



Original Contribution

Occupational Risk Factors for Esophageal and Stomach Cancers among Female Textile Workers in Shanghai, China

Karen J. Wernli^{1,2}, E. Dawn Fitzgibbons¹, Roberta M. Ray¹, Dao Li Gao³, Wenjin Li¹, Noah S. Seixas⁴, Janice E. Camp⁴, George Astrakianakis⁴, Ziding Feng¹, David B. Thomas^{1,2}, and Harvey Checkoway^{2,4}

¹ Program in Epidemiology, Fred Hutchinson Cancer Research Center, Seattle, WA.

² Department of Epidemiology, School of Public Health and Community Medicine, University of Washington, Seattle, WA.

³ Department of Epidemiology, Zhong Shan Hospital Cancer Center, Shanghai, China.

⁴ Department of Environmental and Occupational Health Sciences, School of Public Health and Community Medicine, University of Washington, Seattle, WA.

Received for publication June 27, 2005; accepted for publication November 16, 2005.

The authors evaluated associations between occupational exposures in the textile industry and the risks of esophageal cancer and stomach cancer. The authors conducted a case-cohort study nested in a cohort of female textile workers in Shanghai, China. One hundred and two workers with incident esophageal cancer and 646 workers with incident stomach cancer diagnosed between 1989 and 1998 were compared with an age-stratified reference subcohort ($n = 3,188$). Work histories were ascertained for all study subjects from factory personnel records or interviews. Exposures were reconstructed for chemicals and dusts by linking work history data with a job-exposure matrix developed for the Shanghai textile industry. Hazard ratios and 95 percent confidence intervals were calculated with Cox proportional hazards modeling adapted for the case-cohort design. Risk of esophageal cancer was associated with long-term (≥ 10 years) exposure to silica dust (hazard ratio = 15.8, 95% confidence interval: 3.5, 70.6) and metals (hazard ratio = 3.7, 95% confidence interval: 1.9, 7.1). Cumulative exposure to endotoxin, a contaminant of cotton dust, was inversely related to risks of both esophageal cancer (p -trend = 0.01) and stomach cancer (p -trend < 0.001) when exposures were lagged 20 years. Endotoxin has not been previously reported to be a protective factor for either stomach cancer or esophageal cancer and therefore warrants further study.

cotton fiber; endotoxins; esophageal neoplasms; occupational exposure; occupations; silicon dioxide; stomach neoplasms; textile industry

Abbreviations: CI, confidence interval; EU, endotoxin units; HR, hazard ratio; STIB, Shanghai Textile Industry Bureau.

In 2002, the worldwide numbers of incident cases of esophageal and stomach cancer in women were estimated to be 146,000 and 329,000, respectively (1). The burden of these two cancers is a particular concern in developing countries, where they constitute a substantially larger proportion of all cancer cases than in developed countries (1). In China, these two cancers are estimated to represent 19.7

percent of all incident cancer cases diagnosed among women in 2005 (2).

Established risk factors for esophageal cancer include cigarette smoking, alcohol consumption, and Barrett's esophagus, resulting from gastroesophageal reflux disease (3). *Helicobacter pylori* infection is the predominant established risk factor for stomach cancer (4, 5); other potential risk

factors include dietary factors (i.e., low intakes of fruit and vegetables and high intakes of salt and cured foods) and exposure to high-dose ionizing radiation (4).

Few occupational exposures have been consistently associated with either esophageal cancer or stomach cancer. Polycyclic aromatic hydrocarbons, silica, and mixed dusts have been consistently shown to increase risk of esophageal cancer (6–12). A decreased risk of stomach cancer has been reported among education employees (13) and technical workers (14). Although several agents have been hypothesized as potential risk factors for stomach cancer, no clear associations have been established.

Previous research on these two cancers among female textile workers has been limited and inconclusive. Simpson et al. (15) detected a proportionate increased risk of stomach cancer incidence among textile spinners, doublers, and twisters (proportional incidence ratio = 1.5, 95 percent confidence interval (CI): 1.2, 1.9) and textile winders and reelers (proportional incidence ratio = 1.4, 95 percent CI: 1.0, 1.7). In contrast, Aragonés et al. (13) detected a significantly decreased risk of stomach cancer among female sewers (relative risk = 0.7, 95 percent CI: 0.6, 1.0) but not among textile workers in general (relative risk = 1.0, 95 percent CI: 0.7, 1.6). Neither study investigated associations with esophageal cancer. Moreover, these studies did not consider associations with specific textile industry chemicals or physical agents.

Weiderpass et al. (6) reported a modestly increased risk of esophageal cancer associated with textile dust among women in the highest exposure category (relative risk = 1.3, 95 percent CI: 0.9, 1.8), although there was no association between stomach cancer and textile dust (relative risk = 1.0, 95 percent CI: 0.9, 1.2). The type of textile dust studied was not specified. We previously reported lower-than-expected rates of esophageal cancer (standardized incidence ratio = 0.5, 95 percent CI: 0.4, 0.7) and stomach cancer (standardized incidence ratio = 0.8, 95 percent CI: 0.7, 0.9) in the cohort of female textile workers on which this study is based (16).

