Occupation and Risk of Esophageal and Gastric Cardia Adenocarcinoma

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Background *Adenocarcinomas of the esophagus and gastric cardia have risen dramatically in incidence over the past few decades, however, little research has been conducted on the occupational risk factors for these cancers.*

Methods *In this population-based case-control study, lifetime job histories were compared between cases of esophageal adenocarcinoma (n = 283), gastric cardia adenocarcinoma (n = 259), and population controls (n = 689). Odds ratios (OR) and 95% confidence intervals (CI) for ever employment and by duration in various occupational and industrial categories were calculated using unconditional logistic regression.*

Results *The risk of esophageal adenocarcinoma was elevated for persons ever employed in administrative support (OR = 1.5; 95%CI = 1.0–2.1); financial, insurance, and real estate (OR = 1.6; 95%CI = 1.0–2.4); and health services (OR = 2.2; 95%CI = 1.2–3.9). The risk of gastric cardia adenocarcinoma was increased among transportation workers (OR = 1.7; 95%CI = 1.1–2.6), as well as among carpenters (OR = 1.8; 95%CI = 0.9–3.9) and workers in the furniture manufacturing industry (OR = 2.4; 95%CI = 0.9–6.3). However, we observed few duration–response relations between length of employment in any category and cancer risk.*

Conclusions *This study revealed associations of esophageal adenocarcinoma with employment in administrative support, health services, and a category of financial, insurance, and real estate industries, and of gastric cardia adenocarcinoma with transportation and certain woodworking occupations. Some of these findings may be due to the play of chance associated with the multiple comparisons made in this study. Our results suggest that, overall, workplace exposures play a minor role in the etiology and upward trend of esophageal and gastric cardia adenocarcinomas.* Am. J. Ind. Med. 42:11–22, 2002. *Published 2002 Wiley-Liss, Inc.*†

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Accepted 27 February 2002
DOI 10.1002/ajim.10077. Published online in Wiley InterScience (www.interscience.wiley.com)

KEY WORDS: occupational diseases; esophageal adenocarcinoma; gastric cardia adenocarcinoma

INTRODUCTION

Esophageal and gastric cardia adenocarcinomas have increased sharply in incidence in the United States and western Europe over the past few decades [Yang and Davis, 1988; Powell and McConkey, 1992; Hansson et al., 1993; Devesa et al., 1998]. In contrast, the incidence rates for esophageal squamous cell carcinoma and noncardia gastric adenocarcinoma have remained stable or decreased [Devesa et al., 1998]. While smoking, obesity, and gastroesophageal reflux account for a large proportion of esophageal and gastric cardia adenocarcinomas [Gammon et al., 1997; Chow et al., 1998a; Farrow et al., 2000], much of the increasing trend remains unexplained.

Esophageal adenocarcinomas often occur in the lower third of the esophagus near the gastroesophageal junction, and can be difficult to distinguish from gastric cardia adenocarcinomas [Kalish et al., 1984; Wang et al., 1986; Gammon et al., 1997]. Similar incidence patterns [Devesa et al., 1998] and risk factors [Gammon et al., 1997] for these cancers suggest a common etiology, which appears to be distinct from that of esophageal squamous cell carcinoma and other gastric adenocarcinomas. While a number of epidemiologic studies have linked esophageal or gastric cancers to employment in certain occupations or industries, most have not distinguished between the cell types of esophageal cancer or the subsites of gastric cancer. For esophageal and/or gastric cancer, elevated risks have been reported for several occupations including administrators, health professionals, rubber and chemical manufacturing workers, janitors, truck drivers, painters, dry cleaners, publishing and printing industry workers, pulp and paper mill workers, or for occupational exposures including metalworking fluids, acid mists, silica dust, asbestos, metal dust, wood dust, and polycyclic aromatic hydrocarbons or other combustion byproducts [Wegman and Eisen, 1981; Blair et al., 1985, 1990, 1998; Siemiatycki et al., 1986; Yu et al., 1988; Jakobsson et al., 1990; Kneller et al., 1990; Gustavsson et al., 1993, 1998; Lindsay et al., 1993; Ruder et al., 1994; Ward et al., 1994; Xu et al., 1996; Kang et al., 1997; Vaughan et al., 1997; Walker et al., 1997; Cocco et al., 1998; Sullivan et al., 1998; Straif et al., 1998; Bulbulyan et al., 1999; Pan et al., 1999].

To identify reasons for the increasing incidence of esophageal and gastric cardia adenocarcinomas, we examined data from a multi-center population-based case-control study in the United States. Several analyses examining nonoccupational risk factors in our study, including clinical, lifestyle, and socioeconomic factors, have already been published [Gammon et al., 1997; Farrow et al., 1998, 2000; Vaughan et al., 1998; Chow et al., 1998a,b]. The present analysis examines the risks related to occupation and industry in an effort to generate new hypotheses and test previously noted associations. This is the first phase of analysis of occupational risk factors in our study; based on these and other findings, future analyses will examine specific exposures estimated using the occupation and industry data provided. This is one of the first studies with detailed occupational histories and confounder data to look at these associations specifically for adenocarcinomas of the esophagus and gastric cardia. For comparison, we also examined occupational risk factors for squamous cell carcinoma of the esophagus and for noncardia gastric adenocarcinoma.

MATERIALS AND METHODS

Subjects

The methods for this study have been described in detail in Gammon et al. [1997]. In brief, a population-based case-control study was conducted during 1993–1995 in New Jersey, Connecticut, and western Washington State. Incident cases of esophageal and gastric cancers (esophageal adenocarcinoma, gastric cardia adenocarcinoma, esophageal squamous cell carcinoma, and noncardia gastric adenocarcinoma) between the ages of 30 and 79 years were identified through rapid reporting systems. Population-based controls were obtained via random-digit dialing for those under 65 years of age and from Health Care Financing Administration records for those 65 years of age or older. Controls and cases of esophageal squamous cell carcinoma and noncardia gastric adenocarcinoma (comparison cases) were frequency matched to cases of esophageal adenocarcinoma and gastric cardia adenocarcinoma (target cases) by geographic area, 5-year age group, gender (in New Jersey and Washington), and race (white or other, in New Jersey). Study pathologists reviewed histologic materials and reports from surgery, radiology, and endoscopy in order to classify cases by anatomic site of origin (esophagus, gastric cardia including gastroesophageal junction, or noncardia gastric sites) and histology (adenocarcinoma or squamous cell). The site of origin of tumors involving the distal esophagus as well as the gastric cardia or proximal stomach was determined by estimating the tumor's center using endoscopic, surgical, and pathologic data. The study protocol was approved by the Institutional Review Boards of all participating institutions, and all subjects provided signed informed consent.

