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Silicosis and Lung Cancer in North Carolina Dusty Trades Workers

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Since 1940, 760 cases of silicosis have been diagnosed as part of the State of North Carolina's (NC) pneumoconiosis surveillance program for dusty trades workers. Vital status was ascertained through 1983 for 714 cases that had been diagnosed since 1940 and death certificates were obtained for 546 of the 550 deceased.

Mortality from tuberculosis, cancer of the intestine and lung, pneumonia, bronchitis, emphysema, asthma, pneumoconiosis, and kidney disease was significantly increased in whites. Mortality from tuberculosis, ischemic heart disease, and pneumoconiosis was significantly increased in non-whites. The standardized mortality ratio (95% CI) for lung cancer based on U.S. rates was 2.6 (1.8–3.6) in whites, 2.3 (1.5–3.4) in those who had no exposure to other known occupational carcinogens, and 2.4 (1.5–3.6) in those who had no other exposure and who had been diagnosed for silicosis while employed in the NC dusty trades.

Age-adjusted lung cancer rates in silicotics who had no exposure to other known occupational carcinogens were 1.5 (.8–2.9) times higher than that in a referent group of coal miners with coalworkers' pneumoconiosis (CWP) and 2.4 (1.5–3.9) times higher than that in a referent group of non-silicotic metal miners. Age- and smoking-adjusted rates in silicotics were 3.9 (2.4–6.4) times higher than that in metal miners. This analysis effectively controls for confounding by age, cigarette smoking, and exposure to other known occupational carcinogens, and it is unlikely that other correlates of silica exposure could explain the excess lung cancer mortality in the silicotics.

Key words: silicosis, lung cancer, mining, construction trades, foundry workers, quarry exposures, asbestos products, coal workers' pneumoconiosis, tuberculosis, non-whites

INTRODUCTION

The literature on the carcinogenicity of silica in humans is difficult to interpret and remains controversial [Goldsmith et al., 1982; Heppleston, 1985; IARC, 1987;

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McDonald, 1989]. Although results of necropsy studies have not indicated a relationship between silica and cancer [Heppleston, 1985; Hessel and Sluis-Cremer 1986; Hessel et al., 1990], other reports (Table I) of increased lung-cancer rates in silicotics have been published. However, the International Agency for Research on Cancer [IARC, 1987] has suggested that bias, confounding, or chance may have explained these results. Short-comings of some studies include: 1) non-comparability of reference groups; 2) differences between countries in the definition of compensable silicosis; 3) potential differences in disease detection methods; and 4) potential confounding by other carcinogenic risk factors such as cigarette smoking, radon, and polycyclic aromatic hydrocarbons.

In this paper we present results of a mortality study of North Carolina (NC) workers who were diagnosed with silicosis during 1940–1983. These data have several advantages over those available to previous investigations. Silicotics were identified from workers periodically examined by the NC State Industrial Commission and thus represent silicotics in the North Carolina dusty trades population who have had occupational silica exposure. Silicosis was defined based on radiographic evidence. Individual data were available on cigarette-smoking habit and on work history of jobs with potential occupational carcinogenic exposures. Data on referent groups of non-silicotics were available with comparable risk-factor information.

METHODS

Silicotic Study Group

In 1935, the State of North Carolina inaugurated a program of periodic radiographic examinations of every worker who was employed in the NC dusty trades and this program has continued nearly annually to the present. If evidence of silicosis was found, workers were further evaluated for compensation benefits. North Carolina dusty trades have included mining, foundries, quarrying, stone crushing, asbestos and silica manufacturing products, and construction. Workers are offered examinations every 1–2 years and participation has been voluntary. Details of the program and examples of recording forms have been described in further detail by Rice [1983].

Medical examinations are administered by the NC Industrial Commission's mobile medical unit and consist of a PA chest radiograph and questionnaire on work history, medical symptoms, and since 1964, cigarette-smoking habits. Determinations of pneumoconiosis are made by the Advisory Medical Committee (AMC), consisting of 3 physicians. All films are evaluated for pneumoconiosis according to the procedure described in the 1930 Johannesburg Conference Report [Gardner et al., 1930]. Diagnosis of silicosis is based on the film reading and history of silica exposure.

Radiographs taken as part of the periodic examination have been 35 mm, 4×5 inch, or 4×4 inch films depending on the year. These small films are interpreted by one AMC reader. If evidence of silicosis is indicated or if a retake is necessary, then a standard 14×17 inch film is taken at a local hospital or clinic.

In addition to medical examinations administered by the NC Industrial Commission's mobile medical unit, some workers who left the NC dusty trades had examinations submitted by their personal physicians to the NC Industrial Commission for compensation claims. These radiographs were evaluated for pneumoconiosis similar to those taken by the NC Industrial Commission.