In this report, we present findings from analyses of associations between occupational exposures in the Shanghai, China, textile industry and cancers of the esophagus and stomach. Our aim was to investigate previously reported associations and to identify potentially important new associations between occupational exposures and these two cancers in the textile industry.

MATERIALS AND METHODS

Study subjects

Details on the enumeration and follow-up of the cohort have been published elsewhere (17, 18). Briefly, in 1989–1991, 267,400 active and retired female workers from 526 textile factories operated by the Shanghai Textile Industry Bureau (STIB) were enrolled in a randomized trial of breast self-examination. The cohort was restricted to women born between January 1, 1925, and December 31, 1958. A baseline questionnaire elicited data on several risk factors, including smoking history, alcohol consumption, and reproductive history.

Cancer incidence was ascertained for the period ranging from enrollment in the trial through December 31, 1998. We identified 103 cases of esophageal cancer (*International Classification of Diseases*, Ninth Revision, code 150) and 653 cases of stomach cancer (*International Classification of Diseases*, Ninth Revision, code 151). As part of the planned economy in China, both active and retired study women received all initial medical care through health clinics in their factories. The factories reported all incident cancer diagnoses to the STIB Tumor and Death Registry. For verification of cancer diagnosis, all cancer cases were matched to the Shanghai Cancer Registry on the woman's name, date of birth, cancer site, and diagnosis date. Trained field-workers reviewed medical records to confirm the diagnosis for cancer cases that did not match to the registry (16). We confirmed cancer diagnoses through a cancer registry match or medical record review for 91.2 percent of esophageal cancer cases and 93.3 percent of stomach cancer cases. Women whose cancers were not confirmed were more likely to be older, retired workers. Cases not confirmed by these methods were included in the analyses presented.

A subcohort ($n = 3,199$) was selected from the entire cohort for comparison with the cancer cases. The subcohort was selected as a stratified random sample of the cohort to match the combined birth-year distribution (in 5-year age strata) of all cancer cases included in a series of nested case-cohort studies of multiple cancer sites. One esophageal cancer case and 13 stomach cancer cases were selected for inclusion in the subcohort.

The study was approved by the institutional review boards of the Fred Hutchinson Cancer Research Center (Seattle, Washington) and the Station for Prevention and Treatment of Cancer of the STIB (Shanghai, China), in accordance with an assurance filed with the Office for Human Research Protections of the US Department of Health and Human Services (Washington, DC).

Data collection

To assess work history in the textile industry, experienced field-workers visited all 503 factories where the study subjects worked and abstracted information regarding all textile-industry jobs that the women had held. The information collected included the textile process involved, a task description, and dates of employment. Data were collected from factory personnel records or interviews with co-workers, supervisors, or subjects. Field-workers collected information from factory personnel records for 79.6 percent of noncases, 75.9 percent of esophageal cancer cases, and 81.2 percent of stomach cancer cases. If subjects were contacted for in-person interviews, they provided oral consent to the field-workers. We were able to collect occupational information for 102 esophageal cancer cases (99.0 percent) and 646 stomach cancer cases (98.9 percent). In the subcohort, 11 women did not have complete information on their work history and were excluded. This resulted in a final comparison group of 3,188 women (99.7 percent).

For each factory where a woman worked, experienced local industrial hygienists collected information regarding the textile processes operated within the factory,

manufacturing dates, types of work performed, and hazardous agents present. In addition, the industrial hygienists collected measurement data from historical monitoring records maintained by the Shanghai Municipal Centers for Disease Control or the STIB.

Exposure assessment

A job-exposure matrix was developed for the Shanghai textile industry (K. J. W., unpublished manuscript). The job-exposure matrix was based on a composite of two sources: 1) a-priori assessment of exposures by textile process determined by US industrial hygienists for classification of fiber/process combinations according to the likely presence of various categories of dusts, chemicals, and physical agents; and 2) the prevalence of exposures reported by the Chinese industrial hygienists in specific textile processes within the factory. A positive exposure assignment was indicated in the job-exposure matrix if either assessment indicated that exposure was present. We classified exposure to 23 different chemical or dust groupings (e.g., synthetic fiber dust; mixed fiber dust; solvents; acids, bases, and caustics; bleaching agents; dyes; inks; gases; salts; resins and coatings; metals; and electromagnetic fields/nonionizing radiation). There was sufficient detail in the historical records to allow exposure assignment to 12 specific hazardous agents: cotton, wool, and silica dusts; formaldehyde; benzene; styrene; trichloroethane; tetrachloroethylene; sulfuric and chromic acids; chrome pigment; and acrylonitrile.