In-person, structured interviews were conducted on subjects or next of kin of deceased subjects, eliciting

information on demographic characteristics, tobacco and alcohol use, medical history, diet, and occupational history up to 1 year prior to date of diagnosis for cases or date of interview for controls (i.e., reference date). The occupational history included job title and duration of the subject's usual job and, for each job the subject reported holding for at least 1 year, the job title, activities, business or industry, starting and ending years, and full-time/part-time status.

Interviews were conducted on 554 target cases (80.6% of those eligible), consisting of 293 esophageal adenocarcinomas and 261 gastric cardia adenocarcinomas; 589 comparison cases (74.1% of eligible), consisting of 221 esophageal squamous cell carcinomas and 368 gastric cardia adenocarcinomas; and 695 controls (70.2% of eligible). Interviews were conducted with the next of kin (usually the spouse) in place of the subject for 29.6% of target cases, 32.2% of comparison cases, and 3.5% of controls.

Data Analysis

Each job and industry reported by a subject was coded according to the 1980 Standard Occupational Classification (SOC) system [U.S. Department of Commerce, 1980] and the 1987 Standard Industrial Classification (SIC) system [Executive Office of the President, 1987], respectively. For the purposes of these analyses, jobs were compressed into 51 occupational and 34 industrial categories corresponding largely to the SOC and SIC major grouping schemes. Specific job titles or industries were examined separately when either a category in this study indicated increased risk for any of the cancers investigated or the occupation or industry was previously associated with any of these cancers. We considered only occupations and industries reported by at least five controls and five cases of any one cancer (but not necessarily of all four cancers) and presented results for a given cancer or stratum when the occupation or industry was reported by at least three controls and three cases. Three or four digit SOC and SIC groupings were used when there were sufficient subjects in that category.

Cumulative duration of employment in a given occupation or industry, in years, was calculated by summing the durations of all jobs in that occupation or industry until the reference date, weighting part-time jobs by 0.5. Employment in a given occupation or industry (for ever/never analyses) was based on a subject's having spent at least 1 year in that occupation or industry. To account for possible changes in employment due to early symptoms of cancer and for disease latency, these measures were also assessed using a lagged reference date 10 years before the original reference date. Since detailed recall of recent employment is likely to be good, jobs for which the subject (or next of kin) was able to report only duration and not specific dates were assumed to have ended by the lagged reference date. Jobs for which part-time/full-time status was unknown were treated as full-time.

We used unconditional logistic regression to calculate odds ratios (ORs) and 95% confidence intervals (CIs) comparing each of the four case groups to the controls. All analyses were adjusted for age (linear), gender, race (white, other), study center, respondent type (study subject or proxy), and smoking (non-smoker, former smoker, current smoker). Esophageal adenocarcinoma and gastric cardia adenocarcinoma analyses were further adjusted for body mass index (in quartiles). Esophageal squamous cell carcinoma analyses were additionally adjusted for alcohol consumption (five categories of drinks per day: none; ≤ 1; > 1, but ≤ 2; > 2, but ≤ 6; > 6). Ever/never analyses compared subjects with at least 1 year employment in a given occupation or industry to those with no employment in that occupation or industry. Tests of trend to determine whether risk increased significantly with increasing duration of exposure were performed by adding the exposure variable of interest in grouped linear (i.e., ordered categorical) form to the model containing the covariates. Duration–response analyses compared subjects with 1–9 years and those with 10 or more years employment to those with no employment in a given occupation or industry. Duration–response results were presented for only those occupations or industries showing an association in ever/never analyses or for which previous studies suggested an association. All of the above analyses were also performed separately with jobs unweighted by full-time/part-time status, restricted to self-respondents (i.e., excluding proxies), with the 10 year lag, and with additional adjustment for education (five categories: < 12 years, 12 years, vocational school, some college, college graduate) and income (five categories of dollars per year: $< 15{,}000$; 15,000–29,999; 30,000–49,999; 50,000–74,999; $\geq 75{,}000$).

Two subjects with questionable job histories (e.g., reporting three or more concurrent full-time jobs) and all subjects with missing work histories ($n = 42$) were excluded from all analyses, leaving a total of 283 esophageal adenocarcinomas, 259 gastric cardia adenocarcinomas, 208 esophageal squamous cell carcinomas, 357 noncardia gastric adenocarcinomas, and 689 controls.

RESULTS

Subject Characteristics

Demographic and other characteristics of controls and each of the four case groups have been described in detail previously [Gammon et al., 1997]. In brief, the mean ages of controls and of all cases combined were 62.8 and 64.8 years, respectively. Males comprised 80.0% of controls, and 84.5% of esophageal adenocarcinoma, 85.3% of gastric cardia adenocarcinoma, 81.7% of esophageal squamous cell

carcinoma, and 70.0% of noncardia gastric adenocarcinoma cases. Subjects were mostly white, accounting for 93.0% of controls and 98.9% of esophageal adenocarcinoma, 96.9% of gastric cardia adenocarcinoma, 76.9% of esophageal squamous cell carcinoma, and 83.8% of noncardia gastric adenocarcinoma cases. Controls were less likely than cases to have ever smoked, with 30.8% of controls reporting never smoking compared to 9.1–25.8% of cases. Average alcohol consumption was much lower among controls (2.1 drinks per day) than among cases with esophageal squamous cell carcinoma (6.7 drinks per day). Average usual BMI was lower among controls (BMI = 25.4) than among cases with adenocarcinoma of the esophagus (BMI = 26.7) or gastric cardia (BMI = 26.5).

The 1,796 participants reported a total of 9,206 separate jobs. Controls reported an average of 5.5 jobs over an average work history of 38.0 years; cases reported an average of 5.0 jobs over an average work history of 38.8 years. Among cases, proxy respondents reported an average of 4.2 jobs of mean duration 11.5 years, whereas self-respondents reported an average of 5.3 jobs of mean duration 8.9 years. This suggests that proxy respondents provided a relatively less detailed work history than self-respondents.

