The National Bladder Cancer Study: Employment in the Chemical Industry[1,2]

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ABSTRACT—The relationship between bladder cancer and employment in the chemical industry was assessed in a study of 2,982 incident cases and 5,782 population controls. There were 190 cases and 369 controls who had ever been employed in the chemical industry [odds ratio (OR)=1.0; 95% confidence interval (CI)=0.8, 1.2]. Employment in the production of organic chemicals was associated with a 1.3-fold increased risk among men (95% CI=0.8, 2.1). Risk increased with duration of employment, reaching an OR of 2.4 for 20 or more years (chi for trend=1.57; P=.06). Women who had worked in the plastics industry had a 3.3-fold increased bladder cancer risk. Within the plastics and rubber industry, increased risks for bladder cancer were found for men in mixing, filtering, grinding, and other dusty operations (OR=4.6; 95% CI=1.0, 20.4) and men in heat-associated operations (OR=2.8; 95% CI=0.5, 15.3). A 1.4-fold risk among men in agricultural chemicals was attributable to risks in the pesticides subdivision (OR=2.3; 95% CI=0.6, 8.2). Men performing dusty operations (Le., mixing, filtering, sifting, grinding, and crushing) in any industry had an OR of 1.4 (95% CI=0.8, 2.7). Despite the large number of study subjects, few statistically significant findings were observed and should be evaluated with consideration of the large number of comparisons made in the analysis. The statistical power of case-control studies to detect risks associated with particular occupational exposures is limited by the small proportion of the population employed in any specific occupation or industry.—JNCI 1987; 79:217-222.

In 1895, Rehn (*1*) observed that 4 of his patients diagnosed with bladder cancer had worked in dyestuffs manufacturing in a process that converts aniline to magenta. Since that time, numerous chemicals and processes have been linked to the development of bladder cancer (2, ***3***). However, case-control studies often have had too few subjects to identify or quantify the bladder cancer risk for specific processes and occupations within the chemical industry (***4***). We therefore evaluated the relationship between employment in the chemical industry and bladder cancer using interview data from a large case-control study conducted in 10 geographic areas of the United States (***5***). The study included the State of New Jersey, which has a high concentration of chemical-manufacturing establishments (***6***, 7).

SUBJECTS AND METHODS

A Population-based case-control study was conducted in the following 10 geographic areas of the United States: Atlanta, GA; Detroit, MI; New Orleans, LA; San Francisco, CA; Seattle, WA; and the States of Connecticut, Iowa, New Jersey, and Utah. The study methods are presented in detail elsewhere (***5***).

Cases consisted of all residents of the 10 areas who were aged 21–84 years and who were diagnosed with histologically confirmed bladder cancer during a 1-year period beginning in December 1977. Approximately 2 controls per case were selected by an age- and sex-stratified random sample of the general population in the 10 study areas. Controls aged 21–64 years were selected by telephone with the use of a two-staged random-digit-dialing technique (*8*), whereas controls aged 65–84 years were selected from the Health Care Financing Administration (Medicare) file, which listed approximately 98% of all Americans older than age 64 in 1978 (***5***).

There were 4,086 eligible cases and 6,985 eligible controls. In-person interviews conducted in the study subjects' homes were obtained from 2,982 (73%) cases and 5,782 (83%) controls. The interviews covered demographic characteristics, lifetime occupational and residential histories, beverage consumption, medical history, and use of tobacco, artificial sweeteners, and hair dyes.

The occupational data were originally coded according to the scheme developed by the U.S. Bureau of the Census (***9***). We examined the job titles, duties, and industry descriptions for all cases and controls who ever worked in the chemical industry (code: 347–369), research and development laboratories (code: 729), ordinance manufacturing (code: 258), the rubber industry (code: 379, 387), or the textile and fibers industry (code: 317, 318). We then recoded the occupational data for the subjects who had jobs in the chemical industry as defined by the SIC (*10*), which distinguishes the subdivisions within the chemical industry better than the Census code (***11***). Job titles were coded according to an exposure-oriented scheme based loosely on the ***Dictionary of Occupational Titles*** (***12***).

ABBREVIATIONS USED: CI = confidence interval; OR = odds ratio; SIC = Standard Industrial Classification.

[1] Received August 7, 1986; revised February 12, 1987; accepted February 20, 1987.

[2] Sponsored by the U.S. Food and Drug Administration, the National Cancer Institute, and the U.S. Environmental Protection Agency.