In addition, we obtained quantitative data on cotton dust and endotoxin. Details on this assessment are provided elsewhere (19). Briefly, quantitative assessment of cotton dust exposure was estimated for each specific textile process based on historical measurements made by industrial hygienists from 56 factories between 1975 and 1999. Endotoxin concentrations were estimated using the predicted cotton dust estimates (mg/m^3) and average concentrations of endotoxin, in endotoxin units (EUs), per milligram of dust mass (EU/mg dust) in each major process from the studies conducted by Christiani et al. (20, 21) and Olenchock et al. (22) and from additional cotton and endotoxin measurement data collected for this study (19). These quantitative estimates were combined with each subject's work history for estimation of cumulative historical exposures to cotton dust and endotoxin by years of employment ($\text{EU}/\text{m}^3 \times \text{years}$). Women who had ever held jobs as machinists or sanitation workers or in wool production were not included in the endotoxin analyses, because measurement data were not available for these processes, which entail potential endotoxin exposure from sources other than cotton dust.

Statistical analyses

We utilized Cox proportional hazards modeling, adapted for the case-cohort design, to estimate relative risks (hazard ratios and 95 percent confidence intervals). The software used was Stata, version 8SE (Stata Corporation, College Station, Texas). A weight of 1 was applied for each case, and weights equal to the reciprocal of the sampling fractions in each 5-year age stratum were applied for all of the noncases

TABLE 1. Demographic characteristics of subcohort members and esophageal and stomach cancer cases among female textile workers, Shanghai, China, 1989–1998

Characteristic	Subcohort (<i>n</i> = 3,188)		Esophageal cancer (<i>n</i> = 102)		Stomach cancer (<i>n</i> = 646)	
	No.	%	No.	%	No.	%
Year of birth						
1925–1929	936	29.4	50	49.0	203	31.4
1930–1934	918	28.8	36	35.3	174	26.9
1935–1939	367	11.5	6	5.9	68	10.5
1940–1944	163	5.1	5	4.9	29	4.5
1945–1949	282	8.8	3	2.9	45	7.0
1950–1954	322	10.1	2	2.0	60	9.3
1955–1958	200	6.3	0		67	10.4
Marital status						
Married	2,899	90.9	80	78.4	581	89.9
Widowed	238	7.5	18	17.6	60	9.3
Divorced	22	0.7	2	2.0	2	0.3
Never married	29	0.9	2	2.0	3	0.5
Smoking*						
Never	3,043	95.5	87	85.3	602	93.2
Ever	145	4.5	15	14.7	44	6.8
Duration of smoking (years)†						
<10	29	0.9	6	5.9	9	1.4
10–19	32	1.0	4	3.9	11	1.7
≥20	84	2.6	5	4.9	24	3.7
Alcohol consumption						
Never	2,612	81.9	86	84.3	545	84.4
<1 occasion per month	433	13.6	11	10.8	76	11.8
≥1 occasion per month	143	4.5	5	4.9	25	3.8
Ever pregnant						
No	110	3.5	7	6.9	20	3.1
Yes	3,078	96.5	95	93.1	626	96.9

* Ever smoking regularly for 6 months or more.

† Among current or former smokers.

in the subcohort (23). Robust variance estimates were used to calculate the standard error of the hazard ratio (24). For cases, person-time was contributed from the time of enrollment in the cohort to the time of cancer diagnosis. For non-case subcohort members, person-time was accumulated from the date of enrollment in the original study to the date of death, the date the woman left employment at any factory within the STIB, or December 31, 1998, whichever came first. Risks associated with various textile manufacturing processes were estimated according to duration of employment or exposure (never exposed, <10 years, or ≥10 years). Risk trends associated with exposures to various dusts and chemical agents were estimated in the same manner. Each exposure variable was added individually to the model.

TABLE 2. Hazard ratios for esophageal and stomach cancer among female textile workers, by duration of work in textile processes, Shanghai, China, 1989–1998

Textile process and duration of work	Distribution in subcohort (no.)	Esophageal cancer			Stomach cancer		
		No.	HR*, †	95% CI*	No.	HR†	95% CI
Warehouse							
Never	2,668	95	1.0	Referent	545	1.0	Referent
<10 years	182	2	0.4	0.1, 1.5	45	1.2	0.9, 1.7
≥10 years	338	5	0.4	0.2, 1.1	56	0.8	0.6, 1.1
<i>p</i> -trend			0.07			0.24	
Cotton							
Never	2,590	81	1.0	Referent	531	1.0	Referent
<10 years	123	1	0.2	0.1, 1.4	30	1.1	0.8, 1.7
≥10 years	475	20	1.1	0.7, 1.9	85	0.8	0.6, 1.1
<i>p</i> -trend			0.63			0.14	
Wool							
Never	3,086	97	1.0	Referent	625	1.0	Referent
<10 years	20	1	1.3	0.2, 10.0	3	0.7	0.2, 2.4
≥10 years	82	4	1.1	0.4, 3.2	18	1.1	0.6, 1.8
<i>p</i> -trend			0.80			0.87	
Synthetic fiber							
Never	3,100	96	1.0	Referent	633	1.0	Referent
<10 years	31	3	2.1	0.6, 7.2	2	0.3	0.1, 1.2
≥10 years	57	3	1.2	0.4, 4.2	11	0.9	0.4, 1.6
<i>p</i> -trend			0.65			0.52	
Mixed fiber							
Never	2,745	93	1.0	Referent	532	1.0	Referent
<10 years	126	1	0.2	0.0, 1.3	37	1.5	1.0, 2.2
≥10 years	317	8	0.7	0.3, 1.4	77	1.3	1.0, 1.6
<i>p</i> -trend			0.28			0.08	
Dyeing							
Never	3,132	100	1.0	Referent	635	1.0	Referent
<10 years	19	1	2.1	0.3, 17.8	4	0.9	0.3, 2.8
≥10 years	37	1	1.0	0.1, 7.3	7	0.9	0.4, 2.0
<i>p</i> -trend			0.91			0.78	

