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Lung cancer and occupational exposures other than cotton dust and endotoxin among women textile workers in Shanghai, China

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Abstract

Objectives—Numerous epidemiological studies of lung cancer among textile workers worldwide consistently indicate reduced risks related to cotton dust exposure, presumably due to endotoxin contamination. Our objective was to investigate associations with other exposures potentially related to lung cancer, including wool and synthetic fibre dusts, formaldehyde, silica, dyes and metals, that have only been studied to a limited extent in the textile industry.

Methods—We conducted a cas–ecohort study nested within a cohort of 267 400 women textile workers in Shanghai, China. We compared work assignments and exposure histories of 628 incident lung cancer cases, diagnosed during 1989–1998, with those of a reference subcohort of 3188 workers. We reconstructed exposures with a job–exposure matrix developed specifically for textile factories. Cox proportional hazards modelling was applied to estimate age/smoking-adjusted relative risks (hazard ratios) and risk gradients associated with job assignments and specific agents other than cotton dust and endotoxin.

Results—No associations were observed for lung cancer with wool, silk or synthetic fibre dusts, or with other agents. However, increased risks, although statistically imprecise, were noted for ≥10 years' exposures to silica (adjusted HR 3.5, 95% CI 1.0 to 13) and ≥10 years' exposures to formaldehyde (adjusted HR 2.1, 95% CI 0.4 to 11).

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Competing interests None.

Patient consent Obtained.

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Conclusions—Exposures to silica and formaldehyde, although not widespread among the cohort, may have increased lung cancer risk. Silica is an established human lung carcinogen, whereas there is only weak prior evidence supporting an association with formaldehyde. Both exposures warrant consideration as potential lung carcinogens in textile manufacturing.

Textile and clothing manufacturing is one of the world's largest industries, with women comprising approximately 40% of the workforce.[1] Industrial processes include weaving, spinning, dyeing, knitting and finishing of numerous types of natural and synthetic fibres, maintenance, and textile machine manufacture and repair. Various jobs and textile industry exposures that have been investigated in relation to risk of lung cancer include cotton, wool, silk and synthetic fibre dusts, formaldehyde and mineral oils.[2] The most consistent epidemiological finding from occupational cohort studies has been an inverse exposure–response relationship between lung cancer risk and cotton dust.[3-8] The presumed protective agent in cotton textile factories is endotoxin contamination,[9] which may exert immune-mediated anti-carcinogenic effects.[10]

We observed a reduced lung cancer incidence in the cohort on which this study is based compared to rates for Shanghai women during 1989–1998.[6] The standardised incidence ratio (SIR) was 0.8 (95% CI 0.7 to 0.9) for the entire cohort, and a slightly larger deficit (SIR 0.7, 95% CI 0.6 to 0.8) was found for women whose primary work assignment was in cotton factories.[6] We subsequently demonstrated a strong inverse dose–response trend for quantitative estimates of endotoxin exposure.[11]

There has only been limited research on lung cancer in relation to exposures other than cotton dust in the textile industry. Findings from a large hospital-based case–control study in Montreal[12] indicated reduced lung cancer risks associated with exposures to cotton, wool and synthetic textile dusts. Excess lung cancer risks were observed in several operations in a French cohort study of synthetic fibre (polyester, polyamide) spinning workers, although specific causative factors could not be identified, nor could confounding by asbestos be discounted.[13]

Several studies of lung cancer conducted in China are also relevant to our investigation, despite not having focused on specific workplace exposures. Levin *et al*[14] reported a significantly reduced lung cancer risk for cotton textile employment in Shanghai, with similar results observed for men and women, smokers and non-smokers. In contrast, no associations with textile employment were observed in case–control studies conducted in Shenyang and Harbin, China[15] and Tianjin, China.[16]

Among other characteristic textile industry exposures, there is very limited epidemiological evidence for causal associations of lung cancer with formaldehyde[17] or machining fluids.[18] Exposures to dyes, solvents, bleaches and finishing agents, all of which occur in various textile processes, have not been associated with lung cancer.