Occupation

ORs associated with ever having been employed in a given occupation are presented in Table I. Significantly increased risk of esophageal adenocarcinoma was observed for administrative support workers (OR = 1.5; 95%CI = 1.0–2.1), while non-significantly elevated risks were seen for health service workers and miscellaneous mechanics. For gastric cardia adenocarcinoma, risks were non-significantly elevated for administrative support workers, carpenters, roofers and pavers, and welders and solderers. Modestly increased risks were also seen for esophageal squamous cell carcinoma among health service workers, cleaning and building service workers, other precision workers (not in metal or food occupations), and rail and water transportation operators. The risks of noncardia gastric adenocarcinoma were increased significantly among motor vehicle operators (OR = 1.7; 95%CI = 1.1–2.6), and non-significantly among electricians, painters, and hand working occupations. Risk of esophageal adenocarcinoma was decreased for some occupations, including engineers, architects, and surveyors (OR = 0.5; 95%CI = 0.2–0.9) as well as writers, artists, entertainers, and athletes (OR = 0.3; 95%CI = 0.1–0.9).

Industry

Table II shows ORs associated with ever having been employed in a given industry. A significantly elevated risk of esophageal adenocarcinoma was associated with the financial, insurance, and real estate category (OR = 1.6; 95%CI = 1.0–2.4) and the health services industry (OR = 2.2; 95%CI = 1.2–3.9). Employment in transportation was a significant risk factor for gastric cardia adenocarcinoma (OR = 1.7; 95%CI = 1.1–2.6), with the excess risk primarily among railroad workers (OR = 3.3; 95%CI = 1.3–8.7) and postal workers (OR = 3.3; 95%CI = 1.2–8.8) (data not shown). Non-significant excess risks for this cancer were associated with furniture manufacturing, petroleum refining and manufacturing and stone, clay, glass, and concrete product manufacturing. For esophageal squamous cell carcinoma, risks were modestly increased for the lumber and furniture industries. Risk of noncardia gastric adenocarcinoma was increased significantly for paper product manufacturing (OR = 3.0; 95%CI = 1.3–7.1) and primary metal industries (OR = 2.1; 95%CI = 1.0–4.2), and non-significantly for furniture manufacturing, chemical manufacturing, and personal services. Based on only three exposed cases, there was a decreased risk of gastric cardia adenocarcinoma for employment in miscellaneous manufacturing (OR = 0.3; 95%CI = 0.1–0.9).

Duration–Response Relations

A significant duration–response trend ($P = 0.04$) for esophageal adenocarcinoma was observed for the financial, insurance, and real estate industry, with ORs of 1.2 (95%CI = 0.6–2.3) and 2.0 (95%CI = 1.1–3.4) among subjects employed in that industry for 1–9 years and more than 10 years, respectively (Table III). Similar modestly elevated risks for esophageal adenocarcinoma were associated with long-term employment in both the primary metal industries (OR = 1.8; 95%CI = 0.4–7.9) and the metal product manufacturing industry (OR = 1.7; 95%CI = 0.7–4.0), while risk was reduced for long-term employment among engineers, architects, and surveyors (OR = 0.3; 95%CI = 0.1–0.8). There were no trends indicating increasing or decreasing risk for gastric cardia adenocarcinoma; however, risk was non-significantly elevated for long-term employment among metal and plastic working machine operators (OR = 2.1; 95%CI = 0.8–5.2) and in the primary metal industries (OR = 3.1; 95%CI = 0.8–11.0) (Table IV). For esophageal squamous cell carcinoma, there was a suggestion of duration–response trends among metal and plastic working machine operators and subjects employed in the automotive dealership/gas station industries, as well as moderately elevated risks associated with short- and long-term employment in cleaning and building service (Table V). Risk of esophageal squamous cell carcinoma was increased for long-term employment in the printing and publishing industry and among plumbers and pipefitters; risk was reduced for long-term employment in industrial and commercial machinery manufacturing. There were several

TABLE I. ORs for Esophageal Adenocarcinoma, Gastric Cardia Adenocarcinoma, Esophageal Squamous Cell Carcinoma, and Noncardia Gastric Adenocarcinoma by Occupational Group

