Journal of Occupational and Environmental Medicine
Volume 40 • Number 10 • October 1998

ORIGINAL ARTICLES

Occupational Risk Factors for Cancer of the Gastric Cardia
Analysis of Delhi Certificates From 24 US States

Pierluigi Cocco [1] **MD**
Mary H. Ward [2] **PhD**
Mustafa Dosemeci [2] **PhD**

[1] Institute of Occupational Medicine, University of Cagliari Italy (Dr Cocco)
[2] Occupational Epidemiology Branch, Division of Cancer Epidemiology and Genetics, National Cancer Institute Bethesda, Md. (Dr Ward, Dr Dosemeci).

Address correspondence to: Mary H. Ward, PhD, Occupational Epidemiology Branch, Division of Cancer Epidemiology and Genetics National Cancer Institute, 6130 Executive Boulevard, EPN Room 418, Bethesda, MD 20892.

We evaluated the risk of gastric cardia cancer by occupation and industry in a case-control study using information from death certificates for 24 US states in 1984- 1992. One thousand fifty-six cases of gastric cardia cancer were identified among men aged 20 years or more, including 1,023 whites and 33 blacks. Controls were 5,280 subjects who died of nonmalignant diseases, 5:1 matched to cases by geographic region, race, gender, and 5-year age group. Among white men, occupations with elevated risk included financial managers (odds ratio [OR] = 6.1; 95% confidence interval [CI], 1.3- 28.8), janitors and cleaners (OR = 1.7; 95% CI, 1.0- 2.9), production inspectors (OR = 3.2; 95% CI, 1.5- 6.9), and truck drivers (OR = 1.5; 95% CI, 1.0- 2.2). Industries with elevated risk included pulp and paper mills (OR = 2.0; 95% CI, 1.0- 37), newspaper publishing and printing (OR = 2.6; 95% CI, 1.0- 6.3), industrial and miscellaneous chemicals (OR = 2.0; 95% CI, 1.0- 3.9), water supply and irrigation (OR = 5.6; 95% CI, 1.6- 19.9). Among black men, risks were nonsignificantly increased for subjects employed in railroads (3 cases, 2 controls) and for carpenters (3 cases, 0 controls). We created job-exposure matrices for asbestos, inorganic dust, metal dust, lead, polycyclic aromatic hydrocarbons, nitrogen oxides, nitrosamines, sulfuric acid, fertilizers, herbicides, other pesticides, and wood dust. Among white men, a consistent pattern of risk increase by level and probability of

exposure was observed only for sulfuric acid mists, with a twofold excess (95% CI, 0.6- 7.3) associated with high probability of high intensity exposure. A significant 30% increase in risk was observed for those subjects with a high probability of exposure (all levels combined) to lead, and a 60% increase was observed for subjects with high-level exposure to lead (all probabilities combined). However, crosstabulation of gastric cardia cancer risk by probability and level of exposure to lead did not show consistent trends. Asbestos exposure also showed an overall 50% increase but no consistent trends among white men. None of the 12 occupational hazards showed an association with risk for black men.

While stomach cancer incidence and mortality have been declining worldwide over the past decades, [1] [2] there has been a recent rise in cancer of the **gastric** cardia and adenocarcinoma of the esophagus. [3] Among whites, the male-to-female ratio for cancer of the **gastric** cardia is 5.6:1. Improved diagnostic capability does not seem to account for this time trend because other cancers of the upper digestive tract have not shown a similar increase. [3]

Few studies have specifically evaluated risk factors for cancer of the **gastric** cardia. Smoking and alcohol consumption were associated with risk in some [4] [5] [5A] but not in all studies. [6] Dietary risk factors for **gastric** cancer have also been positively associated with the cardia subsite. [6] A predominance of higher social class and professional occupations among incident male cases of **gastric** cardia cancer [4] [7] has been reported. However, a recent study [5A] found no association between education and income levels and risk of **gastric** Cardia Cancer. Occupational associations were recently evaluated among men and women by broad categories, using the 24 US states' death certificate database, [8] and a significant increase in risk was reported for white men and white women among administrative managers, health professionals, and rubber and chemical manufacturing workers. Among women, an increase in risk was associated also with work in the wholesale trade. We extended the previous investigation among men to

---

include death certificates of an additional 3 years. Also, we evaluated more detailed occupation and industries and applied a priori job-exposure matrices for 12 occupational exposures that have previously been postulated as stomach cancer risk factors.