Table continues

Cumulative exposures to endotoxin and cotton dust were categorized into quartiles according to the distributions of the subcohort members. We also evaluated risks related to endotoxin and cotton dust exposures with lag intervals of 10 years and 20 years to examine possible latency effects. Tests for trend were conducted using the median values of duration within each category for the subcohort.

Because subcohort women were not matched to individual cancer cases but were chosen for a study of multiple cancer sites, the age distribution of some of the cancer case groups (e.g., esophageal cancer) differed from that of the subcohort women. The results did not differ when we controlled for age as a continuous or categorical variable. We present results adjusted for age as a continuous variable. All estimates were also adjusted for smoking history (ever/never) as ascertained at baseline.

RESULTS

Women with esophageal cancer tended to be older, were more likely to be widowed, and were less likely to have ever been pregnant than women in the subcohort (table 1). Nearly 15 percent of esophageal cancer cases were current or former regular smokers, as compared with only 4.5 percent of the subcohort (hazard ratio (HR) = 2.5, 95 percent CI: 1.4, 4.5). Stomach cancer cases were similar to the subcohort with respect to demographic, lifestyle, and reproductive factors (table 1).

There were few significantly increased or decreased risks for either cancer associated with work in textile processes (table 2). A significant trend of increasing risk of esophageal cancer with duration of employment in other textile manufacturing jobs was observed (for ≥10 years, HR = 4.0,

TABLE 2. Continued

Textile process and duration of work	Distribution in subcohort (no.)	Esophageal cancer			Stomach cancer		
		No.	HR†	95% CI	No.	HR†	95% CI
Weaving							
Never	2,068	65	1.0	Referent	402	1.0	Referent
<10 years	231	8	1.1	0.5, 2.3	58	1.3	1.0, 1.8
≥10 years	889	29	0.9	0.6, 1.5	186	1.1	0.9, 1.3
<i>p</i> -trend			0.77			0.43	
Cutting and sewing							
Never	2,892	93	1.0	Referent	585	1.0	Referent
<10 years	87	3	1.4	0.4, 4.6	12	0.7	0.4, 1.3
≥10 years	209	6	1.1	0.5, 2.5	49	1.2	0.9, 1.7
<i>p</i> -trend			0.81			0.30	
Maintenance							
Never	3,082	99	1.0	Referent	621	1.0	Referent
<10 years	48	1	1.0	0.1, 7.1	9	1.0	0.5, 2.0
≥10 years	58	2	1.3	0.3, 5.5	16	1.4	0.8, 2.4
<i>p</i> -trend			0.80			0.30	
Administration and nonproduction							
Never	2,279	80	1.0	Referent	474	1.0	Referent
<10 years	339	11	1.3	0.7, 2.5	78	1.1	0.9, 1.5
≥10 years	570	11	0.7	0.4, 1.4	94	0.8	0.6, 1.0
<i>p</i> -trend			0.33			0.08	
Other manufacturing‡							
Never	3,023	90	1.0	Referent	610	1.0	Referent
<10 years	59	2	1.6	0.4, 7.0	11	0.9	0.5, 1.8
≥10 years	106	10	4.0	2.0, 8.2	25	1.2	0.7, 1.8
<i>p</i> -trend			<0.01			0.57	

* HR, hazard ratio; CI, confidence interval.

† Adjusted for age (years; continuous variable) and smoking status (ever/never) at baseline.

‡ "Other manufacturing" included metal machining, welding, foundry work, forging, metal finishing, gluing, paper-parts formation, wood-shuttle-making, cement production, and steel wire production.

95 percent CI: 2.0, 8.2). Working in warehousing resulted in a 60 percent reduction in esophageal cancer (for ≥10 years, HR = 0.4, 95 percent CI: 0.2, 1.1), though there were few case women who worked in these jobs. Working in jobs with mixed fiber exposure was associated with an increased risk of stomach cancer, but there was no trend in risk with duration of employment.

Risk of esophageal cancer was significantly associated with exposures to metals (for ≥10 years, HR = 3.7, 95 percent CI: 1.9, 7.1) and silica (for ≥10 years, HR = 15.8, 95 percent CI: 3.5, 70.6), with significant trends of increasing risk with increasing duration of exposure (table 3). There was also an increased risk of esophageal cancer associated with 10 or more years of exposure to acids, bases, and caustics (HR = 2.3, 95 percent CI: 1.2, 4.6). There were only modestly increased risks of stomach cancer associated with exposure to electromagnetic fields and lubricants, though there were no trends of sharply increasing risk with duration of exposure.