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TABLE 1.—Number of bladder cancer cases and controls and ORs according to employment in the chemical industry, by race and sex, adjusted for age, geographical area, and cigarette smoking

Race and sex	Employed in the chemical industry	Cases	Controls	OR (95%CI)
White men	Never	1,972	3,615	
	Ever	144	277	0.9 (0.7, 1.2)
White women	Never	654	1,304	
	Ever	35	62	0.9 (0.6, 1.5)
Nonwhite men	Never	124	365	
	Ever	9	25	1.0 (0.4, 2.6)
Nonwhite women	Never	42	129	
	Ever	2	5	0.9 (0.03, 14.6)

The measure of association between employment in the chemical industry and risk of bladder cancer was the OR. The effects of potential confounding factors, such as sex, race, age (21-44, 45-64, 65-84 yr), geographic area (New Jersey, Detroit, other), cigarette smoking (nonsmokers, ex-smokers, current smokers), and occupations with ORs greater than 1.5 (e.g., metal workers and machinists, truck drivers, artists, and painters), were taken into account by stratification. In general, the unadjusted and adjusted risk estimates did not differ by more than 10%, so unadjusted estimates are usually presented. When appropriate, adjusted and stratum-specific estimates are also presented. Maximum likelihood estimates of the OR and 95% CIs were computed by Gart's method (*13*). For duration-response relationships, significance was assessed with the use of Mantel's one-tailed test for linear trend (*14*).

RESULTS

There were 190 bladder cancer cases and 369 controls who had ever been employed in the chemical industry, yielding a crude OR of 1.0 (95% CI = 0.8, 1.2). Adjustment for age, sex, race, geographical area, and cigarette smoking did not change the overall risk estimate. Table 1 shows the race- and sex-specific estimates of risk for ever employment in the chemical industry, adjusted for age, geographical area, and smoking. The small number of nonwhites precluded more detailed analysis, and subsequent tables are limited to white men and women. No relationship between bladder cancer risk and duration of employment in the chemical industry was seen among white men or women (table 2). There was also no association between bladder cancer risk and geographical area, year or age started employment, or time since initial employment in the chemical industry.

Bladder cancer risks among white men and women by employment in occupations and in subdivisions of the chemical industry are shown in tables 3 and 4, respectively. The results are described below.

Industry

Industrial inorganic chemicals (SIC 2810-2819).—A nonsignificant deficit of bladder cancer was seen among men and women ever employed in the production of industrial inorganic chemicals. However, among men employed for at least 20 years, the OR was 2.3 (95% CI = 0.6, 8.2).

Plastics and rubber (SIC 2820-2829).—No association with bladder cancer was seen among men ever employed in the production of plastics and synthetic rubber (OR = 1.1; 95% CI = 0.7, 1.7). Men who began employment after 1959 had an OR of 1.6 (95% CI = 0.5, 4.6). Risk was limited to the New Jersey area where men in the plastics and rubber industry had an OR of 1.3 (95% CI = 0.7, 2.3). Among women, the risk associated with employment in plastics and synthetic rubber production was attributable to the plastics subdivision (OR = 3.3; 95% CI = 0.9, 12.9). The small number of women precluded geographical or other more detailed analyses.

Industrial organic chemicals (SIC 2860-2869).—Employment in the production of organic chemicals was associated with a 1.3-fold increased risk of bladder cancer among men (95% CI = 0.8, 2.1). Risk increased somewhat inconsistently with duration of employment, reaching an OR of 2.4 (95% CI = 0.9, 6.8) for 20 or more years (table 5). The risk was limited to men who were first employed after 1939 (OR = 1.8; 95% CI = 1.0, 3.1). Men who were first employed before 1940 had a deficit

TABLE 2.—Number of bladder cancer cases and controls and ORs according to duration of employment in the chemical industry for white men and women

Duration, yr[a]	Cases	Controls	OR (95%CI)
White men			
Never	1,972	3,615	
<5	65	115	1.0 (0.8, 1.4)
5-9	20	35	1.1 (0.6, 1.8)
10-19	18	52	0.6 (0.4, 1.1)
≥20	35	58	1.1 (0.7, 1.7)
Chi for trend = −0.360; P = .36 (one-tailed)			
White women			
Never	654	1,304	
<5	21	30	1.4 (0.8, 2.5)
5-9	6	12	1.0 (0.4, 2.7)
10-19	3	8	0.8 (0.2, 2.8)
≥20	4	5	1.6 (0.4, 5.9)
Chi for trend = 0.626; P = .27 (one-tailed)			

[a] Excludes 7 cases (6 men and 1 woman) and 24 controls (17 men and 7 women) with unknown duration.