	Controls	Esophageal adenocarcinoma[b]		Gastric cardia adenocarcinoma[b]		Esophageal squamous cell carcinoma[c]		Noncardia gastric adenocarcinoma[d]	
Occupational group[a]	**n**	**n**	**OR (95%CI)**	**n**	**OR (95%CI)**	**n**	**OR (95%CI)**	**n**	**OR (95%CI)**
Administrators, managers	153	67	1.2 (0.8–1.7)	57	1.0 (0.7–1.4)	35	1.4 (0.8–2.3)	52	0.8 (0.6–1.2)
Engineers, architects, surveyors	58	11	0.5 (0.2–0.9)*	21	1.1 (0.6–1.9)	7	0.9 (0.3–2.2)	15	0.7 (0.4–1.3)
Math and computer scientists	19	4	0.7 (0.2–2.1)	4	0.6 (0.2–1.9)	2	—	8	1.2 (0.5–3.1)
Social, recreational, religious, legal	21	6	1.0 (0.4–2.8)	6	0.9 (0.3–2.5)	7	1.2 (0.4–3.5)	6	0.7 (0.3–2.0)
Educators, librarians	67	14	0.6 (0.3–1.2)	19	0.8 (0.4–1.4)	10	0.6 (0.3–1.4)	21	0.8 (0.5–1.5)
Nurses, pharmacists, therapists	12	6	1.5 (0.5–4.8)	2	—	2	—	6	0.6 (0.2–2.0)
Writers, artists, entertainers, athletes	38	7	0.3 (0.1–0.9)*	13	0.8 (0.4–1.6)	6	0.6 (0.2–1.8)	14	0.8 (0.4–1.6)
Non-health technicians	59	18	0.8 (0.4–1.4)	18	0.8 (0.4–1.4)	12	1.3 (0.6–2.9)	20	1.0 (0.6–1.8)
Sales	194	88	1.1 (0.8–1.5)	77	1.1 (0.8–1.6)	46	1.1 (0.7–1.8)	94	1.0 (0.7–1.3)
Administrative support	180	79	1.5 (1.0–2.1)*	70	1.3 (0.9–1.9)	56	1.2 (0.7–1.9)	93	1.0 (0.7–1.3)
Fire fighting and prevention	13	5	0.9 (0.3–2.8)	5	0.8 (0.3–2.5)	2	—	5	1.0 (0.3–3.0)
Law enforcement and guards	32	15	1.3 (0.7–2.5)	8	0.6 (0.3–1.4)	10	1.1 (0.4–2.8)	16	0.9 (0.5–1.9)
Food service	74	26	0.9 (0.6–1.6)	27	1.1 (0.6–1.7)	25	0.7 (0.4–1.3)	40	1.1 (0.7–1.7)
Health service	15	9	2.3 (0.9–5.7)	5	1.3 (0.4–3.6)	9	3.0 (1.0–9.5)	10	1.5 (0.6–3.6)
Cleaning and building service	34	13	0.5 (0.2–1.2)	17	1.1 (0.6–2.2)	27	1.9 (0.9–3.7)	29	1.2 (0.7–2.3)
Personal service	29	8	1.0 (0.5–2.4)	5	0.5 (0.2–1.4)	5	0.6 (0.2–1.8)	14	0.9 (0.5–1.9)
Farm workers	48	21	1.1 (0.6–2.0)	23	1.3 (0.7–2.2)	19	1.0 (0.5–2.0)	23	0.9 (0.5–1.6)
Vehicle mechanics	61	21	0.7 (0.4–1.4)	23	0.7 (0.4–1.3)	14	0.6 (0.3–1.4)	18	0.6 (0.3–1.2)
Electrical equipment repairers	28	7	0.7 (0.3–1.6)	13	1.1 (0.5–2.4)	7	1.4 (0.5–3.7)	8	0.7 (0.3–1.7)
Miscellaneous mechanics	30	17	1.7 (0.9–3.4)	15	1.5 (0.7–2.9)	2	—	10	0.7 (0.3–1.6)
Carpenters	21	7	0.6 (0.2–1.8)	14	1.8 (0.9–3.9)	8	1.5 (0.5–4.6)	9	1.0 (0.4–2.3)
Electricians	13	9	1.7 (0.6–4.3)	7	1.1 (0.4–3.0)	3	1.2 (0.3–6.1)	9	2.4 (1.0–6.1)
Painters	12	1	—	3	0.6 (0.1–2.2)	2	—	12	2.4 (1.0–6.2)
Plumbers, pipefitters	17	7	0.7 (0.2–1.8)	3	0.3 (0.1–1.1)	8	1.3 (0.4–4.0)	2	—
Roofers, pavers	6	5	1.1 (0.3–4.4)	7	2.2 (0.7–7.1)	3	1.9 (0.4–9.9)	4	1.1 (0.3–4.5)
Other construction	47	20	0.8 (0.4–1.5)	12	0.6 (0.3–1.1)	12	0.5 (0.2–1.3)	18	0.9 (0.5–1.6)
Precision metal workers	51	25	1.4 (0.8–2.3)	18	0.9 (0.5–1.6)	12	0.7 (0.3–1.5)	25	1.0 (0.6–1.8)
Precision food workers[e]	6	3	1.2 (0.3–5.0)	3	1.4 (0.3–5.8)	2	—	6	1.7 (0.5–6.1)
Other precision workers	25	15	1.5 (0.7–3.1)	12	1.4 (0.7–3.0)	15	2.4 (1.0–5.5)	9	0.7 (0.3–1.7)
Metal and plastic working machine operators	47	17	0.9 (0.5–1.8)	17	1.0 (0.5–1.8)	19	1.4 (0.7–2.8)	19	0.9 (0.5–1.7)
Printing machine operators	14	2	—	4	1.1 (0.3–3.4)	5	1.7 (0.5–6.1)	5	0.9 (0.3–2.6)
Textile machine operators	25	5	0.4 (0.1–1.3)	8	1.1 (0.5–2.6)	8	0.8 (0.3–2.3)	23	1.1 (0.6–2.2)
Other machine operators	85	27	0.9 (0.5–1.5)	30	1.1 (0.7–1.8)	22	0.6 (0.3–1.2)	47	1.2 (0.8–1.9)
Welders, solderers	13	4	0.7 (0.2–2.4)	10	2.0 (0.8–5.2)	2	—	7	0.8 (0.3–2.3)
Hand working occupations	50	21	1.3 (0.7–2.4)	15	0.9 (0.5–1.7)	21	1.0 (0.5–2.1)	43	1.4 (0.9–2.3)
Motor vehicle operators	77	36	1.2 (0.7–1.9)	33	1.0 (0.6–1.6)	32	0.9 (0.5–1.6)	53	1.7 (1.1–2.6)*
Rail and water transportation operators	23	7	0.5 (0.2–1.4)	10	0.9 (0.4–2.0)	14	2.1 (0.8–5.2)	11	1.2 (0.5–2.6)
Material moving equipment operators	20	10	1.0 (0.4–2.6)	4	0.4 (0.1–1.5)	7	0.8 (0.3–2.5)	15	1.7 (0.8–3.5)
Handlers, equipment cleaners, laborers	122	45	0.9 (0.6–1.3)	50	1.1 (0.7–1.6)	43	0.9 (0.5–1.5)	60	1.0 (0.7–1.5)
Garage and service station occupations	20	12	1.2 (0.5–2.7)	8	0.7 (0.3–1.7)	8	1.7 (0.6–4.8)	9	1.2 (0.5–2.8)

*$P < 0.05$.

[a]Ever/never analyses compared subjects with at least 1 year employment in a given occupation to those with no employment in that occupation.

[b]Adjusted for age, gender, race, study center, respondent type, smoking, BMI.

[c]Adjusted for age, gender, race, study center, respondent type, smoking, alcohol consumption.

[d]Adjusted for age, gender, race, study center, respondent type, smoking.

[e]Includes butchers, meat cutters, bakers, and batchmakers.