Methods

Since 1984, the National Cancer Institute, the National Institute for Occupational Safety and Health, and the National Center for Health Statistics have supported the coding of occupation and industry titles on death certificates from 24 US states according to the 1980 US Census occupation and industry codes. [9] This database currently consists of a total of 4.5 million death certificates, covering the years 1984-1992. Details on the 24 US states' death certificates database have been reported elsewhere. [10] Only usual occupation and industry is reported on the death certificate, and no duration of employment is available. Mortality records among male subjects aged 20 years or more were used to evaluate the risk of **gastric** cardia cancer associated with usual employment in a specific occupation and industry. Of 13,040 stomach cancer deaths among men aged 25 years or older, there were 1,056 deaths (8.1%) from cancer of the **gastric** cardia (ICD-9 code 151.1), including 1,023 whites and 33 blacks. Subjects of other race groups were also excluded because of small numbers. An evaluation of **gastric** cardia cancer risk by broad occupation and industry categories among women was included in the above-cited report. [8] Five

controls per case were selected from among subjects who died of non-malignant diseases, and were frequency-matched to cases by geographic region, race, gender, and 5-year age-group. Decedents in each occupation or industry were compared with all others.

Based on the 1980 US Census list of occupations and industries, [9] we used job-exposure matrices to evaluate occupational exposure to 12 potential

TABLE 1 -- Risk of Mortality From **Gastric** Cardia Cancer Associated With 3-Digit Census Industry Codes Among White Males *

Census Code	Industry	No. of Cases	OR (95% CI)
010	Agricultural production, crops	34	0.8 (0.5-1.3)
011	Agricultural production, livestock	13	1.3 (0.6-2.5)
041	Coal mining	6	0.5 (0.2-1.2)
042	Crude petroleum and natural gas extraction	5	0.8 (0.3-2.2)
060	Construction	84	0.8 (0.6-1.0)
100	Meat products	5	2.0 (0.6-6.2)
111	Bakery	7	3.9 (1.3-11.2)
120	Beverage industries	6	2.3 (0.8-6.5)
142	Yarn, thread and fabric mills	13	0.8 (0.4-1.5)
160	Pulp, paper, and paperboard mills	15	2.0 (1.0-3.7)
171	Newspapers publishing and printing	8	2.6 (1.0,6.3)
172	Printing and publishing, except newspapers	11	1.3 (0.6-2.6)
192	Industrial and miscellaneous chemicals	14	2.0 (1.0-3.9)
210	Tires and inner tubes	5	1.2 (0.4-3.1)
211	Other rubber products, plastic footwear and belting	5	0.7 (0.3-2.0)
231	Sawmills, planing mills, and millwork	5	0.9 (0.3-3.0)
242	Furniture and fixtures	5	1.2 (0.4-3.4)
270	Blast furnaces, steelworks, rolling, and finishing	23	1.2 (0.8-2.0)
271	Iron and steel foundries	5	2.7 (0.9-8.3)
300	Miscellaneous fabricated metal products	6	1.6 (0.6-4.3)
320	Metalworking machinery	8	1.1 (0.5-2.5)
331	Machinery except electrical, not elsewhere classified	14	1.1 (0.6-2.1)
341	Radio, TV, and communication equipment	5	2.6 (0.8-8.3)
342	Electrical machinery, equipment and supplies	10	0.9 (0.4-1.8)
351	Motor vehicles and motor vehicle	22	1.0 (0.6-1.7)