TABLE 3.—*Number of bladder cancer cases and controls and ORs among white men and women employed in subdivisions of the chemical industry*

Industry (SIC No.)[a]	Men			Women		
	Cases	Controls	OR (95%CI)	Cases	Controls	OR (95%CI)
Never employed in chemical industry	1,972	3,615		654	1,304	
Industrial inorganic chemicals (2810–2819)	18	39	0.8 (0.5, 1.5)	0	4	—
Plastics, synthetic rubber, and other synthetic fibers (2820–2829)	27	46	1.1 (0.7, 1.7)	5	4	2.5 (0.7, 8.9)
Plastics (2821)	23	37	1.1 (0.7, 1.9)	5	3	3.3 (0.9, 12.9)
Drugs (2830–2839)	22	39	1.0 (0.6, 1.7)	9	16	1.1 (0.5, 2.6)
Soaps and cleansers (2841–2843)	13	25	1.0 (0.5, 1.9)	3	5	1.2 (0.3, 5.0)
Perfumes and cosmetics (2844)	8	19	0.8 (0.3, 1.8)	8	10	1.6 (0.6, 4.0)
Paints, varnishes, lacquers, and enamels (2850–2859)	17	30	1.0 (0.6, 1.9)	3	7	0.9 (0.2, 3.3)
Industrial organic chemicals (2860–2869)	28	40	1.3 (0.8, 2.1)	1	0	—
Aromatic organic chemicals (2865)	12	23	1.0 (0.5, 1.9)	1	0	—
Nonaromatic and unspecified organic chemicals (2869)	17	22	1.4 (0.8, 2.7)	0	0	—
Agricultural chemicals (2870–2879)	6	8	1.4 (0.5, 4.0)	1	2	1.0 (0.1, 12.4)
Fertilizers (2873)	1	4	0.5 (0.1, 3.9)	1	2	1.0 (0.1, 12.4)
Pesticides (2879)	5	4	2.3 (0.6, 8.2)	0	0	—
Adhesives (2891)	3	11	0.5 (0.1, 1.8)	0	0	—
Explosives (2892)	11	14	1.4 (0.7, 3.2)	2	2	2.0 (0.3, 13.7)
Chemicals, NEC[b] (2899)	22	49	0.8 (0.5, 1.4)	3	14	0.4 (0.1, 1.4)

[a] SIC, Office of Management and Budget, 1972.
[b] Not elsewhere classified.

of bladder cancer (OR = 0.5; 95%CI = 0.2, 1.4). No elevation of risk was seen in New Jersey (OR = 1.0; 95% CI = 0.6, 1.8). In fact, higher risks were seen among men residing outside New Jersey or Detroit (OR = 2.8; 95%CI = 1.0, 7.6).

We separated the men who produced aromatic compounds (OR = 1.0) from those who produced unspecified or nonaromatic organic compounds, such as acids, solvents, alcohols, and esters (OR = 1.4; 95%CI = 0.8, 2.7). Among the unspecified and nonaromatic producers, ORs of 1.2, 0.5, 1.8, and 5.5 were observed for men employed less than 5, 5–9, 10–19, and 20 or more years, respectively (chi for trend = 2.11; $P = .017$).

Agricultural chemicals (SIC *2870–2879*).—The 1.4-fold risk among men in the agricultural chemicals industry was attributable to risks in the pesticides subdivision (OR = 2.3; 95%CI = 0.6, 8.2). Although based on small numbers, fertilizer production was associated with a deficit of bladder cancer.

Explosives (SIC *2892*).—Men ever employed in the explosives industry had an OR of 1.4 (95%CI = 0.7, 3.2). No association with duration of employment was seen.

Occupation

Sales occupations.—Although no overall increased risk of bladder cancer was seen among salespeople, a 1.5-fold increased risk was seen among white men employed in sales occupations for at least 10 years. ORs of 0.8, 0.6, 1.4, and 1.8 were observed for men employed less than 5, 5–9, 10–19, and 20 or more years, respectively (chi for trend = 0.42; $P = .34$).

Chemists and engineem—A significant deficit of bladder cancer was seen among male chemists, engineers, and other research and technical occupations. However, men with at least 20 years' employment in these occupations had a twofold increased risk (OR = 1.8; 95%CI = 0.6, 5.6).