TABLE II. ORs for Esophageal Adenocarcinoma, Gastric Cardia Adenocarcinoma, Esophageal Squamous Cell Carcinoma, and Noncardia Gastric Adenocarcinoma by Industry Group

	Controls	Esophageal adenocarcinoma[b]		Gastric cardia adenocarcinoma[b]		Esophageal squamous cell carcinoma[c]		Noncardia gastric adenocarcinoma[d]	
Industry group[a]	**n**	**n**	**OR (95%CI)**	**n**	**OR (95%CI)**	**n**	**OR (95%CI)**	**n**	**OR (95%CI)**
Agriculture	56	20	0.9 (0.5–1.7)	24	1.1 (0.7–2.0)	23	1.0 (0.5–1.9)	29	1.0 (0.6–1.7)
Mining	11	4	0.7 (0.2–2.9)	3	0.8 (0.2–3.2)	1	—	8	1.7 (0.6–4.8)
Construction	117	47	0.8 (0.5–1.3)	41	0.8 (0.5–1.2)	36	0.8 (0.4–1.4)	57	1.0 (0.7–1.5)
Food product manufacturing	32	15	0.9 (0.5–1.9)	17	1.4 (0.8–2.7)	10	0.9 (0.4–2.3)	19	1.2 (0.6–2.3)
Textile manufacturing	23	8	0.8 (0.3–2.0)	4	0.5 (0.2–1.7)	7	0.5 (0.2–1.5)	13	0.9 (0.4–1.9)
Lumber, except furniture	18	6	0.7 (0.3–2.1)	6	0.7 (0.2–1.9)	10	1.9 (0.5–7.7)	11	1.6 (0.7–3.7)
Furniture manufacturing	10	3	1.1 (0.3–4.2)	9	2.4 (0.9–6.3)	4	2.0 (0.4–9.0)	8	1.9 (0.7–5.1)
Paper product manufacturing	13	5	1.1 (0.3–3.4)	3	0.9 (0.2–3.1)	5	1.6 (0.4–6.3)	13	3.0 (1.3–7.1)*
Printing and publishing	41	10	0.6 (0.3–1.3)	13	1.1 (0.6–2.1)	11	1.7 (0.7–3.7)	15	0.8 (0.4–1.6)
Chemical manufacturing	44	14	0.8 (0.4–1.6)	13	1.1 (0.6–2.2)	13	1.0 (0.4–2.4)	24	1.5 (0.9–2.7)
Petroleum refining and manufacturing	6	1	—	5	2.8 (0.7–10.8)	1	—	2	—
Rubber and plastic product manufacturing	26	5	0.4 (0.1–1.1)	8	0.8 (0.3–1.9)	6	0.5 (0.1–1.6)	13	0.9 (0.4–1.8)
Leather product manufacturing	8	1	—	2	—	3	1.1 (0.2–5.0)	7	1.0 (0.3–3.3)
Stone, clay, glass, concrete product manufacturing	10	6	1.6 (0.5–5.0)	9	2.4 (0.9–6.6)	5	1.2 (0.3–4.8)	7	1.0 (0.3–2.9)
Primary metal industries	21	13	1.3 (0.6–2.9)	12	1.4 (0.7–3.1)	6	0.8 (0.3–2.7)	18	2.1 (1.0–4.2)*
Metal product manufacturing, except machinery	48	26	1.3 (0.8–2.3)	17	1.0 (0.5–1.8)	15	0.8 (0.3–1.8)	29	1.1 (0.6–1.9)
Industrial and commercial machinery manufacturing	75	19	0.7 (0.4–1.2)	26	1.1 (0.6–1.8)	14	0.7 (0.3–1.4)	24	0.7 (0.4–1.1)
Electrical equipment manufacturing	58	16	0.7 (0.4–1.3)	11	0.6 (0.3–1.1)	12	0.7 (0.3–1.5)	28	1.1 (0.7–1.9)
Transportation equipment manufacturing	102	40	0.9 (0.6–1.4)	42	1.0 (0.7–1.6)	28	0.9 (0.5–1.6)	44	0.8 (0.5–1.2)
Measuring and analyzing equipment manufacturing	32	10	0.8 (0.3–1.7)	12	1.2 (0.6–2.5)	9	1.3 (0.5–3.3)	13	0.8 (0.4–1.7)
Miscellaneous manufacturing	28	6	0.5 (0.2–1.3)	3	0.3 (0.1–0.9)*	10	1.5 (0.6–3.5)	15	0.8 (0.4–1.7)
Transportation	78	37	1.2 (0.7–1.9)	48	1.7 (1.1–2.6)*	33	1.2 (0.7–2.2)	35	0.8 (0.5–1.3)
Communications	36	9	0.5 (0.2–1.3)	16	1.5 (0.8–3.0)	4	0.5 (0.1–1.9)	11	0.9 (0.4–1.8)
Public utilities	21	5	0.6 (0.2–1.8)	10	1.3 (0.6–3.0)	10	1.6 (0.6–4.6)	5	0.7 (0.2–1.9)
Wholesale trade	77	30	0.9 (0.5–1.4)	32	1.1 (0.7–1.8)	20	0.8 (0.4–1.6)	31	0.8 (0.5–1.3)
Retail trade	247	108	1.2 (0.8–1.6)	90	1.0 (0.7–1.4)	77	1.1 (0.7–1.6)	134	1.1 (0.8–1.5)
Automotive dealers, gas stations	45	26	1.1 (0.6–2.0)	22	1.1 (0.6–2.0)	18	1.7 (0.8–3.5)	21	1.3 (0.8–2.4)
Financial, insurance, real estate	83	48	1.6 (1.0–2.4)*	34	1.2 (0.7–1.9)	22	1.1 (0.6–2.0)	39	0.9 (0.6–1.5)
Personal services	25	5	0.7 (0.2–1.9)	8	0.9 (0.4–2.2)	5	0.5 (0.1–2.0)	23	1.7 (0.9–3.3)
Automotive repair and services	21	7	1.6 (0.6–3.9)	2	—	6	0.7 (0.2–2.3)	11	1.0 (0.4–2.3)
Miscellaneous repair services	15	6	1.5 (0.6–4.0)	8	1.2 (0.4–3.1)	1	—	7	1.3 (0.5–3.3)
Health services	43	25	2.2 (1.2–3.9)*	19	1.4 (0.8–2.6)	10	0.6 (0.2–1.6)	30	1.3 (0.7–2.3)
Public administration	385	164	0.8 (0.6–1.2)	154	0.9 (0.6–1.3)	120	0.8 (0.5–1.4)	189	1.0 (0.7–1.4)

*$P < 0.05$.

[a]Ever/never analyses compared subjects with at least 1 year employment in a given industry to those with no employment in that industry.

[b]Adjusted for age, gender, race, study center, respondent type, smoking, BMI.

[c]Adjusted for age, gender, race, study center, respondent type, smoking, alcohol consumption.