	equipment		
352	Aircrafts and parts	11	0.9 (0.5-1.8)
360	Ship and boat building and repairing	5	1.5 (0.5-4.2)
391	Miscellaneous manufacturing industries	10	3.3 (1.3-8.4)
392	Not specified manufacturing industries	26	0.9 (0.6-1.4)
400	Railroads	23	1.3 (0.8-2.2)
410	Trucking service	30	1.0 (0.7-1.6)
412	U.S. Postal Service	14	1.1 (0.6-2.0)
441	Telephone (wire and radio)	9	1.0 (0.4-2.4)
460	Electric light and power	12	1.0 (0.5-1.9)
470	Water supply and irrigation	5	5.6 (1.6-19.9)
530	Machinery, equipment and supplies	8	1.3 (0.6-3.0)
550	Groceries and related products	8	2.2 (0.9-5.4)
580	Lumber and building material retailing	7	1.7 (0.7-4.2)
601	Grocery stores	16	1.4 (0.8-2.5)
612	Motor vehicle dealers	8	0.7 (0.3-1.5)
620	Auto and home supply stores	5	1.4 (0.4-4.3)
621	Gasoline service stations	6	1.2 (0.5-3.0)
630	Apparel and accessories stores, except shoe	5	2.0 (0.6-6.2)
632	Furniture and home furnishings stores	5	1.0 (0.4-2.8)
641	Eating and drinking places	13	0.7 (0.4-1.3)
691	Not specified retail trade	7	1.0 (0.4-2.4)
711	Insurance	18	1.7 (0.9-3.2)
712	Real estate	8	0.6 (0.3-1.4)
721	Advertising	5	2.2 (0.7-7.1)
742	Business services	7	1.7 (0.7-4.1)
751	Automotive repair shops	14	0.7 (0.4-1.4)
760	Miscellaneous repair services	5	0.8 (0.3-2.4)
812	Offices of physicians	7	1.8 (0.6-5.3)
831	Hospitals	9	0.7 (0.3-1.8)
841	Legal services	5	1.0 (0.2-3.8)
842	Elementary and secondary schools	23	1.1 (0.7-1.8)
850	Colleges and universities	16	2.1 (1.1-4.2)
882	Engineering, architectural, and surveying services	5	0.9 (0.3-2.6)
890	Accounting, auditing, and bookkeeping services	6	2.2 (0.6-7.0)
901	General government, not elsewhere	20	1.4 (0.8-2.5)

	classified		
910	Justice, public order, and safety	25	1.5 (0.9-2.4)
931	Administration and economic programs	8	1.5 (0.5-3.9)
932	National security and international affairs	8	0.8 (0.3-1.7)
942	Armed Forces	21	1.0 (0.6-1.6)

* Only occupations with five or more exposed cases are reported. OR, odds ratio; 95% CI, 95% confidence interval.

carcinogenic exposures; namely, inorganic dust, asbestos, metal dust, lead, polycyclic aromatic hydrocarbons, nitrogen oxides, nitrosamines, sulfuric acid, fertilizers, herbicides, other pesticides, and wood dust. Most of these occupational hazards were discussed as risk factors for stomach cancer in a recent review. [11] An estimate of intensity level (none = 0, low = 1, medium = 2, high = 3) and probability (none = 0, low = 1, medium = 2, high = 3) of exposure to each of the 12 occupational hazards was developed by an experienced industrial hygienist (M.D.) and an occupational physician (P.C.) for each 3-digit occupation and industry code.

Intensity of exposure was estimated based upon literature information, computerized exposure databases (Occupational Safety and Health Administration files, National Institute for Occupational Safety and Health inspections database), and personal experience of the same professionals. The probability index was estimated based on the proportion of exposed workers within a given job title or industry and the number of occupations or industries with the same 1980 Census code. In addition, occupations were characterized into two groups depending upon the sources of exposure. If exposure was determined by the occupation itself regardless of industry, final intensity and probability scores were obtained by squaring the occupational scores. If exposure was determined by both occupation and industry, then the probability of exposure was dependent upon the industry, and the final score of intensity resulted from multiplying the intensity scores of both the occupation and industry. The final scores of probability and intensity of exposure were further categorized within four levels (none = 0, low = 1-2, medium = 3-4, high = 6-9).

Odds ratios (ORs) were estimated by logistic regression, and 95% confidence intervals (95% CI) by the Wald method, using the GMBO program in the Epicure software. [12] Included in the logistic regression model were age (5-year age categories), marital status (never married vs ever married), rural vs urban residence, and socioeconomic status (SES) (five categories, based on Green's Standardized Scores for Specific Occupations [13]). Statistical significance of trends in risk by increasing intensity level and probability of exposure were tested by dividing the regression coefficients of the variables assumed as non-categorical by their standard error to generate a Z-statistic. Under the null hypothesis, this test behaves as a normal standard deviate. [14] *P* values were two-tailed.

Results

Average age at death of **gastric** cardia cancer cases did not vary by race (white men, 64.2 ± 11.1 years; black men, 64.4 ± 10.9). Among white men, never having been married was associated with a significantly reduced risk of **gastric** cardia cancer (OR = 0.6; 95% CI, 0.4-0.8), while the risk was positive among black men (OR = 2.4; 95% CI, 0.9-6.1). A 20% increase in risk among both study

groups was associated with rural residence, defined as residence in the countryside or in a city with less than 250,000 inhabitants (white men: OR = 1.2; 95% CI, 1.0-1.4; black men: OR = 1.2; 95% CI, 0.5-2.7).