Inspectors and quality-control occupations.—An increased risk of bladder cancer was observed among women ever employed as inspectors or in other quality-control occupations (OR = 2.5; 95%CI = 0.7, 8.9).

Operators.—Although operators might be the most heavily exposed workers in the chemical industry, the men in this study did not experience significant excess bladder cancer risk (OR = 1.2; 95% CI = 0.8, 1.7). The ORs did not vary significantly by duration, year or age started employment, or time since initial employment. Only operators in New Jersey had an excess risk (OR = 1.3; 95%CI = 0.8, 1.9).

Among men performing dusty operations (i.e., mixing, filtering, sifting, grinding, crushing, etc.), an OR of 1.7 (95%CI = 1.0, 3.0) was observed. Adjustment for age, geographical area, and smoking lowered the risk to 1.4 (95%CI = 0.8, 2.7). There were no consistent patterns of risk associated with duration, year started employment, or time since initial employment. However, risk was inversely related to age started employment in dusty operations. The ORs were 2.1, 1.2, and 0.7 for men who began employment before age 26, 26–40, and over 40 years, respectively.

Among men performing operations requiring heat (i.e., distilling, heating, baking, furnace tender, casting, etc.), an OR of 1.3 (95%CI = 0.6, 2.5) was observed. No meaningful relationships with duration, latency, geographical location, or other employment characteristics were seen.

Baggers, bottlers, canners, and assemblers.—These occupations potentially involve high levels of exposure to the chemical products being bagged, bottled, and

TABLE 4.—*Number of bladder cancer cases and controls and ORs among white men and women employed in occupations within the chemical industry*

Occupation	Men			Women		
	Cases	Controls	OR (95%CI)	Cases	Controls	OR (95%CI)
Never employed in chemical industry	1,972	3,615		654	1,304	
Office occupations	24	47	0.9 (0.6, 1.5)	11	28	0.8 (0.4, 1.6)
Sales occupations	11	20	1.0 (0.5, 2.1)	1	3	0.7 (0.1, 6.3)
Chemists, engineers, and other research and technical occupations	18	64	0.5 (0.3, 0.9)	0	5	—
Foremen and supervisors	13	28	0.9 (0.4, 1.6)	0	0	—
Inspectors and quality-control occupations	6	11	1.0 (0.4, 2.7)	5	4	2.5 (0.7, 8.9)
Operators	47	73	1.2 (0.8, 1.7)	2	2	2.0 (0.3, 13.7)
Op A Mixing, blending, compounding, and frothing	17	18	1.7 (0.9, 3.3)	0	0	—
Op B: Filtering, straining, separating, sifting, precipitation, centrifuging, and extracting	1	1	1.8 (0.1, 28.1)	0	0	—
Op C: Distilling	1	4	0.5 (0.1, 3.9)	0	0	—
Op D: Heating, baking, drying, seasoning, melting, autoclaving, and furnace tender	10	14	1.3(0.6, 2.9)	1	0	—
Op E: Coating, calendering, laminating, and dyeing	0	3	—	0	0	—
Op F: Grinding, crushing, smashing, pulverizing, shredding, and cutting	5	6	1.5 (0.5, 5.0)	0	0	—
Op G: Casting, molding, pressing, and pilling	3	3	1.8(0.4, 8.9)	1	0	—
Op H: Not otherwise specified	18	30	1.1 (0.6, 2.0)	0	2	—
Op A, B, and F (i.e., dusty operations)	23	25	1.7 (1.0, 3.0)	0	0	—
Op C, D, and G (i.e., heat operations)	14	20	1.3 (0.6, 2.5)	2	0	—
Baggers, bottlers, canners, and assemblers	9	9	1.8 (0.7, 4.6)	11	15	1.5 (0.7, 3.2)
Tank cleaners	2	1	3.7 (0.4, 34.5)	0	0	—
Laborers	15	25	1.1(0.6, 2.1)	1	1	2.0 (0.1, 30.3)
Fork lift operators, tow-motor operators, and bulldozer operators	0	8	—	0	0	—
Stock persons, wrappers, packers, shipping clerks, and warehousemen	15	29	0.9 (0.5, 1.8)	4	3	2.7 (0.6, 11.3)
Truck drivers and deliverymen	1	8	0.2 (0.03, 1.5)	0	0	—
Maintenance occupations(e.g., mechanics, welders, plumbers, electricians, millwrights, pipefitters and carpenters)	17	36	0.9 (0.5, 1.5)	0	0	—
Groundskeepers and security guards	3	8	0.7 (0.2, 2.6)	0	0	—
Other and unknown	1	8	0.2 (0.03, 1.5)	1	2	1.0 (0.1, 12.4)

canned. Both sexes had nonsignificant increases of bladder cancer associated with these occupations.