[d]Adjusted for age, gender, race, study center, respondent type, smoking.

positive trends of borderline significance for noncardia gastric cancers, including employment as an electrician (OR = 1.2; 95%CI = 0.3–4.7 and OR = 5.3; 95%CI = 1.3–21.2 for short- and long-duration, respectively; $P = 0.05$), as a motor vehicle operator (OR = 1.6; 95%CI = 0.9–2.8 and OR = 1.8; 95%CI = 1.0–3.2; $P = 0.05$), and in primary metal industries (OR = 1.8; 95%CI = 0.8–4.3 and OR = 2.8; 95%CI = 0.8–9.1; $P = 0.05$), while a non-significant trend

TABLE III. ORs for Esophageal Adenocarcinoma by Duration of Employment in Selected Occupational and Industrial Groups

	Duration 1–9 yrs			Duration ≥ 10 yrs			
Exposure	**n cases**	**n controls**	**OR (95% CI)[a]**	**n cases**	**n controls**	**OR (95% CI)[a]**	**Trend *P***
Occupational categories							
Administrators, managers	19	48	1.2 (0.6–2.1)	48	105	1.2 (0.8–1.9)	0.63
Engineers, architects, surveyors	6	13	1.0 (0.3–2.9)	5	45	0.3 (0.1–0.8)*	0.002
Administrative support	50	106	1.6 (1.0–2.4)*	29	74	1.4 (0.8–2.3)	0.66
Health service	8	12	2.8 (1.1–7.5)*	1	3	—	—
Plumbers, pipefitters	1	9	—	6	8	1.3 (0.4–4.4)	—
Precision metal workers	15	29	1.5 (0.8–3.0)	10	22	1.2 (0.5–2.7)	0.78
Metal and plastic working machine operators	11	35	0.8 (0.4–1.7)	6	12	1.3 (0.5–3.9)	0.52
Industry categories							
Printing and publishing	7	31	0.6 (0.2–1.5)	3	10	0.6 (0.1–2.6)	0.13
Primary metal Industries	7	16	1.1 (0.4–2.9)	6	5	1.8 (0.4–7.9)	0.24
Metal product manufacturing, except machinery	13	32	1.1 (0.6–2.3)	13	16	1.7 (0.7–4.0)	0.26
Industrial and commercial machinery manufacturing	7	38	0.5 (0.2–1.3)	12	37	0.8 (0.4–1.7)	0.08
Transportation equipment manufacturing	21	45	1.1 (0.6–2.0)	19	57	0.7 (0.4–1.3)	0.20
Financial, insurance, real estate	18	43	1.2 (0.6–2.3)	30	40	2.0 (1.1–3.4)*	0.04
Health services	15	23	2.8 (1.4–5.9)*	10	20	1.6 (0.7–3.8)	0.14

*$P < 0.05$.

[a]Adjusted for age, gender, race, study center, respondent type, smoking, BMI; reference group, with OR = 1.0, consists of all subjects with no employment in that occupation or industry.

TABLE IV. ORs for Gastric Cardia Adenocarcinoma by Duration of Employment in Selected Occupational and Industrial Groups

	Duration 1–9 yrs			Duration ≥ 10 yrs			
Exposure	**n cases**	**n controls**	**OR (95% CI)[a]**	**n cases**	**n controls**	**OR (95% CI)[a]**	**Trend *P***
Occupational categories							
Administrators, managers	12	48	0.7 (0.3–1.3)	45	105	1.2 (0.8–1.8)	0.86
Administrative support	41	106	1.3 (0.8–2.0)	29	74	1.5 (0.9–2.6)	0.32
Cleaning and building service	12	19	1.8 (0.8–4.1)	5	15	0.4 (0.1–1.4)	0.62
Carpenters	9	5	6.3 (2.0–20.3)*	5	16	0.6 (0.2–2.1)	0.56
Precision metal workers	11	29	1.0 (0.5–2.2)	7	22	0.7 (0.3–1.8)	0.60
Metal and plastic working machine operators	8	35	0.6 (0.3–1.5)	9	12	2.1 (0.8–5.2)	0.88
Welders, solderers	9	8	3.0 (1.1–8.5)*	1	5	—	—
Motor vehicle operators	18	44	1.0 (0.5–1.8)	15	33	1.0 (0.5–2.0)	0.80
Industry categories							
Construction	16	56	0.6 (0.3–1.2)	25	61	0.9 (0.5–1.6)	0.56
Furniture manufacturing	7	8	2.4 (0.8–7.2)	2	2	—	—
Printing and publishing	10	31	1.1 (0.5–2.4)	3	10	1.0 (0.3–3.8)	0.75
Chemical manufacturing	7	23	1.2 (0.5–3.0)	6	21	1.0 (0.4–2.6)	0.60
Primary metal industries	6	16	0.9 (0.3–2.5)	6	5	3.1 (0.8–11.0)	0.20
Metal product manufacturing, except machinery	11	32	1.0 (0.5–2.1)	6	16	0.9 (0.3–2.6)	0.70
Transportation	26	38	2.0 (1.1–3.5)*	22	40	1.4 (0.7–2.6)	0.03
Communications	7	10	2.9 (1.0–8.4)	9	26	1.1 (0.5–2.6)	0.68
Health services	11	23	1.6 (0.7–3.6)	8	20	1.2 (0.5–3.0)	0.52

*$P < 0.05$.

[a]Adjusted for age, gender, race, study center, respondent type, smoking, BMI; reference group, with OR = 1.0, consists of all subjects with no employment in that occupation or industry.

TABLE V. ORs for Esophageal Squamous Cell Carcinoma by Duration of Employment in Selected Occupational and Industrial Groups

	Duration 1–9 yrs			Duration ≥ 10 yrs			
Exposure	**n cases**	**n controls**	**OR (95% CI)[a]**	**n cases**	**n controls**	**OR (95% CI)[a]**	**Trend *P***
Occupational categories							
Health service	7	12	3.1 (0.9–10.7)	2	3	—	—
Cleaning and building service	15	19	2.0 (0.8–5.0)	13	15	1.9 (0.7–5.4)	0.03
Plumbers, pipefitters	2	9	—	6	8	2.0 (0.5–8.3)	—
Precision metal workers	7	29	0.8 (0.3–2.2)	5	22	0.6 (0.2–2.0)	0.16
Other precision workers	8	9	3.0 (0.9–10.3)	7	16	1.9 (0.6–6.1)	0.03
Metal and plastic working machine operators	13	35	1.3 (0.6–3.0)	6	12	1.7 (0.4–6.9)	0.61
Garage and service station occupations	6	18	1.5 (0.4–5.2)	2	2	—	—
Industry categories							
Lumber, except furniture	7	9	1.4 (0.3–7.1)	3	9	3.3 (0.4–28.5)	0.10
Printing and publishing	4	31	0.8 (0.2–2.6)	7	10	3.3 (1.0–10.6)*	0.34
Primary metal industries	5	16	0.9 (0.3–3.4)	1	5	—	—
Metal product manufacturing, except machinery	6	32	0.6 (0.2–1.7)	9	17	1.4 (0.4–4.6)	0.81
Industrial and commercial machinery manufacturing	10	38	1.2 (0.5–2.8)	4	37	0.3 (0.1–0.9)*	0.02
Transportation equipment manufacturing	12	45	0.9 (0.4–2.2)	17	57	1.0 (0.5–2.1)	0.51
Automotive dealers, gas stations	12	30	1.5 (0.6–3.6)	6	15	2.2 (0.7–6.9)	0.33

*$P < 0.05$.