Among white men, risk increased significantly by SES category: ORs were 1.3 (95% CI, 1.0-1.6), 1.7 (95% CI, 1.4-2.2), 2.1 (95% CI, 1.6-2.6), and 2.5 (95% CI, 1.9-3.4) in consecutive, increasing SES categories, compared with the lowest category. A significant 2.5-fold increase in risk was also observed among black men in the second-lowest SES category, compared with the lowest, but numbers in the higher SES categories were not sufficient to confirm the trend observed among whites. These covariates and age in five-year groups were included in logistic regression models to estimate risk associated with each industry, occupation, or exposure.

Table 1 shows the risks for **gastric** cardia cancer associated with specific industries with five cases or more among white men. A significant or borderline significant increase in risk was observed among the following industries: bakery products (OR = 3.9; 95% CI, 1.3-11.2); pulp, paper, and paperboard mills (OR = 2.0; 95% CI, 1.0-3.7); newspaper publishing and printing (OR = 2.6; 95% CI, 1.0-6.3); industrial and miscellaneous chemicals manufacturing (OR = 2.0; 95% CI, 1.0-3.9); miscellaneous manufacturing industries (OR = 3.3; 95% CI, 1.3-8.4); water supply and irrigation (OR = 5.6; 95% CI, 1.6-19.9); colleges and universities (OR = 2.1; 95% CI, 1.1-4.2); and social services not elsewhere classified (OR = 7.8; 95% CI, 1.6-37.8). Notably, among industries reported to be associated with stomach cancer in other studies, risk was not increased for farming, mining, the construction industry, manufacturing of tires and other rubber products, or woodworking.

TABLE 2 -- Risk of Mortality From **Gastric** Cardia Cancer Associated With 3-Digit Census Occupational Codes Among White Males*

Census Code	Occupation	No. of Cases	OR (95% CI)
005	Administrators and officials, public administration	7	1.0 (0.4-2.7)
007	Financial managers	6	6.1 (1.3-28.8)
013	Managers, marketing, advertising and public relations	9	2.2 (0.8-5.7)
019	Managers and administrators not elsewhere classified	90	1.2 (0.8-1.7)
023	Accountants and auditors	12	1.3 (0.6-2.9)
053	Civil engineers	5	0.5 (0.1-1.8)
055	Electrical and electronic engineers	12	1.6 (0.7-3.6)
059	Engineers, not elsewhere classified	6	2.1 (0.6-6.8)
084	Physicians	7	1.3 (0.5-3.6)
156	Teachers, elementary school	7	0.8 (0.3-2.0)
178	Lawyers	6	1.3 (0.4-4.5)
243	Supervisors and proprietors, sales occupations	42	0.9 (0.7-1.4)

253	Insurance sales occupations	11	1.5 (0.7-3.3)
254	Real estate sales occupations	8	1.0 (0.4-2.3)
259	Sales representatives, mining, manufacturing, wholesale	12	0.7 (0.4-1.4)
274	Sales workers, other commodities	11	1.0 (0.5-2.0)
355	Mail carriers, postal service	8	1.3 (0.5-3.1)
379	General office clerks	5	0.7 (0.3-2.0)
417	Firefighting occupations	7	2.2 (0.9-5.6)
418	Police and detectives, public service	5	0.8 (0.3-2.1)
426	Guards and police, except public service	7	0.4 (0.2-1.1)
453	Janitors and cleaners	23	1.7 (1.0-2.9)
473	Farmers, except horticultural	40	0.9 (0.6-1.4)
479	Farm workers	6	1.0 (0.3-2.8)
503	Supervisors, mechanics and repairers	6	1.9 (0.6-6.1)
505	Automobile mechanics	20	1.3 (0.7-2.2)
518	Industrial machinery repairers	9	1.7 (0.8-3.8)
544	Millwrights	7	1.8 (0.7-4.3)
549	Not specified mechanics and repairers	8	1.1 (0.5-2.5)
558	Supervisors, not elsewhere classified	6	0.5 (0.2-1.3)
563	Brickmasons and stonemasons	5	1.7 (0.6-5.0)
567	Carpenters	19	1.2 (0.7-2.0)
575	Electricians	15	1.4 (0.7-2.5)
579	Painters, construction and maintenance	6	0.6 (0.2-1.4)
585	Plumbers, pipefitters, and steamfitters	10	0.7 (0.4-1.5)
633	Supervisors, production occupations	26	1.1 (0.7-1.7)
637	Machinists	26	1.2 (0.8-2.0)
696	Stationary engineers	8	0.8 (0.3-1.7)
734	Printing machine operators	6	1.4 (0.5-3.7)
777	Miscellaneous machine operators	8	0.7 (0.3-1.7)
779	Machine operators, not specified	17	1.1 (0.6-1.9)
783	Welders and cutters	10	1.1 (0.5-2.4)
785	Assemblers	7	1.2 (0.5-2.8)
796	Production inspectors, checkers, and examiners	13	3.2 (1.5-6.9)
804	Truck drivers, heavy	41	1.5 (1.0-2.2)
823	Railroad conductors and yard masters	6	1.7 (0.6-4.6)
824	Locomotive operating occupations	5	2.5 (0.8-7.6)
869	Construction laborers	14	1.5 (0.8-2.9)
883	Freight, stock, and material handlers	6	1.7 (0.6-5.1)