Stock persons, wrappers, packers, shipping clerks, and warehousemen.—*No* excess bladder cancer was seen overall among men who packed, moved, and shipped chemicals. Risk increased slightly with increasing years since first employment. Examining the years the men started employment revealed that risk was highest among those who began work during 1930–39 (OR=1.8; 95% CI=0.6, 5.6). Men who began work in these jobs before age **26** were at higher risk (OR=1.4; 95% CI=0.7, 3.2) than those who began those jobs later in life (OR=0.5; 95%CI=0.2, 1.6).

TABLE 5.—*Number of white male bladder cancer cases and controls and ORs according to duration of employment in the production of industrial organic chemicals (SIC 2860-2869)*

Duration, yr[a]	Cases	Controls	OR (95%CI)
Never	1,972	3,615	
<5	10	15	1.2 (0.5, 2.7)
5–9	4	5	1.5 (0.4, 5.4)
10–19	5	9	1.0 (0.3, 3.0)
220	8	6	2.4 (0.9, 6.8)
Chi for trend = 1.57; P=.058 (one-tailed)			

[a] Excludes 1 case and 5 controls with unknown duration.

Maintenance occupations.—Theseoccupations include mechanics, welders, electricians, plumbers, pipefitters, millwrights, and carpenters. The men in these occupations often sustain heavy exposures when they repair malfunctioning machinery and factory structural elements. Men employed for less than 20 years in maintenance occupations had less bladder cancer than expected (OR=0.7), but the OR for men employed **20** or more years was 1.5 (95%CI=0.4, 5.4).

Occupations Within Specific Industries

We examined all occupations within each subdivision of the chemical industry. Several operator groups in the plastics and rubber industry had significantly elevated risks of bladder cancer. The mixing, filtering, grinding,

and other dusty operator occupations were associated with an almost fivefold increased risk of bladder cancer (OR = 4.6; 95% CI = 1.0, 20.4). The heat-associated operations, e.g., distilling, heating, casting, and furnace tending, were associated with an almost threefold increased risk (OR = 2.8; 95% CI = 0.5, 15.3). Operators in the organic chemical industry had a bladder cancer risk (OR = 1.3; 95% CI = 0.6, 2.9) similar to that of the overall organic chemical industry; however, the operators, not otherwise specified, had a significant threefold risk (OR = 3.2; 95% CI = 1.0, 10.3). Operators in the explosives industry incurred greater bladder cancer risk (OR = 2.4; 95% CI = 0.6, 10.4) than other occupational categories in that industry. Three cases and no controls performed operations involving heat (i.e., distilling, heating, casting, etc.). Associations for other occupational groups within industries were unremarkable or were based on very small numbers of subjects.

DISCUSSION

In this large 10-area case–control study, there was no association between bladder cancer incidence and employment in the chemical industry overall. Bladder cancer risk was increased among men employed in the organic chemical industry. Risk rose with increasing duration of employment. Operators exposed to dusty or thermally degraded chemicals had increased risk of bladder cancer in the chemical industry overall and, in particular, in the plastics and rubber industry. Other modest increases in risk were associated with employment in specific industries or occupations, although most were not statistically significant and should be evaluated with consideration of the large number of comparisons made in the analysis. The findings that demonstrate internal consistency, such as the overall association and the duration–response relationship in the organic chemical industry, or consistency with previous research, however, should be given more credence.

Increased risk of bladder cancer was observed among some groups within the plastics industry. Operators exposed to dusty or hot processes had a threefold to fivefold increased risk, and women had an OR of 3.3. These data are consistent with the report of Najem et al. ***(15)*** of a significant 3.4-fold excess risk of bladder cancer among persons ever employed in the plastics industry. The risk in the present study appeared to be limited to New Jersey. It is interesting that Najem and co-workers' Prevalent bladder cancer cases were from northern New Jersey and were identified in approximately the same time period as the present study subjects. Therefore, this study may not be an independent confirmation of the hypothesis of Najem et al. but could merely be a second study of the same group of people or factories. It is also not known if the risk was limited to New Jersey because of the small numbers of people in the plastics industry in the other study areas or because of some hazard unique to the New Jersey plastics industry. Other bladder cancer case–control studies in the literature do not report on employment in the plastics industry specifically; they usually combine the plastics and rubber industries.