The trends for cotton dust did not indicate consistent associations for either cancer (table 4). Markedly decreased risks of esophageal and stomach cancer were observed in relation to cumulative exposure to endotoxin, and the inverse gradient became more pronounced when exposures were lagged by 20 years (table 5).

DISCUSSION

Our results indicate that there were increased risks of esophageal cancer associated with exposures to silica dust and metals. These two exposures are often present in other manufacturing processes that are not directly related to fabric and garment manufacturing. The Shanghai textile industry is comprehensive and includes fabric-making, garment assembly, and other manufacturing processes (i.e., metal work, foundry work, welding and forging, cementing, and making steel wire). Exposures to welding dust, lead fumes,

TABLE 3. Hazard ratios for esophageal and stomach cancer among female textile workers, by duration of exposure to the hazardous agent present in the textile process, Shanghai, China, 1989–1998

Hazardous agent and duration of exposure	Distribution in subcohort (no.)	Esophageal cancer			Stomach cancer		
		No.	HR*,†	95% CI*	No.	HR†	95% CI
Wool							
Never	2,738	91	1.0	Referent	553	1.0	Referent
<10 years	94	2	0.5	0.1, 2.1	16	0.8	0.5, 1.4
≥10 years	356	9	0.7	0.3, 1.3	77	1.1	0.8, 1.4
<i>p</i> -trend			0.20			0.81	
Synthetic fiber dust							
Never	1,922	65	1.0	Referent	385	1.0	Referent
<10 years	238	7	0.9	0.4, 2.1	47	1.0	0.7, 1.4
≥10 years	1,028	30	0.8	0.5, 1.3	214	1.0	0.9, 1.2
<i>p</i> -trend			0.42			0.71	
Mixed fiber dust (synthetic/natural)							
Never	3,049	95	1.0	Referent	620	1.0	Referent
<10 years	43	1	0.5	0.1, 4.1	7	0.8	0.4, 1.8
≥10 years	96	6	1.5	0.6, 3.5	19	1.0	0.6, 1.6
<i>p</i> -trend			0.52			0.76	
Solvents							
Never	2,730	86	1.0	Referent	547	1.0	Referent
<10 years	169	5	1.3	0.5, 3.3	33	1.0	0.7, 1.4
≥10 years	289	11	1.5	0.8, 2.9	66	1.1	0.8, 1.5
<i>p</i> -trend			0.19			0.51	
Acids, bases, and caustics							
Never	2,925	90	1.0	Referent	589	1.0	Referent
<10 years	90	2	1.1	0.2, 4.5	20	1.1	0.6, 1.8
≥10 years	173	10	2.3	1.2, 4.6	37	1.0	0.7, 1.5
<i>p</i> -trend			0.02			0.80	
Dyes							
Never	3,092	97	1.0	Referent	630	1.0	Referent
<10 years	30	2	3.3	0.7, 15.5	3	0.5	0.1, 1.5
≥10 years	66	3	1.7	0.5, 5.6	13	0.9	0.5, 1.7
<i>p</i> -trend			0.18			0.58	
Metals							
Never	2,961	87	1.0	Referent	594	1.0	Referent
<10 years	87	3	1.6	0.5, 5.3	17	1.0	0.6, 1.7
≥10 years	140	12	3.7	1.9, 7.1	35	1.3	0.9, 1.8
<i>p</i> -trend			<0.001			0.29	
Silica dust							
Never	3,180	98	1.0	Referent	645	1.0	Referent
<10 years	2	1	34.8	2.5, 476.5	0		
≥10 years	6	3	15.8	3.5, 70.6	1	0.8	0.1, 6.6
<i>p</i> -trend			<0.001			0.75	
Electromagnetic fields or nonionizing radiation							
Never	1,016	34	1.0	Referent	178	1.0	Referent
<10 years	345	6	0.5	0.2, 1.3	85	1.5	1.1, 1.9
≥10 years	1,827	62	0.9	0.6, 1.3	383	1.2	1.0, 1.5
<i>p</i> -trend			0.59			0.10	
Lubricants							
Never	1,211	36	1.0	Referent	214	1.0	Referent
<10 years	331	9	0.9	0.4, 1.8	82	1.4	1.1, 1.9
≥10 years	1,646	57	1.0	0.6, 1.5	350	1.2	1.0, 1.4
<i>p</i> -trend			0.87			0.08	

* HR, hazard ratio; CI, confidence interval.

† Adjusted for age (years; continuous variable) and smoking status (ever/never) at baseline.