889	Laborers except construction	26	0.9 (0.6-1.6)
905	Military	20	0.9 (0.6-1.6)
913	Retired, no occupation reported	11	1.1 (0.5-2.2)

* Only occupations with five or more exposed cases are reported.

Non-significant increases of twofold or more were observed for meat products and iron and steel foundries. Among black men, a non-significant positive association was observed only among persons employed in railroads (OR = 13.1, based on three cases and two controls).

Table 2 presents the ORs for occupations with five exposed deaths or more among white men. A significant or borderline significant increase in risk was observed for financial managers (OR = 6.1; 95% CI, 1.3-28.8); janitors and cleaners (OR = 1.7; 95% CI, 1.0-2.9); production inspectors, checkers, and examiners (OR = 3.2; 95% CI, 1.5-6.9); and drivers of heavy trucks (OR = 1.5; 95% CI, 1.0-2.2).

Some non-significant excess risks corresponded to results among industries: printing machine operators (OR = 1.4; 95% CI, 0.5-3.7), bakers (OR = 2.0; 95% CI, 0.5-7.8), and water and sewage treatment plant operators (OR = 5.2; 95% CI, 1.1-25.0). The last two occupations, both based on three cases, are not reported in the tables. Other non-significant increases in risk among occupations previously associated with stomach cancer [11] were observed for firefighters, brickmasons and stonemasons, and construction laborers, but not for farmers, farmworkers, and butchers and meatcutters. Among blacks, only carpenters showed a non-significant excess risk (three cases and no controls).

The application of the 12 job-exposure matrices for potential occupational risk factors for **gastric** cardia cancer showed an increase in risk associated with the probability of exposure to asbestos and sulfuric acid among white men (Table 3) , with a significant positive trend for sulfuric acid. The increase in risk associated with high probability of exposure to asbestos was based on only one death. High probability of exposure to lead was associated with a significant 30% increase in risk among white men, and the risk was 1.2 for all probability categories combined among black men (data not shown). Risk patterns by intensity of exposure (Table 4) showed an inverse trend for asbestos, while sulfuric acid again showed a significantly positive trend ($P < 0.01$). The highest intensity level of lead exposure was associated with a significant 60% increase in risk.

TABLE 3 -- Risk of Mortality From **Gastric** Cardia Cancer, by Probability of Exposure to Specified Occupational Hazards (All Intensity Levels Combined)

	Unexposed		**All Exposed**		**Probability of Exposure**					
					Low		**Medium**		**High**	
Exposure	***n***	**OR**	***n***	**OR (95% CI)**	***n***	**OR (95% CI)**	***n***	**OR (95% CI)**	***n***	**OR (95% CI)**
Asbestos	13	1.0	1010	1.5 (0.8-2.8)	819	1.5 (0.8-2.8)	190	1.5 (0.8-2.9)	1	2.6 (0.2-28.7)