Men employed in the manufacture of pesticides had a 2.3-fold increase in bladder cancer. Although the excess was not statistically significant, the association is interesting in light of the extremely large risks for bladder cancer observed by Howe et al. ***(16)*** for crop sprayers (OR = 7.0; 95% CI = 0.9, 315.5) and nurserymen (OR = 5.5; 95% CI = 1.2, 51.1). Two studies of pesticide applicators *(17, 18)* showed nonsignificant excesses of bladder cancer, based on small numbers. However, a recent review of 12 studies of farmers (*19*), obviously a group exposed to pesticides, did not cite any reports of excess bladder cancer. In fact, seven of the studies reported statistically significant deficits. Several studies of employees at pesticide-manufacturing factories showed no excess of bladder cancer (20–24).

The associations with employment in the organic chemical industry and with heavily exposed operator jobs are consistent with several previous case–control studies and with what is known about the carcinogenicity of aromatic amines and other organic chemicals ***(4,*** 25). A striking aspect of our findings, however, is their apparent divergence from the findings of most previous cohort studies of chemical workers. Some studies of workers producing aromatic amines and other chemicals have reported relative risks in the range of 10–50 (26). No excess risks of that magnitude were found in this generally "negative" study. Possible explanations for this difference include misclassification of exposure status, reductions of hazardous workplace exposures, overmatching in control selection, and lack of statistical power.

Previous research has usually focused on people in one company or one small geographic area where definitions of job titles and industry were consistent throughout the study population. Our subjects were employed in at least the 10 study areas, in many different companies, spanning several decades. There may have been considerable variation in exposures in these different settings. Inappropriately grouping by job title introduces misclassification and dilutes risk estimates.

Results of this study may differ from previous research because of changing occupational exposures. While new agents are being introduced continuously, improvements in industrial hygiene and engineering controls as well as Government regulation have eliminated some exposures and reduced levels of other exposures. Many of the studies reporting large relative risks for employees in the chemical industry date back several decades when exposures may have been higher than for our subjects who were diagnosed in 1978. However, the importance of this factor may be minor in this study because of the long average latency of bladder cancer. The average latency for chemically induced bladder cancer is generally estimated to be approximately 30 years. Cases diagnosed in 1978 might have been caused by chemical exposures sustained around 1948. The industrial clean-up of even the most potent bladder carcinogens (e.g., aromatic amines) did not occur until the late 1950's, 10 years later. There-

fore, we would not expect to observe much reduction in disease due to lowered exposures in this study. In addition, the analyses of workers in the plastics and organic chemical industries showed greater bladder cancer risks among the persons who began that work more recently.

One recent study that also observed no excess bladder cancer risk associated with employment in the chemical industry was criticized for possible overmatching in control selection (27). The cases and controls, residents of the State of New Jersey, were matched on age, sex, and county of residence. In small counties with few employers, matching on county may have been equivalent to matching on occupation. Hence no association between bladder cancer and occupation was observed. Regardless of whether this was a justifiable criticism of the cited study, it is unlikely to explain the current results. The National Bladder Cancer Study covered 10 large geographic areas, including 5 entire States, with numerous employers of various types.

Finally, although the study population was large, many times larger than previous case-control studies of bladder cancer that were often based on 300 cases or less, the study's statistical power was limited by the small proportion of the population in any specific industry or occupation. For example, only 1% reported any employment in the organic chemical industry. At that exposure rate, this study would have required over 16,000 cases and 33,000 controls to detect the **OR** of 1.3 for employment in the chemical industry with 90% power. To study the effects of specific chemicals with lower exposure rates would require an even larger study. We believe that the small proportion of the population in the industries of interest was the most important reason for this study's generally "negative" findings. Most of the earlier studies, though smaller, have been conducted in areas selected for their unusual distribution of occupations and industries.

In summary, our findings demonstrate the limited ability to detect specific occupational hazards with the use of a multicenter case-control design. Even with an extremely large number of subjects, few meaningful associations were observed between occupation and bladder cancer. Study locations must be targeted carefully with large proportions of the populations employed in the specific occupations or industries of interest to have the necessary statistical power. However, this multicenter study was useful for generating some hypotheses. For example, we observed an association with employment in the plastics industry, which has been reported only in one other study. An investigation designed to test this specific hypothesis seems warranted.

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