TABLE 4. Hazard ratios for esophageal and stomach cancer by cumulative exposure to cotton dust, in quartiles, Shanghai, China, 1989–1998

Lag and cotton dust exposure (mg/m ³ × years)	Distribution in subcohort (no.)	Esophageal cancer			Stomach cancer		
		No.	HR*,†	95% CI*	No.	HR†	95% CI
No lag							
None	1,016	36	1.1	0.6, 2.0	201	1.0	0.8, 1.3
>0–55.9	543	17	1.0	Referent	111	1.0	Referent
>55.9–97.0	543	17	0.9	0.5, 1.8	109	1.0	0.7, 1.3
>97.0–143.4	543	11	0.5	0.2, 1.1	101	0.9	0.7, 1.2
>143.4	543	21	0.9	0.5, 1.8	124	1.1	0.8, 1.5
<i>p</i> -trend			0.83			0.51	
10-year lag							
None	1,026	36	1.0	0.6, 1.8	208	1.0	0.8, 1.3
>0–55.9	613	19	1.0	Referent	126	1.0	Referent
>55.9–97.0	520	15	0.8	0.4, 1.5	101	1.0	0.7, 1.3
>97.0–143.4	512	11	0.5	0.2, 1.0	103	1.0	0.7, 1.4
>143.4	517	21	0.9	0.5, 1.6	108	1.0	0.8, 1.4
<i>p</i> -trend			0.80			0.92	
20-year lag							
None	1,198	38	1.0	0.6, 1.7	266	1.2	0.9, 1.5
>0–55.9	640	22	1.0	Referent	124	1.0	Referent
>55.9–97.0	456	18	0.8	0.4, 1.6	99	1.1	0.8, 1.5
>97.0–143.4	459	13	0.5	0.3, 1.0	82	0.9	0.7, 1.3
>143.4	435	11	0.5	0.2, 1.0	75	0.9	0.6, 1.2
<i>p</i> -trend			0.03			0.02	

* HR, hazard ratio; CI, confidence interval.

† Adjusted for age (years; continuous variable) and smoking status (ever/never) at baseline.

and steel were the basis of the metal-exposure category. Only foundry work was classified with exposure to silica dust in the job-exposure matrix.

Crystalline silica has been classified as carcinogenic to humans (group 1) by the International Agency for Research on Cancer, mainly because of associations with lung cancer in occupational settings (25). Previous studies have also suggested a relation between silica dust and esophageal cancer (7, 9). A case-control study among men in Japan detected a moderately elevated risk (odds ratio = 1.5, 95 percent CI: 0.6, 3.9) of esophageal cancer mortality in relation to silica exposure (9). A nearly threefold excess risk was detected in a cohort of silica-exposed iron-steel workers in China (7). However, an association between silica dust and esophageal cancer has not been observed consistently (26). To our knowledge, our study is the only study that has focused on the textile industry. In addition, these prior studies only included men and assessed cancer mortality as the main outcome.

Exposure to silica and metals as assessed in the job-exposure matrix might have been correlated with other potential hazards, specifically exposure to polycyclic aromatic hydrocarbons that were not assessed in the job-exposure matrix. Nonetheless, our results are consistent with findings from studies of esophageal cancer and silica in other industrial settings (6, 7, 9, 11).

The acids, bases, and caustics category included such chemicals as acetic acid, sulfuric acid, and ammonia hydroxide, which would most likely be used in scouring, bleaching, and dyeing of raw material, yarn, and fabric. The main route of exposure would be either skin contamination or inhalation. Acids might play a role in altering the pH of the esophagus and stomach, resulting in gastroesophageal reflux disease, which is a risk factor for esophageal cancer (27). Bases and caustics are corrosive, which might alter the epithelial cells of the esophagus or lead to corrosive esophagitis (27).

The inverse risk gradients observed for the relation between endotoxin exposure and both cancers were unanticipated. The association with endotoxin was stronger for esophageal cancer than for stomach cancer. Endotoxin is a lipopolysaccharide derived from Gram-negative bacteria and is present in high concentrations in cotton dust (28). Endotoxin elicits a systemic inflammatory response after inhalation that entails the release of macrophages and increases production of inflammatory mediator interleukin 1 and tumor necrosis factor- α (29). It has been suggested that the anticarcinogenic effect of endotoxin is mediated through activation of macrophages and tumor necrosis factor- α release (28, 30). There has been a suggestion of acute gastrointestinal effects (i.e., diarrhea and vomiting) due to endotoxin

TABLE 5. Hazard ratios for esophageal and stomach cancer by cumulative exposure to endotoxin, in quartiles, Shanghai, China, 1989–1998*

Lag and endotoxin exposure (EU†/m ³ × years)	Distribution in subcohort (no.)	Esophageal cancer			Stomach cancer		
		No.	HR‡,§	95% CI†	No.	HR‡	95% CI
No lag							
Unexposed	916	30	1.0	0.5, 1.8	178	0.9	0.7, 1.1
>0–1,517.4	531	17	1.0	Referent	123	1.0	Referent
>1,517.4–2,430.0	531	18	0.9	0.5, 1.9	106	0.9	0.7, 1.2
>2,430.0–3,530.6	531	17	0.8	0.4, 1.6	105	0.9	0.7, 1.2
>3,530.6	530	11	0.5	0.2, 1.1	101	0.8	0.6, 1.1
<i>p</i> -trend			0.06			0.20	
10-year lag							
Unexposed	926	30	1.0	0.6, 1.9	184	0.9	0.7, 1.1
>0–1,517.4	629	17	1.0	Referent	145	1.0	Referent
>1,517.4–2,430.0	502	19	1.0	0.5, 2.1	101	0.9	0.7, 1.2
>2,430.0–3,530.6	481	17	0.9	0.4, 1.7	93	0.9	0.6, 1.2
>3,530.6	501	10	0.5	0.2, 1.1	90	0.8	0.6, 1.1
<i>p</i> -trend			0.05			0.05	
20-year lag							
Unexposed	1,093	32	0.9	0.5, 1.5	242	1.0	0.8, 1.3
>0–1,517.4	666	23	1.0	Referent	148	1.0	Referent
>1,517.4–2,430.0	465	22	1.0	0.5, 1.8	90	0.9	0.7, 1.2
>2,430.0–3,530.6	401	7	0.3	0.1, 0.7	69	0.8	0.5, 1.1
>3,530.6	414	9	0.4	0.2, 0.8	64	0.7	0.5, 0.9
<i>p</i> -trend			0.01			<0.001	