Inorganic dust	652	1.0	371	0.9 (0.8-1.1)	72	0.9 (0.7-1.2)	116	1.0 (0.8-1.3)	183	0.9 (0.9-1.1)
Metal dust	830	1.0	193	1.0 (0.8-1.2)	23	0.8 (0.5-1.2)	100	1.1 (0.8-1.4)	70	0.9 (0.7-1.3)
Lead	841	1.0	182	0.9 (0.8-1.1)	69	0.9 (0.7-1.2)	25	0.9 (0.6-1.4)	88	1.3 (1.0-1.7)
Polycyclic aromatic hydrocarbons	723	1.0	300	1.0 (0.8-1.2)	63	0.9 (0.7-1.2)	91	1.0 (0.7-1.2)	146	1.0 (0.8-1.3)
Nitrogen oxides	727	1.0	296	0.9 (0.7-1.0)	55	0.8 (0.6-1.1)	37	0.8 (0.6-1.2)	204	0.9 (0.7-1.1)
Nitrosamines	839	1.0	30	0.8 (0.5-1.2)	113	1.0 (0.8-1.3)	41	1.0 (0.7-1.4)	184	0.9 (0.8-1.1)
Sulfuric acid *	729	1.0	294	1.2 (1.0-1.4)	229	1.1 (0.9-1.3)	35	1.4 (0.9-2.1)	30	1.3 (0.8-2.1)
Fertilizers	965	1.0	58	0.9 (0.6-1.3)	6	0.8 (0.3-2.1)	8	1.2 (0.5-3.0)	44	0.9 (0.6-1.4)
Herbicides	966	1.0	57	0.9 (0.6-1.4)	7	1.3 (0.5-3.3)	7	1.1 (0.4-3.0)	43	0.8 (0.5-1.3)
Other pesticides	915	1.0	108	1.1 (0.8-1.5)	52	1.3 (0.9-1.8)	11	1.0 (0.5-2.1)	45	0.9 (0.6-1.5)
Wood dust	958	1.0	65	0.8 (0.6-1.1)	34	0.8 (0.5-1.2)	9	0.9 (0.4-1.8)	22	0.9 (0.5-1.4)

* Test for trend: $P < 0.05$.

TABLE 4 -- Risk of Mortality From **Gastric** Cardia Cancer by Intensity of Exposure to Occupational Hazards (All Probabilities Combined)

	Unexposed		**All Exposed**		**Intensity Level of Exposure**					
					Low		**Medium**		**High**	
Exposure	***n***	**OR**	***n***	**OR (95% CI)**	***n***	**OR (95% CI)**	***n***	**OR (95% CI)**	***n***	**OR (95% CI)**
Asbestos	13	1.0	1010	1.5 (0.8-2.8)	873	1.5 (0.8-2.9)	120	1.4 (0.7-2.7)	17	1.0 (0.5-2.4)
Inorganic dust	652	1.0	371	0.9 (0.8-1.1)	192	1.0 (0.8-1.2)	134	1.0 (0.8-1.2)	45	0.8 (0.5-1.1)
Metal dust	830	1.0	193	1.0 (0.8-1.2)	47	0.8 (0.6-1.1)	75	1.0 (0.8-1.4)	71	1.1 (0.8-1.5)
Lead	841	1.0	182	0.9 (0.8-1.1)	105	1.0 (0.8-1.3)	59	1.0 (0.7-1.3)	18	1.6 (1.0-2.8)

Polycyclic aromatic hydrocarbons	723	1.0	300	1.0 (0.8-1.2)	173	1.0 (0.8-1.3)	99	0.9 (0.7-1.2)	28	1.0 (0.6-1.6)
Nitrogen oxides	727	1.0	296	0.9 (0.7-1.0)	157	0.9 (0.7-1.1)	95	0.9 (0.7-1.2)	44	0.7 (0.5-1.0)
Nitrosamines	839	1.0	30	0.8 (0.5-1.2)	22	1.0 (0.6-1.6)	142	0.9 (0.8-1.2)	20	0.9 (0.5-1.5)
Sulfuric acid *	729	1.0	294	1.2 (1.0-1.4)	209	1.1 (0.9-1.3)	74	1.5 (1.1-2.0)	11	1.8 (0.9-3.8)
Fertilizers	965	1.0	58	0.9 (0.6-1.3)	5	1.4 (0.4-5.0)	46	0.9 (0.6-1.4)	7	0.7 (0.3-1.9)
Herbicides	966	1.0	57	0.9 (0.6-1.4)	2	1.1 (0.1-13.9)	6	2.9 (1.0-8.4)	49	0.8 (0.5-1.2)
Other pesticides	915	1.0	108	1.1 (0.8-1.5)	29	1.5 (0.9-2.4)	26	1.0 (0.7-1.7)	53	1.1 (0.7-1.7)
Wood dust	958	1.0	65	0.8 (0.6-1.1)	32	0.9 (0.6-1.4)	24	0.7 (0.5-1.2)	9	1.0 (0.5-2.2)

* Test for trend: $P < 0.01$.

More detailed analyses were possible only for white men. Among whites, risk patterns associated with exposure to asbestos, lead, and sulfuric acid were also explored within categories of probability and intensity of exposure (Table 5) . A consistent pattern of increasing risk by probability within intensity level categories and by intensity level within probability categories was observed for sulfuric acid, with a few significantly positive trends. Lead showed some increase in the highest level of exposure, but only one case was represented in the high-level/high probability of exposure cell. Risk patterns associated with probability and intensity of exposure to asbestos were inconsistent. However, only one subject had a high probability of exposure to asbestos.