[a]Adjusted for age, gender, race, study center, respondent type, smoking, alcohol consumption; reference group, with OR = 1.0, consists of all subjects with no employment in that occupation or industry.

was observed among persons employed in the chemical manufacturing industry (Table VI).

Results were similar when analyses excluded full-time/part-time job status (i.e., unweighted) and when education or income were included in the models (data not shown). Using a 10-year lagged reference date also produced similar results, although ORs became significant for esophageal adenocarcinoma among subjects employed as health service workers (OR = 3.2; 95%CI = 1.2–8.2) and for esophageal squamous cell carcinoma among subjects employed as cleaning and building service workers (OR = 2.7; 95% CI = 1.3–5.5). In addition, the duration–response trend for noncardia gastric adenocarcinoma among painters became more evident (OR = 2.0; 95%CI = 0.5–8.1 and OR = 2.7; 95%CI = 0.7–9.9 for short- and long-duration, respectively, $P = 0.05$). Restricting analyses to self-respondents did not change interpretation of results, although the OR for esophageal squamous cell carcinoma associated with cleaning and building service became more pronounced (OR = 3.3; 95%CI = 1.6–6.9).

DISCUSSION

This study examined the risks associated with various occupations and industries for esophageal and gastric cardia adenocarcinoma. For comparison, we also examined these occupations and industries in relation to esophageal squamous cell carcinoma and noncardia gastric adenocarcinoma. We found an increased risk of esophageal adenocarcinoma associated with employment in administrative support positions; in the financial, insurance, and real estate industries; and in the health services industry. The risk of gastric cardia adenocarcinoma was increased among workers in the transportation industry, while the risk of noncardia gastric adenocarcinoma was elevated among motor vehicle operators and among workers in the paper product manufacturing and primary metal industries. However, the generally modest number of exposed cases, the relatively low levels of risk observed, and the lack of clear duration–response trends for most associations suggest that workplace exposures play a minor role in the etiology of these cancers.

TABLE VI. ORs for Noncardia Gastric Adenocarcinoma by Duration of Employment in Selected Occupational and Industrial Groups

	Duration 1–9 yrs			Duration ≥ 10 yrs			
Exposure	**n cases**	**n controls**	**OR (95% CI)[a]**	**n cases**	**n controls**	**OR (95% CI)[a]**	**Trend *P***
Occupational categories							
Food service	25	55	1.0 (0.6–1.8)	15	19	1.2 (0.6–2.5)	0.73
Carpenters	4	5	2.1 (0.5–9.2)	5	16	0.6 (0.2–1.9)	0.70
Electricians	3	9	1.2 (0.3–4.7)	6	4	5.3 (1.3–21.2)*	0.05
Painters	5	5	2.7 (0.7–11.5)	7	7	2.2 (0.6–7.4)	0.06
Precision metal workers	15	29	1.1 (0.6–2.3)	10	22	0.9 (0.4–2.1)	0.95
Metal and plastic working machine operators	14	35	0.9 (0.5–1.8)	5	12	1.1 (0.4–3.4)	0.42
Motor vehicle operators	27	44	1.6 (0.9–2.8)	26	33	1.8 (1.0–3.2)	0.05
Material moving equipment operators	8	12	1.6 (0.6–4.3)	7	8	1.8 (0.6–5.4)	0.37
Industry categories							
Agriculture	23	44	1.1 (0.6–2.0)	6	12	0.7 (0.2–2.2)	0.79
Construction	16	56	0.6 (0.3–1.2)	41	61	1.4 (0.9–2.3)	0.39
Food product manufacturing	10	19	1.0 (0.4–2.4)	9	14	1.4 (0.6–3.5)	0.56
Lumber, except furniture	10	9	2.5 (0.9–7.1)	1	9	—	—
Furniture manufacturing	7	8	2.4 (0.8–7.0)	1	2	—	—
Paper product manufacturing	7	11	1.7 (0.6–5.1)	6	2	—	—
Chemical manufacturing	12	23	1.3 (0.6–2.7)	12	21	1.8 (0.8–3.8)	0.47
Primary metal industries	10	16	1.8 (0.8–4.3)	8	5	2.8 (0.8–9.1)	0.05
Metal product manufacturing, except machinery	21	32	1.2 (0.6–2.3)	8	17	0.9 (0.3–2.2)	0.92

*$P < 0.05$.
[a]Adjusted for age, gender, race, study center, respondent type, smoking; reference group, with OR = 1.0, consists of all subjects with no employment in that occupation or industry.

Our study is one of the first with lifetime occupational histories and detailed confounder information to examine occupational risk factors separately for adenocarcinoma and squamous cell carcinoma of the esophagus, as well as for cardia and noncardia subsites of gastric adenocarcinoma. Because the incidence rates for adenocarcinomas of the esophagus and gastric cardia have increased sharply in the past couple of decades and because most prior studies examined the time period when squamous cell carcinoma accounted for most cases of esophageal cancer, while noncardia tumors predominated in gastric cancer, we can make only limited inferences from earlier studies.

The elevated risk of esophageal adenocarcinoma associated with the health services industry was spread over a broad category of healthcare workers (including dental assistants, health and nursing aides, orderlies, and attendants), with only a slight excess among those employed as nurses, pharmacists, or therapists. A modest excess risk of esophageal squamous cell carcinoma was also seen among persons employed in the health services occupational category, but there were too few subjects in other healthcare-related positions (e.g., physicians, dentists, veterinarians, and health technicians) to analyze separately for these cancers. It is noteworthy that Ward et al. [1994] observed an excess mortality from cancers of the gastric cardia and lower esophagus among health professionals, although they did not report on other healthcare workers.