We conducted a nested case–cohort study of lung cancer incidence in relation to workplace exposures among women employed in the textile industry in Shanghai, China. Our primary objectives were to examine associations of lung cancer with dust and chemical exposures other than cotton dust and endotoxin to identify other potential occupational risk or protective factors in a large cohort of women with very low smoking prevalence.

METHODS

Study subjects and cancer incidence ascertainment

The base cohort consisted of 267 400 women textile workers from 526 factories who were enrolled in the late 1980s in an intervention trial of breast self-examination. A detailed description of the cohort is contained in publications by Thomas *et al.*[19 20] The cohort included active and retired women employees from member companies of the Shanghai Textile Industry Bureau (STIB) who were born between 1 January 1925 and 31 December 1958. At enrolment into the trial, women were administered a baseline questionnaire eliciting data on demographic variables, lifestyle habits, including cigarette smoking and alcohol use, and reproductive history.

Follow-up of the cohort has been described previously.[6 19 20] Cancer incidence was ascertained for the years 1989–1998, inclusive, from annual medical reports submitted by the factory clinics to a cancer registry maintained by the STIB Station for the Prevention and Treatment of Cancer. Only 7.2% of the cohort had left the STIB by 31 December 1998.[20] Cancer diagnoses were confirmed by computerised matching of the cohort with records from the Shanghai Cancer Registry (SCR)[21 22] and by medical record review. Initially, records from the STIB registry were matched to records from the SCR for concordance with diagnosis date (within 6 months), cancer diagnosis (ICD-9), name, date of birth and address. For records without a match in the SCR, field workers reviewed medical records to confirm the cancer diagnosis. We identified 641 lung cancer cases (ICD-9 code 162) during the period of follow-up.[6] Among the 628 cases for whom work history data were available, diagnoses were verified for 522 cases; 209 were confirmed histologically, 197 were based on x-ray and other imaging methods, 14 were diagnosed by clinical exams, 2 were identified surgically, and 100 were based on cytological or immunological testing. One case was identified only by death certificate.

A comparison subcohort of 3188 women was selected as a random sample of the entire cohort, stratified on year of birth, using 5-year interval groupings, to correspond to the birth year distribution of all cancers combined. This subcohort was selected for a series of nested case–cohort analyses of multiple cancer sites in this cohort, including the previous analysis of lung cancer and endotoxin.[11] The subcohort size was set to be twice that of the largest case group (breast cancer). Included in the subcohort were three lung cancers.

The study procedures were approved by the Institutional Review Board (IRB) Committee to Protect Human Subjects, Biomedical Research at the University of Washington, the IRB for Research on Human Subjects at the Fred Hutchinson Cancer Research Center, and the IRB for Research on Human Subjects at the Station for the Prevention and Treatment of Cancer of the STIB at Zhong Shan Hospital, Shanghai, China.

Exposure assessment

The Shanghai textile industry is a vertically integrated system that includes the manufacture of fibres, cloth and ancillary products (eg, raincoats), garment assembly, and textile machine manufacture and repair. With the assistance of a team of occupational hygienists employed by the STIB, we developed a job–exposure matrix (JEM) that permitted classification of workshops, processes and component jobs according to exposures to dusts, chemicals and physical agents potentially associated with cancer risk[23]: cotton, wool, silk and synthetic fibre dusts; endotoxin; solvents; metals; dyes; inks; lubricants (including machining fluids); bleaches; acids, bases and caustics; resins, monomers and coatings; formaldehyde; and silica. Exposure classification was based on factory type (eg, cotton spinning, polyester dyeing), workshop (process and machinery) and job- or task-related information obtained from government and factory inspection reports describing basic processes and materials utilised since each factory was opened. The available historical exposure information only permitted dichotomous (exposed versus not exposed) classifications from the JEM. We derived cumulative exposure durations for job types and exposures by linking the JEM with study subjects' work history data. Quantitative exposure estimates for endotoxin, available from our previous analyses,[11] were derived from historical cotton dust sampling data obtained from factory inspections conducted by the government, and measurements of endotoxin made from cotton dust samples we collected in 2002.[24 25] Complete textile industry work history information could not be obtained from factory records for 13 of the 641 lung cancer cases and three of the 3185 subcohort members without lung cancer. Analyses excluding the 106 cases without diagnostic confirmation were not materially different from those conducted on all 628 cases with work history data. Thus, we will present findings for the 628 cases and 3188 subcohort workers.