Discussion

The results of the present case-control analysis suggest that occupational exposure to sulfuric acid mists may be a risk factor for cancer of the **gastric** cardia. Applying a job-exposure matrix to the occupation/industry combinations in the death certificates of study subjects resulted in significantly increasing risks by probability and intensity level of exposure. Exposure to sulfuric acid mists occurs in the pulp and paper mills industry, where we observed a significant increase in risk. Exposure to acid mists also occurs among water and sewage treatment plant operators, who showed a fivefold increase in risk in this study (OR = 5.2; 95% CI, 1.1-25.0, based on three cases; not shown in the tables).

TABLE 5 -- Risk of Mortality From **Gastric** Cardia Cancer by Probability and Intensity Level of

Exposure to Asbestos, Lead, and Sulfuric Acid

Exposure	Intensity Level	Probability of Exposure					
		Low		Medium		High	
		n	OR (95% CI)	*n*	OR (95% CI)	*n*	OR (95% CI)
Asbestos	Unexposed	13	1.0	13	1.0	13	1.0
	Low	753	1.5 (0.8-3.0)	120	1.7 (0.8-3.7)		--
	Medium	62	1.3 (0.7-2.7)	58	1.3 (0.7-2.8)		--
	High	4	0.8 (0.2-2.9)	12	1.0 (0.4-2.9)	1	--
Lead	Unexposed	841	1.0	841	1.0	841	1.0
	Low	26	0.7 (0.5-1.1)	2	0.3 (0.1-1.4)	77	1.3 (1.0-1.8)
	Medium	30	0.9 (0.6-1.4)	19	1.0 (0.6-1.6)	10	1.1 (0.5-2.2)
	High	13	1.6 (0.9-3.1)	4	1.5 (0.5-4.6)	1	--
Sulfuric acid	Unexposed	729	1.0	729	1.0	729	1.0
	Low	178	1.1 (0.9-1.3)	6	0.8 * (0.3-2.0)	25	1.2 (0.7-2.0)
	Medium	49	1.3 (0.9-1.9)	24	1.7 * (1.0-2.9)	1	0.9 (0.1-11.2)
	High *	2	1.6 (0.3-8.0)	5	2.0 * (0.7-6.4)	4	2.0 (0.6-7.3)

* Tests for trend: $P < 0.05$.

Other exposures in these jobs include chlorine and its acids. Gastroesophageal reflux has been suggested as an important risk factor for adenocarcinomas of the esophagus and **gastric** cardia, [15] possibly through the production of premalignant epithelial changes after contact with the acidic content of the stomach. Whether the inhalation and subsequent ingestion of acid mists in occupational settings might also cause irritation and subsequent premalignant changes in the **gastric** cardia mucosa is unknown. Significant increases in **gastric** cardia cancer risk were also associated with high probability (all levels combined) of and high-level (all probabilities combined) exposure to lead, by crosstabulation of risk by the two exposure metrics did not show consistent trends. Only one death was represented in the high probability/high level of exposure cell. Results for asbestos were also inconsistent. Only one subject had high probability of exposure to asbestos, and risk decreased by increasing level of exposure in the low- and medium-probability categories. None of the other occupational hazards explored using job-exposure matrices showed any pattern of increasing risk either by probability or intensity level of exposure.

The present analysis of risk of **gastric** cardia cancer by occupation and industry showed some similarities with reports in the literature for all stomach cancer combined. [11] However, occupations--such as farmers, and butchers and meatcutters--or industries--such as mining, construction, manufacturing of tires and other rubber products, and wood working, previously associated with stomach cancer, [11] --were not associated with **gastric** cardia cancer risk in this study among white men. A non-significant excess risk for carpenters was limited to black men. Also, exposure to inorganic dust, metal dust, and nitrosamines, possible candidates as occupational carcinogens for **gastric** cancer, [11] did not show an association in this study. These disparities may be due to the limitations of this analysis in evaluating occupational exposures, or they may reflect a different etiology for **gastric** cardia cancer,

compared with other cancers of the stomach.