TABLE I. Follow-Up and Case-Control Studies of Silicosis and Lung Cancer Mortality

Principal author [year]	Source of silicosis records	No. of silicotics	Year of silicosis diagnosis	Year of follow-up	Lung cancer SMR by industry[a]					
					Only mining	Mining, quarry, tunnel, or stone	Foundry	Ceramic	Other	Total[b]
Westerholm [1980]	Pneumocon. registry	3,610	31–48	69	5.9[d]		0.8	1.3	3.3	2.7[d]
			49–69	69	3.8[d]		2.2[d]	2.9	1.0	2.8[d]
Gudbergsson [1984]	Occupational registry dis.	331	64–74	75						3.0[d]
Chiyotani [1984]	Hospital med. records	4,413 (Person-years)	71–81	81						6.5[d]
Schuler [1986]	National insur. fund	2,399	60–78	78	2.5[d]	1.2	3.9[d]	1.9		2.4[d]
Neuberger [1986]	Medical examination	2,212	50–60	80						1.4[d]
Hessel [1986]	Pension fund	Case-contl.	—	—	(1.1)[c]					(1.1)[c]
Westerholm [1986]	Pneumocon. registry	712	59–77	79		5.4[d]	3.9[d]			4.4[d]
Kurppa [1986]	Occupational registry dis.	961	35–77	82	4.4[d]	2.7[d]	2.1[d]		3.4[d]	3.1[d]
Forastiere [1986, 1987]	Compensation	Case-contl.	—	—				2.1[c,d]		2.1[c,d]
Zambon [1986]	Compensation	1,313	59–63	84	1.4[d]	1.8[d]			2.2	1.9[d]
Steenland [1986]	Union death benefits	Case-contl.	—	—		(3.2)				
Finkelstein [1987]	Compensation	1,479	40–75	85	2.3[d]	3.6		2.9	2.7	3.0[d]
Mastrangelo [1988]	Compensation	Case-contl.	—	—						(1.9)[c,d]
Forastiere [1989]	Compensation	952	46–84	84	[2.5][d]	[1.4]	[1.6]	[2.1][d]		[1.5][d]
Infante-Rivard [1989]	Compensation	1,165	38–85	86	3.8[d]	2.0[d]	3.0[d]	5.0[d]	6.9[d]	3.5[d]
Ng [1990]	Compensation	1,419	80	86						2.0[d]
Amandus [1990]	Medical examination	369	59–61	75	(2.0)[c,d]					(2.0)[c,d]

[a]SMR computed from an external reference group; RR computed from an internal reference group (parentheses); MOR computed from an external reference group [brackets].
[b]Total: all workers in study combined.
[c]Adjusted for cigarette-smoking status.
[d]Significantly different from 1.0 (p value $< .05$).

In this analysis, mortality of individuals who were determined to have silicosis from an examination administered by the NC Industrial Commission was evaluated both separately and together with mortality of individuals diagnosed as having silicosis on the basis of a self-initiated examination after termination of employment in the NC dusty trades. The separate analyses were done in order to control for a possible detection bias related to diagnosis of silicosis made incidental to an examination done as part of a medical evaluation of symptoms related to lung cancer [McDonald, 1989].

Work history and cigarette-smoking habit data were abstracted from NC Industrial Commission medical examination files for all 760 male silicotics diagnosed between 1940 and 1983. Vital status was ascertained through 1983 from Social Security death indication records, National Death Index data, NC motor vehicle records, state compensation files, and personal interviews for 714 (94%) of the 760 cases. Death certificates were obtained for 546 (99%) of the 550 deceased. The underlying cause of death was abstracted from the death certificate and coded according to the International Classification of Diseases, Adapted [National Center for Health Statistics, 1968].

Silicotics were classified by their smoking habit (ever or never smoked cigarettes). Information on the number of years cigarettes were smoked was not collected during the examinations. Subjects who ever worked in asbestos product manufacturing, olivine mining, talc mining, insulation work, or foundries were considered potentially exposed to other known carcinogens. Talc and olivine were considered potential carcinogens because of possible amphibole contamination.

REFERENCE GROUPS

Because medical records for non-silicotics who had left the NC dusty trades before 1974 were not retained by the Industrial Commission, external referent groups were selected for analysis. Employing a person-years analysis, mortality of the study population was compared to that of the US and NC male populations. Person-years were accumulated from date of silicosis diagnosis through 1983 over 5 year age intervals, 5 year calendar-time periods, and 5 year intervals since silicosis diagnosis. Expected deaths were computed separately for whites and non-whites from respective US and NC rates. US rates were used from 1940 to 1983 and NC rates from 1950 because NC mortality rates were unavailable prior to 1950.