Data analysis

We conducted Cox proportional hazards modelling, adapted for the case–cohort design,[26] to estimate relative risks (HRs and associated 95% CIs) associated with duration of employment in various jobs and processes, and duration of exposures to specific agents. Robust variance estimates were used to compute standard errors of the hazard ratio.[27] The period of risk was defined as time since entry into the cohort, at the date of the baseline questionnaire, until the date of lung cancer diagnosis, date lost to follow-up, or end of follow-up. We censored follow-up at the dates last employed for the 96 women who permanently left the STIB before 31 December 1998. The three lung cancer cases who overlapped with the subcohort contributed person-time to the subcohort's person-time experience until their dates of diagnosis. We defined exposure strata as 0 (reference), 1–4, 5–9, 10–19 and ≥20 years. In some instances of small numbers, we defined strata as 0, 1–9 and ≥10 years, or simply computed hazard ratios for ever versus never exposed (>0, 0 years).

All effect estimates were adjusted for age and cigarette smoking (ever versus never). The results for models with age adjustment and for models with age and smoking adjustment were nearly identical; consequently, we present the latter. We also performed analyses with and without adjustment of cumulative exposure to endotoxin to address potential confounding. Additional analyses with lagged exposures, by 10 and 20 years, were conducted to take into account disease latency. The findings only changed minimally when we adjusted for endotoxin or when exposures were lagged. Therefore, we only present unlagged data without adjustment for endotoxin. All data analyses were performed with SAS v 9.2.

RESULTS

The cases' and subcohort's (not including the three overlapping lung cancer cases) distributions of demographic, lifestyle and reproductive history details, as of the beginning of follow-up, are shown in table 1. The cases were somewhat older than the non-cases, and, as a consequence of being in earlier birth cohorts, also tended to have more children and earlier year of first employment. As expected, a history of ever having smoked was more common among cases (11.5%) than in the subcohort (4.6%), and proportionately more cases (5.9%) than non-cases (1.6%) smoked for 30 years or longer. Alcohol consumption, defined as at least one drink per month, did not differ between groups.

Analyses by duration of employment in broad process groupings (table 2) did not indicate any notable associations, with the exception of an inverse risk trend for employment in cotton handling, spinning and processing jobs. HR was 0.7 (95% CI 0.5 to 1.0) for ≥20 years' duration. This trend was expected in view of the strong correlation between cotton dust and endotoxin, and the previously observed inverse dose–response relationship with endotoxin.[11]

Results for exposures to chemicals and dusts (other than cotton dust and endotoxin) are presented in table 3. There were no consistent patterns of lung cancer risk associated with any of the dusts or chemicals, with the exceptions of silica and formaldehyde for which elevated risks, albeit statistically imprecise, were observed. The HRs for silica were, respectively, 4.5 (95% CI 0.3 to 59) and 3.5 (95% CI 1.9 to 13) for 1–9 years' and ≥10 years' exposure. We also observed an excess risk related to ≥10 years' exposure to formaldehyde (HR 2.1, 95% CI 0.4 to 11) that was based on very small numbers of exposed cases (N=2) and non-cases (N=5).

DISCUSSION

Cotton dust is the most common exposure experienced by this cohort of women workers, and the association of the contaminant endotoxin with a reduced lung cancer risk is well established.[10] In this analysis, we focused on other dust and chemical exposures that are less common than cotton dust and, with the exception of silica, for which evidence for lung carcinogenesis is either sparse or inconsistent.