* Women who had ever been employed as machinists or in sanitation or wool production were not included in quantitative analyses of endotoxin.

† EU, endotoxin units; HR, hazard ratio; CI, confidence interval.

‡ Adjusted for age (years; continuous variable) and smoking status (ever/never) at baseline.

exposure among sewage treatment plant workers, but these effects have not been associated with cancer (31).

The major strengths of this study were the inclusion of a large number of incident cases with confirmed diagnoses, collection of complete work history data on study subjects in the textile industry, and thorough assessment of potential hazards using a job-exposure matrix developed specifically for the textile industry in Shanghai. The main limitation of the study was the absence of quantified exposure data for workplace agents other than cotton dust and endotoxin. Our assessments for other agents, notably silica and metals, were based on expert classification of jobs in different textile processes and industry sectors and on reports of exposure within the factories by industrial hygienists in Shanghai. Thus, there is the possibility of misclassification of exposure. Misclassification is likely to have been nondifferential and would be expected to have biased risk estimates towards the null. Nonetheless, the assessment of textile industry exposures in our study was far more detailed than in previous investigations of cancer risks among textile workers. Moreover, no previous studies have examined exposure-response relations with quantitative estimates of endotoxin and cotton dust in the textile industry.

There were slight differences in the proportions of work history information obtained from the primary source (fac-

tory personnel records) for esophageal cancer cases and noncase subcohort women. If we take into account interviews with supervisors as the next least-biased source of work history information, nearly 90 percent of work history information for both noncases and esophageal cases was obtained from personnel records or interviews with factory supervisors. It is unlikely that interviews with supervisors, coworkers, or the subjects themselves would have resulted in recall bias. Interviewees were asked specifically about the work the woman conducted in the textile mill but were not asked about exposures to specific agents.

It is unlikely that the results for endotoxin, which causes acute respiratory and gastrointestinal symptoms, were affected by a healthy worker survivor bias caused by selective transfer from jobs with heavy exposure. Movement in the industry was constrained prior to 1994, and subcohort women and both case groups had held a median of two jobs during their lifetime work in the textile industry (data not shown). When we conducted separate analyses restricted to women who had worked in only one job, the results for endotoxin and cotton dust were not materially different from those for the entire study population (data not shown).

To our knowledge, this is the most comprehensive investigation yet undertaken of the relation between exposures in

the textile industry and the risks of esophageal cancer and stomach cancer. Some of the exposures assessed in this analysis, especially silica, metals, and endotoxin, are not unique to the textile industry and might influence risks of esophageal cancer and stomach cancer in other industries. The inverse risk gradients associated with endotoxin exposure observed in this study will need to be replicated before firm conclusions can be reached regarding protective effects.

ACKNOWLEDGMENTS

This research was supported by grant R01CA80180 from the US National Cancer Institute and by training grant ES07262 (K. J. W.) from the US National Institute of Environmental Health Sciences.

The authors thank Drs. Fan Liang Chen, Yong Wei Hu, Guan Lin Zhao, and Lei Dan Pan for their ongoing support. The authors thank Wang Wen Wan for project management; Drs. Dai He Liang, Wang Zhu Ming, Qi A Zhen, Wang Xia Ming, Xiang Wei Ping, and Li Yu Fang for their extensive efforts in collecting factory information; the 30 field-workers for collecting women's personnel records and confirming diagnoses; and Dr. Ilir Agalliu, Georgia Green, Shirley Zhang, Richard Gandolfo, and Ted Grichuhin for technical and administrative support.

Conflict of interest: none declared.

