0	280	1.02	(0.84, 1.25)
>11.0–16.8	15	0.98	(0.55, 1.73)
p value for trend			0.896
Women ≥ 50 years old (977 cases)			
Entire employment period			
0	284	1.00	(ref)
>0–14.5	173	1.23	(0.97, 1.56)
>14.5–24.2	173	0.86	(0.68, 1.09)
>24.2–31.17	174	0.85	(0.67, 1.07)
>31.17	173	0.96	(0.76, 1.23)
p value for trend*			0.430
10-year lag			
0	285	1.00	(ref)
>0–14.5	177	1.22	(0.97, 1.55)
>14.5–24.2	201	0.84	(0.67, 1.06)
>24.2–31.17	156	0.87	(0.68, 1.10)
>31.17	158	0.97	(0.75, 1.25)
p value for trend			0.015
20-year lag			
0	288	1.00	(ref)
>0–14.5	268	1.06	(0.86, 1.30)
>14.5–24.2	225	0.91	(0.73, 1.13)
>24.2–31.17	156	0.91	(0.71, 1.18)
>31.17	40	0.88	(0.59, 1.33)
p value for trend			0.015

[a], [b], * See the footnotes in Table 2

The average duration of follow-up for cases and non-cases was 5.2 and 10.9 years, respectively. Most of the subjects had worked >20 years, and few women had more than two jobs.

Table 4 Risk of breast cancer (1,709 cases) in relation to the number of nights worked among textile workers in the Shanghai textile industry

Cumulative exposure (night shifts)	Cases	HR[a]	95 % CI
Entire employment period[b]			
0	557	1.00	(ref)
>0–1,316.79	288	0.96	(0.81, 1.14)
>1,316.79–2,018.71	287	1.00	(0.84, 1.19)
>2,018.71–2,880	288	0.88	(0.74, 1.04)
>2,880	289	0.89	(0.75, 1.07)
p value for trend*			0.155
10-year lag			
0	577	1.00	(ref)
>0–1,316.79	422	0.99	(0.84, 1.15)
>1,316.79–2,018.71	250	0.99	(0.83, 1.18)
>2,018.71–2,880	207	0.84	(0.70, 1.02)
>2,880	253	0.89	(0.74, 1.08)
p value for trend			0.071
20-year lag			
0	725	1.00	(ref)
>0–1,316.79	497	1.08	(0.94, 1.24)
>1,316.79–2,018.71	175	0.93	(0.77, 1.14)
>2,018.71–2,880	134	0.89	(0.71, 1.11)
>2,880	178	0.92	(0.74, 1.14)
p value for trend			0.046

[a], [b], * See the footnotes in Table 2

Associations between risk of breast cancer and reproductive and life style risk factors for breast cancer cases compared to the breast cancer-free women randomly selected from the cohort, using an age stratification scheme for a series of occupational studies, have been published previously [15]. The analyses were repeated with the expanded comparison group for this study. The results were similar to those previously published. Risk of breast cancer was elevated in nulliparous women and increased with age at first live birth. Risk decreased with increased number of live births and in women who breast fed for more than 4 years. There were few cigarette smokers, and about 20 % of the subjects ever consumed alcohol. Neither of these factors was associated with risk of breast cancer.

Shift work

The hazard ratios for breast cancer in relation to the number of years worked on rotating night shift throughout the entire work history period, and for exposure lagged 10 and 20 years, respectively, are presented in Table 2. All relative risk estimates were close to unity except for a significantly decreased HR estimate for the third quartile in the exposure lagged 10 years. Risk decreased with increasing duration of shift work in the lagged analyses,

Table 5 Risk of breast cancer in relation to the number of nights worked for two groups of women stratified by age