The observed elevated risk among women exposed to silica is not surprising in view of its classification by the International Agency for Research on Cancer (IARC) as a confirmed (category 1) human lung carcinogen.[28] Excessive lung cancer risks have been noted consistently in many silica-exposed occupations,[29] although to our knowledge, this is the first such report from the textile industry. Silica exposure in the Shanghai textile industry occurred almost exclusively in the foundries where textile machines were made and repaired. Although a relatively small number of women workers were exposed to silica, its hazardous potential deserves attention in the textile industry. However, any conclusions about a carcinogenic risk from silica in this cohort should be made with some caution because we could not assess exposures to carcinogenic polycyclic aromatic hydrocarbons that also occur in foundries.[30] Confounding by asbestos is very unlikely, as we did not identify any jobs held by women workers with potential exposures.

Our observation of an elevated lung cancer risk associated with formaldehyde was based on very small numbers of exposed workers. Formaldehyde, similar to silica, is a relatively rare exposure among Shanghai women textile workers, with <1% of workers routinely exposed.[23] There is little epidemiological support for an association of lung cancer with formaldehyde,[17] including null findings from a cohort study of US garment workers[31] whose jobs are similar in some respects to workers in our cohort. In spite of the absence of consistent evidence for lung carcinogenesis, formaldehyde has been classified by IARC as a category 1 carcinogen based on a causal relationship with nasopharyngeal cancer and relatively strong associations with sinonasal cancer and leukaemia.[32] In this study, too few subjects were exposed to formaldehyde to permit any strong conclusions about a possible relationship with lung cancer.

The two-fold elevated risk observed for ≥20 years' employment in dyeing jobs (table 2) was unanticipated, as there little prior evidence to suggest associations with lung cancer,[33] and our findings for exposures to dyes showed no associations (table 3).

There are several important strengths of our study. This study had a substantially larger base cohort, and hence a larger number of of lung cancer cases, than any previously reported study of textile workers. Our exposure assessment was also more extensive, detailed and specific than those in previous occupational cohort or population-based studies because we were able to obtain complete work history data that could be linked with a specifically designed JEM. Confounding by cigarette smoking, which is an obvious concern in any occupational study of lung cancer, was an unlikely source of bias because of the low smoking prevalence in the cohort. Data on smoking habits available from the baseline questionnaire administered on entry into the breast self-examination trial, although possibly incomplete, also enabled control of potential confounding. We did not have data on some other important lung cancer risk factors in China, such as exposure to passive smoke, cooking practices and radon. Nonetheless, exposures to these factors were unlikely to be related to occupational exposure types and levels experienced by the cohort, and thus were probably not confounders. Availability of quantitative data for endotoxin allowed control for potential confounding of associations with other agents, although none was noted.

The main limitation of our study was the absence of quantitative historical exposure data for the agents of interest considered here. Instead, we relied on occupational hygiene ratings and duration of exposure as the dose metric, which does not reflect differences in exposure intensities between jobs and over time. Moreover, our analyses were based on relatively broad groupings for some agents, such as metals, which may have suffered from misclassification that obscured agent-specific associations. There is also the possibility of a healthy worker survivor bias, whereby associations would have been under-estimated, because follow-up (1989–1998) occurred many years after hire for most cohort members. However, such bias was probably minimal because early termination from employment was very rare due to governmentally-regulated work practices in China. Consistent with this pattern, mean employment durations for the lung cancer cases and non-case subcohort members were 25.8 and 25.9 years, respectively. Moreover, during follow-up, cohort members were aged 40–73 years, when most lung cancer incidence typically occurs.

Despite these caveats, both silica and formaldehyde warrant concern as potential lung carcinogens in the textile industry. Similar findings from other textile worker cohort studies would strengthen these causal conclusions. However, unlike the Shanghai textile industry, textile industries in most countries worldwide do not include foundries; consequently, silica may not be a widespread hazard. In contrast, formaldehyde exposures are generally more prevalent in textile manufacturing.