Other external referent groups used in our analysis (Table II) include a nationwide sample of non-silicotic metal miners and a sample of current and ex-Appalachian coal miners with coalworkers' pneumoconiosis (CWP). CWP cases provide an adjustment for competing causes of death, because similar to silicosis, CWP has been associated with high respiratory disease risk but has not been found to be associated with lung cancer [Miller and Jacobsen, 1985; Ames et al., 1984].

During 1959–1961, the US Public Health Service examined 12,258 metal miners as part of a cross-sectional study of silicosis, and vital status was ascertained through 1975 [Costello, 1983]. Each worker was administered a spirometry test; a questionnaire on work history, cigarette-smoking habits, and respiratory symptoms; and a chest radiograph which was interpreted for pneumoconiosis by 3 physicians according to the 1959 ILO Classification [ILO, 1959]. Data on 9,543 non-silicotic

TABLE II. Number of Men and Person-Years in Study and Reference Groups

	No. in cohort	Person-years
NC silicotics		
Whites	655	8,602
Non-whites	105	982
Non-silicotic metal miners	9,543	132,902
Appalachian coal miners with CWP[a]		
Active miners	259	1,373
Ex-miners	218	779

[a]CWP: Coalworkers' pneumoconiosis.

white males [Amandus and Costello, 1990] who were employed in non-dieselized, non-uranium metal mines were available for this study.

During 1963–1965, the US Public Health Service also examined a sample of current and ex-Appalachian coal miners. Similar to the metal miners, every coal miner received a chest radiograph which was interpreted by 3 physicians according to a modified version of the 1959 ILO classification and was administered a questionnaire on cigarette-smoking habits and work history. Vital status of this cohort was ascertained through 1975 [Amandus, 1982]. Data on 259 and 218 white male CWP cases in current and ex-coal miners, respectively, were available for analysis.

STATISTICAL METHODS

Standardized mortality ratios (SMRs) were computed as a ratio of observed to expected number of deaths for comparison of the silicotics to the US and state populations. The Life Table Analysis System computer program [Waxweiler et al., 1983] was used to compute SMRs for categories which have been the same in each ICDA revision (Table III). Tests of significance and 95% confidence intervals (CI) for the SMRs were made by assuming that the observed number of deaths followed a Poisson distribution [Bailar and Ederer, 1964]. For these analyses, 46 subjects whose vital status could not be determined were assumed to have survived through the end of the follow-up period.

Age- and smoking-adjusted lung-cancer rates of the silicotics were compared to those of the metal miner and coal miner referent groups by using the Mantel-Haenzel (MH) estimator for incidence density data. Person-years and observed numbers of lung-cancer deaths were tallied by 10 year age intervals of follow-up from 1959 to 1975 for comparison to metal miners and from 1963 to 1975 for comparison to coal miners. MH rate ratios and 95% test-based confidence intervals were calculated [Kleinbaum et al., 1982].

RESULTS

Mortality rates (Table IV) from tuberculosis, cancer of the intestine and lung, pneumonia, bronchitis, emphysema, asthma, pneumoconiosis, and infectious kidney disease were significantly increased in white silicotics when compared to US rates. Mortality rates from tuberculosis, ischemic heart disease, and pneumoconiosis were

TABLE III. Cause of Death Categories Evaluated in Survey Among NC Dusty Trade Workers*

Causes of death category	ICDA eighth revision code(s)
Tuberculosis	10–19
Respiratory tuberculosis	10–12
Other tuberculosis	13–19
All neoplasms	140–239
Digestive cancer	150–159, 197.8
Stomach cancer	151
Intestional cancer	152–153
Liver cancer	197.8
Pancreatic cancer	157
Respiratory cancer	161–163
Cancer of largnx	161
Cancer of trachea, bronchus, and lung	162–163
Prostate cancer	185
Cancer of lymph and hematopoietic tissue	200–207
Diseases of heart and circulatory system	390–398, 400.1–400.3, 400.9, 401–404, 410–414, 420–438 440–444.1, 444.3–458
Ischemic heart disease	410–413
Diseases of respiratory system	460–519
Influenza	470–474
Pneumonia	480–486
Bronchitis	490–491
Emphysema	492
Asthma	493
Pneumoconiosis & other respiratory disease	500–519
Diseases of digestive system	444.2, 520–537, 540–543, 550–553, 560–577
Diseases of genito-urinary system	80–584, 590–607, 610–629
Chronic and unspecified renal failure	582–584
Infection of kidney	590
Accidents	800–845, 850–877, 880–887, 890–936, 940–949
Transportation	800–845, 900–941
Falls	880–887, 943
Other	890–929, 940–946

*See note in text.

significantly increased in non-whites. The lung cancer SMR in white silicotics was 2.6 (1.8–3.6) based on US rates and 3.0 (2.0–4.2) based on NC rates. Because only one case of lung cancer occurred among non-whites, the remainder of the results presented are for whites only.