Cancer of the **gastric** cardia is largely underreported on the death certificates. SEER incidence data indicate that it accounts for about 25% of all **gastric** cancer among men, [8] while it accounts only for 8.1% of stomach cancer deaths in the 24 US states' death certificate database. We observed an association of **gastric** cardia cancer with higher SES, which may be due to differential underreporting by the SES of the decedent. We adjusted risk estimates by SES to prevent underestimation of the **gastric** cardia cancer risk associated with some occupations and industries belonging to low SES.

Interpretation of results from hypothesis-generating studies is difficult, as chance is a likely explanation when multiple comparisons are involved. Suggestions have been made to correct the level of statistical significance by the number of comparisons. [16] Instead, we presented only risk estimates with at least five exposed deaths and explored the consistency of trends by probability and intensity of exposure.

Another limitation in the present study is that occupational information in the death certificates is limited to only one occupation and industry title, with no duration of employment. Any resulting exposure misclassification would probably be non-differential. As a consequence, underestimation is most likely for risk associated with high-exposure categories, and positive trends such as those that we observed for exposure to sulfuric acid would be possible only under very extreme conditions. [17]

On the other hand, using the 24 US states' database provided the largest number of **gastric** cardia cancer deaths studied to date, which allowed the first detailed exploration of occupational associations. Further studies with more detailed exposure assessments, based on complete work histories and incident cases, are needed to further evaluate hypotheses generated by the present study.

References

1. Parkin DM, Pisani P, Ferlay J. Estimates of the worldwide incidence of eighteen major cancers in 1985. *Int J Cancer.* 1993;54:594-606.

2. Howson CP, Hiyama T, Wynder EL. The decline in **gastric** cancer: epidemiology of an unplanned triumph. *Epidemiol Rev.* 1986;8:1-27.

3. Blot WJ, Devesa SS, Kneller RW, Fraumeni JF Jr. Rising incidence of adenocarcinoma of the esophagus and **gastric** cardia. *JAMA.* 1991;265:1287-1289.

4. Kabat GC, Ng SKC, Wynder EL. Tobacco, alcohol intake, and diet in relation to adenocarcinoma of the esophagus and **gastric** cardia. *Cancer Causes Control.* 1993;4:123-132.

5. Vaughan TL, Davis S, Kristal A, Thomas DB. Obesity, alcohol, and tobacco as risk factors for cancers of the esophagus and **gastric** cardia: adenocarcinoma versus squamous cell carcinoma. *Cancer Epidemiol Biomark Prevent.* 1995;4:85-92.

5A. Gammon MD, Schoenberg JB, Ahsan H, et al. Tobacco, alcohol, and socioeconomic status and adenocarcinomas of the esophagus and **gastric** cardia. *J Natl Cancer Inst*. 1997;89:1277-1284.

6. Palli D, Bianchi S, DeCarli A, et al. A case-control study of cancer of the **gastric** cardia in Italy. *Br J Cancer.* 1992;65:263-266.

7. Powell J, McConkey CC. Increasing incidence of adenocarcinoma of the **gastric** cardia and adjacent sites. *Cancer.* 1990;62:440-443.

8. Ward MH, Dosemeci M, **Cocco** P. Mortality from **gastric** cardia and lower esophagus cancer and occupation. *J Occup Med.* 1994;36:1222-1227.

9. Bureau of the Census. *Alphabetical Index of Industries and Occupations*. [PHC80-R3.] Washington, DC: US Department of Commerce; 1982.

10. Burnett CA, Dosemeci M. Using occupational mortality data for surveillance of work-related diseases of women. *J Occup Med.* 1994;36:1199-1203.

11. **Cocco** P, Ward MH, Buiatti E. Occupational risk factors for **gastric** cancer: an overview. *Epidemiol Rev.* 1996;18:218-234.

12. Preston DL, Lubin JH, Pierce DA. *Epicure*. Seattle, WA: Hirosoft International Corp; 1990.

13. Green L. Manual for scoring socioeconomic status for research on health behavior. *Public Health Rep.* 1970;85:815-827.

14. Breslow NE, Day NE. *Statistical Methods in Cancer Research: Volume I-- The Analysis of Case-Control Studies*. [IARC Scientific Publications No. 32.] Lyon, France: International Agency for Research on Cancer; 1980.

15. Chow WH, Finkle WD, McLaughlin JK, et al. The relation of gastroesophageal reflux disease and its treatment to adenocarcinomas of the esophagus and **gastric** cardia. *JAMA.* 1995;274:474-477.

16. Rothman KJ. *Modern Epidemiology*. Boston, MA: Little, Brown and Co; 1986.

17. Dosemeci M, Wacholder S, Lubin J. Does nondifferential misclassification always bias a true effect toward the null value?