The excess risk of esophageal adenocarcinoma associated with administrative support work in our study was not observed by Ward et al. [1994], although they did note an excess mortality from cancers of the gastric cardia and lower esophagus among administrative managers. To our knowledge, the excess risk of esophageal adenocarcinoma that we observed among persons in the financial, insurance, and real estate industries has not previously been reported. However, these findings may be due in part to residual confounding with lifestyle risk factors.

The increased risks of both esophageal and gastric cardia adenocarcinomas that were suggested for long-term employment in certain metal-related occupations and industries are interesting, since occupational exposure to metal dusts has previously been related to esophageal cancer, particularly in the lower third of the esophagus [Yu et al., 1988], and to gastric cancer [Kneller et al., 1990; Xu et al.,

1996]. However, in our study, there was no excess of esophageal or gastric cardia adenocarcinoma in other occupations or industries having similar exposures.

The increased risk of gastric cardia adenocarcinoma suggested for carpenters (mainly employed in construction) and workers in the furniture manufacturing industry is noteworthy, since both groups are likely to be exposed to wood dust. However, the results of duration–response analyses were unremarkable and based on small numbers of exposed cases, and we are not aware of previous reports linking wood dust exposure to this tumor.

The elevated risk of gastric cardia adenocarcinoma that we observed in the transportation industry was concentrated among railroad and postal workers. Previous studies have noted increased risks of esophageal and gastric cardia cancer among truck drivers and other workers exposed to combustion products from diesel exhaust and other sources [Gustavsson et al., 1993; Cocco et al., 1998]. However, the risk of gastric cardia adenocarcinoma was not excessive among motor vehicle operators or other workers likely to receive heavy exposures to combustion products or motor exhaust, nor did employment in the transportation industry increase the risk for either type of esophageal cancer.

Although esophageal adenocarcinoma appeared to show a positive duration–response trend with employment in the financial, insurance, and real estate industries, other occupational risks in our study showed no clear trend or were more pronounced among subjects with a shorter vs. longer duration of employment. This pattern might be due to unstable risk estimates from a small number of subjects in many duration strata, to the assignment of higher-exposure jobs among short-term workers, or to demographic and lifestyle factors associated with short-term employment that might increase risk despite our efforts to adjust for known confounders. Whatever the explanations for the occupational risks in our study, it is noteworthy that the work-related associations for esophageal and gastric cardia adenocarcinoma were generally dissimilar, despite the concordance observed for other epidemiologic patterns of these tumors [Gammon et al., 1997; Chow et al., 1998a].

In our study, the occupational risk factors (either by job title or by related exposures) for esophageal squamous cell carcinoma and noncardia gastric adenocarcinoma seemed more prominent, although these cancers are also believed to be largely non-occupational in origin [Muñoz and Day, 1996; Nomura, 1996]. While few of the associations between occupation and esophageal squamous cell carcinoma were significant in our study, some have been reported previously, including elevated risks for plumbers and pipefitters (possibly exposed to asbestos and metal dust and fumes [Selikoff et al., 1979; Kaminski et al., 1980; Yu et al., 1988; McDonald et al., 1993; Kang et al., 1997]), roofers and pavers, garage and service station workers (possibly exposed to combustion products [Gustavsson et al., 1993]), and the printing and publishing industry [Bulbulyan et al., 1999]. Many of our findings for noncardia gastric adenocarcinoma also have been observed previously, including increased risks for electricians [Parent et al., 1998], painters [Jedrychowski et al., 1990], motor vehicle operators [Minder and Beer-Porizek, 1992; Burns and Swanson, 1995; Parent et al., 1998], material moving equipment operators [Burns and Swanson, 1995], furniture manufacturing [Gonzalez et al., 1991], paper product manufacturing [Toren et al., 1996], chemical manufacturing [Minder and Beer-Porizek, 1992], mining [Gonzalez et al., 1991; Chow et al., 1994], and primary metal industries [Sorahan et al., 1994; Urbaneja et al., 1995; Xu et al., 1996].

Several limitations should be kept in mind when evaluating the results of our study. First, occupational and industrial categories are only crude surrogates for the workplace exposures that may increase cancer risk. Individual categories are likely to include jobs with a wide variety of exposures, thus introducing exposure misclassification. Even within specific occupations or industries, workers may experience a range of exposures in terms of type and intensity. Despite the relatively large size of this case-control study, we were unable to examine many more narrowly-defined occupational and industrial categories because of small numbers of subjects in those categories. However, any resulting misclassification is probably non-differential with regard to case-control status, and would, therefore, tend to attenuate the estimated risks.

Recall bias may also contribute to the associations observed in this study. However, esophageal cancer is not generally viewed as an occupational disease and would not be expected to appreciably affect one's recall of work history. In fact, among self-respondents, controls and each of the case groups reported a similar number of lifetime jobs and cumulative duration of employment. The proportions of jobs missing occupational or industrial codes were low and similarly distributed between cases and controls. The same was true for the number and cumulative duration of gaps in the work histories. Proxy respondents, who were more common among the cases than among the controls, tended to report fewer jobs than the self-respondents and were slightly more likely to not report occupational title, although they recalled industry and cumulative duration of employment similarly to self-respondents. However, it is unlikely that recall bias due to differential reporting between proxy- and self-respondents affected our results, since we not only adjusted for the type of respondent in all analyses, but we also observed similar results when analyses were restricted to self-respondents.

In addition, since we examined risks for four cancers across 51 occupations and 34 industries, it is possible that as a result of multiple comparisons, some elevated or reduced risks might have occurred by chance alone. While many of the associations we observed have been reported previously,

the new findings generated by our study should be interpreted more cautiously.

In conclusion, this case-control study revealed associations of esophageal adenocarcinoma with employment in administrative support, health services, and the category of financial, insurance, and real estate industries, and of gastric cardia adenocarcinoma with transportation and certain woodworking occupations. At least some of these findings may be due to the play of chance associated with the multiple comparisons made in this study. Our results suggest that occupational exposures play a minor role in the etiology and rising incidence of these tumors.

ACKNOWLEDGMENTS

The authors thank Aaron Blair for helpful comments on this manuscript, Jay Lubin for statistical advice, and Jeremy Miller for programming assistance.

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