What this paper adds

- Little is known about potential aetiological relationships between lung cancer and textile industry exposures apart from associations with cotton dust and endotoxin.
- In this study of women textile workers in Shanghai, China, lung cancer risks were not associated with exposures to most other dusts and chemicals.
- The exceptions were silica and formaldehyde for which elevated risks were observed for exposures longer than 10 years, although these findings were based on small numbers.
- Silica and formaldehyde warrant consideration as potential lung cancer hazards in other textile factories.

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Table 1

Demographic, employment, smoking and reproductive history details of lung cancer cases and subcohort non-cases

	Cases		Non-cases	
	N	**(%)**	**N**	**(%)**
Total	628	100	3185	100
Year of birth				
1925–1929	246	39.2	934	29.3
1930–1934	223	35.5	917	28.8
1935–1939	72	11.5	367	11.5
1940–1944	24	3.8	163	5.1
1945–1949	26	4.1	282	8.9
1950–1954	24	3.8	322	10.1
1955–1958	13	2.1	200	6.3
Year first employed in STIB				
Before 1945	49	7.8	211	6.6
1945–1949	153	24.4	668	21.0
1950–1954	81	12.9	321	10.1
1955–1959	148	23.6	611	19.2
1960–1964	77	12.3	395	12.4
1965–1969	57	9.1	391	12.3
1970 and after	63	10.0	588	18.5
Smoking status at baseline				
Never	556	88.5	3040	95.4
Ever	72	11.5	145	4.6
Former smoker	7	1.1	26	0.8
Current smoker	65	10.4	119	3.7
Smoked <10 years	7	1.1	29	0.9
10 to <20 years	14	2,2	32	1.0
20 to <30 years	14	2.2	32	1.0
Smoked ≥30 years	37	5.9	52	1.6
Ever drink alcohol at baseline				
No	516	82.2	2609	81.9
<Once/month	86	13.7	433	13.6
≥Once/month	26	4.1	143	4.5
Number of live births at baseline				
None	34	5.4	124	3.9
1	79	12.6	751	23.5
2–3	256	40.8	1212	38.1
≥4	259	41.2	1098	34.5

STIB, member companies of the Shanghai Textile Industry Bureau.

Table 2

Relative risks (HRs) for lung cancer in relation to duration of employment in jobs grouped by similar processes

Process grouping/ years worked	Cases	Non-cases	HR*	(95% CI)
Warehouse, packing, quality control				
0	530	2665	1.0	
1–9	36	182	1.1	(0.8 to 1.7)
10–19	32	148	1.2	(0.8 to 1.9)
≥20	30	190	0.8	(0.5 to 1.2)
Cotton handling, processing, spinning				
0	509	2558	1.0	
1–9	35	123	1.2	(0.8 to 1.7)
10–19	30	153	1.0	(0.6 to 1.4)
≥20	54	321	0.7	(0.5 to 1.0)
Wool handling, processing, spinning				
0	608	3084	1.0	
1–9	5	20	1.1	(0.4 to 3.0)
10–19	5	28	0.8	(0.3 to 2.2)
≥20	10	53	0.7	(0.4 to 1.4)
Silk handling, processing, spinning				
0	622	3153	1.0	
>0	6	32	1.0	(0.4 to 2.3)
Synthetic fibre handling, processing, spinning				
0	612	3097	1.0	
1–9	2	31	0.2	(0.1 to 1.0)
10–19	8	25	1.5	(0.7 to 3.5)
≥20	6	32	0.7	(0.3 to 1.8)
Mixed fibre handling, processing, spinning				
0	525	2743	1.0	
1–9	20	126	0.7	(0.4 to 1.2)
10–19	31	114	1.5	(0.9 to 1.7)
≥20	52	202	1.2	(0.9 to 1.7)
Scouring, bleaching				
0	624	3158	1.0	
>0	4	27	0.8	(0.3 to 2.8)
Dyeing				
0	613	3129	1.0	
1–9	5	19	1.5	(0.5 to 4.4)
10–19	4	19	1.0	(0.3 to 2.8)
≥20	6	18	2.3	(0.9 to 6.1)
Finishing				
0	622	3145	1.0	