REFERENCES

- Parkin DM, Bray F, Ferlay J, et al. Global cancer statistics, 2002. *CA Cancer J Clin* 2005;55:74–108.
- Yang L, Parkin DM, Ferlay J, et al. Estimates of cancer incidence in China for 2000 and projections for 2005. *Cancer Epidemiol Biomarkers Prev* 2005;14:243–50.
- Enzinger PC, Mayer RJ. Esophageal cancer. *N Engl J Med* 2003;349:2241–52.
- Kelley JR, Duggan JM. Gastric cancer epidemiology and risk factors. *J Clin Epidemiol* 2003;56:1–9.
- Parkin DM, Bray FI, Devesa SS. Cancer burden in the year 2000. The global picture. *Eur J Cancer* 2001;3(suppl 8):S4–66.
- Weiderpass E, Vainio H, Kauppinen T, et al. Occupational exposures and gastrointestinal cancers among Finnish women. *J Occup Environ Med* 2003;45:305–15.
- Pan G, Takahashi K, Feng Y, et al. Nested case-control study of esophageal cancer in relation to occupational exposure to silica and other dusts. *Am J Ind Med* 1999;35:272–80.
- Gustavsson P, Jakobsson R, Johansson H, et al. Occupational exposures and squamous cell carcinoma of the oral cavity, pharynx, larynx, and oesophagus: a case-control study in Sweden. *Occup Environ Med* 1998;55:393–400.
- Tsuda T, Mino Y, Babazono A, et al. A case-control study of the relationships among silica exposure, gastric cancer, and esophageal cancer. *Am J Ind Med* 2001;39:52–7.
- Jansson C, Johansson AL, Bergdahl IA, et al. Occupational exposures and risk of esophageal and gastric cardia cancers among male Swedish construction workers. *Cancer Causes Control* 2005;16:755–64.
- Yu IT, Tse LA, Wong TW, et al. Further evidence for a link between silica dust and esophageal cancer. *Int J Cancer* 2005;114:479–83.
- Parent ME, Siemiatycki J, Fritschi L. Workplace exposures and oesophageal cancer. *Occup Environ Med* 2000;57:325–34.
- Aragones N, Pollan M, Gustavsson P. Stomach cancer and occupation in Sweden: 1971–89. *Occup Environ Med* 2002;59:329–37.
- Krstevic S, Dosemeci M, Lissowska J, et al. Occupation and risk of stomach cancer in Poland. *Occup Environ Med* 2005;62:318–24.
- Simpson J, Roman E, Law G, et al. Women's occupation and cancer: preliminary analysis of cancer registrations in England and Wales, 1971–1990. *Am J Ind Med* 1999;36:172–85.
- Wernli KJ, Ray RM, Gao DL, et al. Cancer among women textile workers in Shanghai, China: overall incidence patterns, 1989–1998. *Am J Ind Med* 2003;44:595–9.
- Thomas DB, Gao DL, Self SG, et al. Randomized trial of breast self-examination in Shanghai: methodology and preliminary results. *J Natl Cancer Inst* 1997;89:355–65.
- Thomas DB, Gao DL, Ray RM, et al. Randomized trial of breast self-examination in Shanghai: final results. *J Natl Cancer Inst* 2002;94:1445–57.
- Astrakianakis G. Cotton dust, endotoxin exposure and the risk of lung cancer among female textile workers in Shanghai. (Doctoral dissertation). Seattle, WA: School of Public Health and Community Medicine, University of Washington, 2005.
- Christiani DC, Ye TT, Zhang S, et al. Cotton dust and endotoxin exposure and long-term decline in lung function: results of a longitudinal study. *Am J Ind Med* 1999;35:321–31.
- Christiani DC, Ye TT, Wegman DH, et al. Cotton dust exposure, across-shift drop in FEV1, and five-year change in lung function. *Am J Respir Crit Care Med* 1994;150:1250–5.
- Olenchok SA, Christiani DC, Mull JC, et al. Airborne endotoxin concentrations in various work areas within two cotton textile mills in the People's Republic of China. *Biomed Environ Sci* 1990;3:443–51.
- Borgan O, Langholz B, Samuelsen SO, et al. Exposure stratified case-cohort designs. *Lifetime Data Anal* 2000;6:39–58.
- Barlow WE, Ichikawa L, Rosner D, et al. Analysis of case-cohort designs. *J Clin Epidemiol* 1999;52:1165–72.
- International Agency for Research on Cancer. Silica, some silicates, coal dust and para-aramid fibrils. IARC monographs on the evaluation of carcinogenic risks to humans. Lyon, France: International Agency for Research on Cancer, 1997.
- Calvert GM, Rice FL, Boiano JM, et al. Occupational silica exposure and risk of various diseases: an analysis using death certificates from 27 states of the United States. *Occup Environ Med* 2003;60:122–9.
- Goyal R. Diseases of the esophagus. In: Kasper DL, Braunwald E, Fauci AS, et al, eds. *Harrison's online: featuring the complete contents of Harrison's Principles of Internal Medicine, 16th Edition*. New York, NY: McGraw-Hill's AccessMedicine, 2005. (<http://www.accessmedicine.com/resourceTOC.aspx?resourceID=4>).
- Lane SR, Nicholls PJ, Sewell RD. The measurement and health impact of endotoxin contamination in organic dusts from multiple sources: focus on the cotton industry. *Inhal Toxicol* 2004;16:217–29.
- Thorn J. The inflammatory response in humans after inhalation of bacterial endotoxin: a review. *Inflamm Res* 2001;50:254–61.
- Enterline PE, Sykora JL, Keleti G, et al. Endotoxins, cotton dust, and cancer. *Lancet* 1985;2:934–5.
- Thorn J, Kerekes E. Health effects among employees in sewage treatment plants: a literature survey. *Am J Ind Med* 2001;40:170–9.