Cumulative exposure (night shifts)	Cases	HR[a]	95 % CI
Women < 50 years old (732 cases)			
Entire employment period[b]			
0	273	1.00	(ref)
>0–1,114.29	115	0.83	(0.64, 1.07)
>1,114.29–1,603.39	113	0.95	(0.73, 1.23)
>1,603.39–2,116.61	117	1.08	(0.83, 1.40)
>2,116.61	114	0.96	(0.74, 1.26)
p value for trend*			0.200
Exposure window 1: >20 years			
0	292	1.00	(ref)
>0–1,114.29	241	0.91	(0.75, 1.12)
>1,114.29–1,603.39	112	1.10	(0.85, 1.43)
>1,603.39–2,116.61	70	0.92	(0.68, 1.26)
>2,116.61	17	1.12	(0.64, 1.97)
p value for trend			0.533
Exposure window 2: >10–20 years			
0	437	1.00	(ref)
>0–1,114.29	271	1.05	(0.87, 1.26)
>1,114.29–1,603.39	24	1.07	(0.67, 1.71)
Women ≥ 50 years old (977 cases)			
Entire employment period[b]			
Quartiles			
0	284	1.00	(ref)
>0–1,627.5	173	1.09	(0.88, 1.36)
>1,627.5–2,588.21	172	0.84	(0.68, 1.04)
>2,588.21–3,453.78	174	0.91	(0.74, 1.13)
>3,453.78	174	0.93	(0.74, 1.16)
p value for trend*			0.140
Exposure window 1: >20 years			
Quartiles			
0	285	1.00	(ref)
>0–1,208.57	177	1.08	(0.87, 1.35)
>1,208.57–1,883.93	197	0.84	(0.68, 1.03)
>1,883.93–2,911.07	145	0.90	(0.71, 1.13)
>2,911.07	173	0.97	(0.78, 1.22)
p value for trend			0.243
Exposure window 2: >10–20 years			
Quartiles			
0	288	1.00	(ref)
>0–363.75	285	1.02	(0.85, 1.24)
>363.75–630	185	0.94	(0.76, 1.16)
>630–908.57	130	0.90	(0.71, 1.14)
>908.57	89	0.97	(0.74, 1.29)
p value for trend			0.156

[a, b,] * See the footnotes in Table 2

Table 6 Joint effects of shift work and magnetic field exposure on risk of breast cancer (1,709 cases and 4,780 controls)

Stratified group	Cases	HR[b]	95 % CI
Entire employment period[a]			
MF ≤ 6.24 μT-years and shift work duration ≤ 27.5 years	1,101	1.00	(ref)
MF ≤ 6.24 μT-years and shift work duration > 27.5 years	165	0.94	(0.77, 1.14)
MF > 6.24 μT-years and shift work duration ≤ 27.5 years	299	1.02	(0.88, 1.19)
MF > 6.24 μT-years and shift work duration > 27.5 years	122	0.87	(0.70, 1.08)
Redefined shift work groups			
MF ≤ 6.24 μT and shift work = 0	467	1.00	(ref)
MF ≤ 6.24 μT and shift work > 0	799	0.92	(0.81, 1.06)
MF > 6.24 μT and shift work = 0	73	0.91	(0.68, 1.22)
MF > 6.24 μT and shift work > 0	348	0.94	(0.80, 1.11)

[a] The cutoff points for categories were defined by the values at the 75th percentiles for the duration of years working on night-shift work and cumulative exposure of MF (μT-years)

[b] *HR* hazard ratio, *95 % CI* 95 % confidence interval, *MF* magnetic fields

and the trend test for the exposure lagged 20 years was statistically significant, but the 95 % CIs of the risk estimates for all three incremental quartiles included unity.

Similar findings were observed from the age-stratified analyses (<50, ≥ 50 years) in the study population shown in Table 3.

When exposure was assessed based on the cumulative number of nights worked (Table 4), most HRs were also close to unity and not statistically significant, and there were no significant trends in risk with number of nights worked.

The results in Tables 2 and 4 were not appreciably altered by further adjusting for number of live births, age at first live birth, and alcohol intake. Findings from the age-stratified analyses (<50, ≥50 years) were very similar to those observed for the entire study population (Table 5).

There were 1,550 women (973 cases, 577 non-cases) who had changed their shift work pattern from a six morning–six swing–six night cycle to a two morning–two swing–two night cycle in the mid-80s, and had worked on the latter shift cycle for at least 3 years. Risks of breast cancer were not altered significantly for those women compared to the women who had never worked on shift work (data not shown).

There was no evidence of a combined effect on risk of breast cancer by exposures to MFs and durations of shift work (Table 6).

Discussion

We found no evidence for an association between rotating night-shift work and the risk of breast cancer in this large cohort of female textile workers in China. Our findings are consistent with the results of several previous studies [6, 8, 23], including the prospective cohort study among Chinese women [7], but not with the reports from several other studies in Caucasian populations. [3–5, 24–27] In a registry-based cohort study in Sweden, Schwartzbaum et al. [28] observed no increase (SIR 0.97, 95 % CI 0.67–1.4) in risk of breast cancer among female workers who likely worked on shift work. No association between shift work and breast cancer risk was reported in a cohort of telegraph operators in Norway [29]. Of five studies reporting an effect of shift work on breast cancer [3–5, 24, 25], three studies reported an increased risk of breast cancer with long-term rotating shift work (RR 1.36, 95 % CI 1.04–1.78 and RR 2.21, 95 % CI 1.10–4.45 for duration $\geq$30 years; RR 1.79, 95 % CI 1.06–3.01 for the duration $\geq$20 years) [3–5]; two found the increased risk of breast cancer with ever worked night shift (RR 1.6, 95 % CI 1.0–2.5; RR 1.5, 95 % CI 1.3–1.7) [24, 25].