Process grouping/ years worked	Cases	Non-cases	HR*	(95% CI)
>0	6	40	0.7	(0.3 to 1.7)
Weaving				
0	384	2065	1.0	
1–9	61	231	1.4	(1.0 to 1.9)
10–19	67	295	1.2	(0.9 to 1.7)
≥20	116	594	0.9	(0.8 to 1.2)
Sewing, cutting				
0	575	2890	1.0	
1–9	17	87	1.2	(0.7 to 2.0)
10–19	19	96	1.1	(0.7 to 1.9)
≥20	17	112	0.9	(0.5 to 1.6)
Maintenance				
0	610	3079	1.0	
1–9	7	48	1.0	(0.4 to 2.1)
10–19	6	27	1.2	(0.4 to 2.6)
≥20	5	31	1.0	(0.4 to 2.6)
Administration, other non-production				
0	451	2277	1.0	
1–9	74	338	1.8	(1.0 to 1.8)
10–19	55	268	1.3	(1.0 to 1.9)
≥20	48	302	0.9	(0.7 to 1.3)

*HR adjusted for age and smoking.

Table 3

Relative risks (HRs) for lung cancer in relation to duration of exposure to textile industry agents

Agent/years exposed	Cases	Non-cases	HR*	(95% CI)
Wool dust				
0	530	2736	1.0	
1–4	12	56	0.9	(0.5 to 1.7)
5–9	10	111	1.6	(0.7 to 3.2)
10–19	25	38	1.1	(0.7 to 1.8)
≥20	51	244	1.0	(0.7 to 1.4)
Silk				
0	595	3022	1.0	
1–9	9	37	1.3	(0.6 to 2.8)
≥10	24	126	1.0	(0.7 to 1.6)
Synthetic fibre dust				
0	360	1922	1.0	
1–4	23	128	0.9	(0.6 to 1.5)
5–9	26	110	1.5	(0.9 to 2.3)
10–19	71	361	1.1	(0.8 to 1.5)
≥20	148	664	1.2	(0.9 to 1.4)
Solvents				
0	543	2727	1.0	
1–4	16	83	1.2	(0.7 to 2.0)
5–9	17	86	1.2	(0.7 to 2.2)
10–19	23	139	0.9	(0.6 to 1.4)
≥20	29	150	1.2	(0.8 to 1.9)
Acids, bases, caustics				
0	578	2922	1.0	
1–4	12	43	1.9	(0.9 to 3.7)
5–9	9	47	1.3	(0.6 to 2.7)
10–19	17	86	1.1	(0.7 to 1.9)
≥20	12	87	0.8	(0.4 to 1.5)
Dyes				
0	614	3089	1.0	
1–9	4	30	1.0	(0.3 to 3.0)
≥10	10	66	0.9	(0.4 to 1.7)
Resins, monomers, coatings				
0	619	3097	1.0	
1–9	5	31	1.0	(0.4 to 2.6)
≥10	4	57	0.4	(0.1 to 1.1)
Metals				
0	585	2958	1.0	
1–4	8	46	0.9	(0.4 to 2.0)

Agent/years exposed	**Cases**	**Non-cases**	**HR***	**(95% CI)**
5–9	9	41	1.5	(0.7 to 3.1)
10–19	12	58	1.0	(0.5 to 1.9)
≥20	14	82	1.1	(0.6 to 2.0)
Lubricants				
0	204	1210	1.0	
1–4	33	174	1.0	(0.7 to 1.5)
5–9	45	157	1.8	(1.2 to 2.7)
10–19	105	495	1.2	(0.9 to 1.6)
≥20	241	1149	1.0	(0.8 to 1.3)
Silica dust				
0	623	3177	1.0	
1–9	1	2	4.5	(0.3 to 59)
≥10	4	6	3.5	(1.0 to 13)
Formaldehyde				
0	626	3174	1.0	
1–9	0	6	0	–
≥10	2	5	2.1	(0.4 to 11)

*HR adjusted for age, smoking.