To date, our study is the largest study to have examined the association between shift work and breast cancer risk in an Asian population. Pronk et al. [7] investigated the association in a population-based prospective cohort study of 73,049 Shanghai women aged between 40 and 70 years. The cohort was followed for incident breast cancer for an average of 9 years, and 717 breast cancer cases were identified. Similar to our findings, the results from the Pronk et al. cohort study showed no associations with shift work.

There are several possible explanations for the observed null association between breast cancer risk and shift work in our study. Shift work information was collected at the factory level and then linked to subjects' work histories. The main advantage of using such linkage was to avoid recall bias. However, using the aggregate level for exposure assessment has the possibility of exposure misclassification. In the STIB, when a factory instituted a shift work policy, it affected virtually all women in any particular job type; thus, applying the factory-level information on shift work by job to each of the individuals in our study minimized misclassification. Also, misclassification was minimized by the stability of the jobs held by the study subjects. About 85 % of women in our study had only one or two jobs in their whole work history, and 72 % of women worked longer than 20 years. It is also worth noting that, despite some probable degree of misclassification of our shift work assessment, the use of standardized factory shift work policy information and linkage to workers' personnel records avoided inaccuracies typically associated with study subjects' recall bias. Therefore, it seems unlikely that exposure misclassification or other inaccuracies masked any strong associations in this study.

An alternative explanation for our null findings is that the association of shift work and breast cancer may vary by race and ethnicity. In fact, our findings are consistent with the reports in another Chinese population [7], but differ considerably from the findings reported from studies in Caucasians in the USA and Scandinavia. It is possible that the conflicting findings reveal true biological differences between the populations. One of the hypothesized biological mechanisms to explain the possible causal effect of night shift on increasing risk of breast cancer is through melatonin suppression. Exposure to light at night, such as from working night shifts, suppresses the nocturnal rise in melatonin production and release by pineal gland [30]. This suppression results in increased gonadotropin production in the pituitary and leads to increased levels of ovarian hormones, which have a simulative effect on the mammary epithelium. The dark eye color of Chinese women may prevent the suppression of melatonin secretion from nocturnal light. This hypothesis is supported by two recent studies mentioned by Girschik et al. [31] in their letter discussing the findings by Pronk et al. In a small intervention study ($n = 11$), light-filtering goggles' were effective in preventing the suppression of melatonin by nocturnal lighting in Caucasians but not Asian men [32]. In another study comparing the influence of eye colors of Caucasians and Asian on suppression of melatonin secretion by light, two groups of subjects were exposed to light (1,000 lux) for 2 h at night, and suppression of melatonin by light was found to be significantly stronger for Caucasians (88.9 ± 4.2 %) than for Asians (73.4 ± 20.0 %) [33].

There are a number of other reasons that could contribute to inconsistent findings among the published studies, such as different definitions for night-shift work, variations in duration of shift work, differences in workshop light intensity and shift cycle, and uncontrolled confounding by other variables. In addition, it is still unclear which shift cycle or timing of exposure is most relevant to breast carcinogenesis.

There are several noteworthy strengths of our study. Our study was based in a well-defined occupational cohort and included a very large case group. In addition, we were able to collect a complete work history for each woman and detailed information on shift work policy from each factory. We also had detailed shift work information for each job including shift type, schedule of each shift, rotation cycle, and change of shift policy, which enabled us to accurately calculate cumulative exposure to night shifts.

There are also limitations of our study that warrant mention. Because no assigned jobs were exclusively night shift, we could not investigate associations that may be specific to night shift. Instead, night-shift work was embedded within rotating shift work patterns. We did not have direct information on menopause, but instead, used age (<50 vs. $\geq$50 years) as a surrogate stratification variable. Nonetheless, it is unlikely that inferences regarding associations for pre- and postmenopausal women were erroneous. Information on women's body mass index was not available. However, we do not expect women's body mass index to be a confounder as it would be unlikely to relate to shift work. Women enrolled in the study were permanent or retired textile workers in STIB and have health insurance provided by STIB. Therefore, the likelihood of being diagnosed with breast cancer is the same for all workers regardless their work type and schedule.

In summary, rotating shift work was not associated with the risk of breast cancer in a cohort of female textile workers in Shanghai, China. Our results, although in conflict with findings of several studies in Caucasian women, are consistent with the findings in one other Chinese cohort. The effect of shift work on breast cancer risk may be different in Caucasian and Asian populations. More evidence from non-Western populations is needed.

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