Lung cancer SMRs (Tables V, VI) were 2.3 (1.5–3.4) in silicotics with no exposures to other known occupational carcinogens and 4.5 (1.8–9.2) in silicotics who had other possible occupational carcinogenic exposures (asbestos product manufacturing, olivine mining, talc mining, insulation work, and foundries). Lung-cancer mortality was increased in cigarette smokers (SMR = 3.4, 2.0–5.3) and non-smokers (SMR = 1.7, .5–3.9) but only reached statistical significance in smokers. These SMRs for smoking-specific groups should be interpreted cautiously because general population rates were used for calculating expected deaths so that the effect of smoking is not controlled. Lung cancer SMRs tend to be overestimated for smokers and underestimated for non-smokers.

TABLE IV. Observed (O) and Expected (E) Number of Deaths From Selected Causes, and SMR for NC Silicotics by Race*

	Whites			Non-whites		
Cause of death	0	E	SMR	0	E	SMR
Tuberculosis	71	2.3	30.7[a]	11	0.5	20.5[a]
Respiratory tuberculosis	71	2.2	32.4[a]	10	0.5	20.4[a]
Other tuberculosis	0	—	—	1	0.0	21.7
All neoplasms	67	44.8	1.5[a]	6	5.2	1.2
Digestive cancer	16	14.2	1.1	1	1.7	0.6
Stomach cancer	2	3.1	0.6	0	0.5	0.0
Intestinal cancer	10	4.3	2.3[a]	0	0.3	0.0
Liver cancer	1	0.4	2.3	0	0.1	0.0
Pancreatic cancer	3	2.5	1.2	1	0.3	3.7
Other digestive cancer	0	3.8	0.0	0	0.6	0.0
Respiratory cancer	34	13.7	2.5[a]	1	1.6	0.6
Cancer of larynx	1	0.7	1.4	0	0.1	0.0
Cancer of trachea, bronchus & lung	33	12.9	2.6[a]	1	1.5	0.7
Other respiratory cancer	0	0.2	0.0	0	0.0	0.0
Prostate cancer	7	3.8	1.9	0	0.6	0.0
Cancer of lymph. and hematopoietic tissue	6	3.6	1.7	1	0.3	3.3
All other cancer	4	9.3	.4	3	1.5	2.0
Diseases of heart & circulatory systems	150	128.5	1.2	17	12.8	1.3
Ischemic heart disease	93	86.2	1.1	13	6.2	2.1[a]
All other heart & circulatory diseases	57	42.3	1.4	4	6.6	0.6
Diseases of respiratory system	152	14.3	10.6[a]	23	1.5	14.9[a]
Influenza	1	0.4	2.6	0	0.1	0.0
Pneumonia	13	5.5	2.4[a]	3	0.8	3.6
Acute resp. (excluding flu & pneumonia)	0	0.1	0.0	0	0.0	0.0
Bronchitis	6	0.8	7.9[a]	0	0.0	0.0
Emphysema	12	3.4	3.6[a]	0	0.2	0.0
Asthma	2	0.6	3.1	0	0.1	0.0
Pneumoconiosis and other respiratory diseases	118	3.6	32.9[a]	20	0.4	56.4[a]
Diseases of digestive system	11	9.8	1.1	0	1.1	0.0
Diseases of genito-urinary system	6	3.6	1.6	2	0.8	2.5
Chronic & unspecified renal failure	2	1.4	1.4	0	0.4	0.0
Infection of kidney	4	0.6	6.5[a]	1	0.1	8.9
Other	0	1.6	0.0	1	0.3	0.3
Accidents	9	8.3	1.1	1	1.3	0.8
Transportation	5	3.7	1.4	1	0.5	1.9
Falls	1	1.8	0.6	0	0.2	0.0
Other accidents	3	2.7	1.1	0	0.6	0.0
All other deaths	20	16.3	1.2	4	3.0	1.0
All deaths	486	226.6	2.1[a]	64	26.2	2.4[a]

*SMR is significantly different from 1.0 (p value < .05).
[a]US white male rates.

Lung cancer mortality was also increased in subjects diagnosed with silicosis while still employed in the NC dusty trades (SMR = 2.5, 1.7–3.7) even in those who had no exposures to other known occupational carcinogens (SMR = 2.4, 1.5–3.6). Lung-cancer mortality was increased in cigarette smokers who had been diagnosed with silicosis after leaving employment (SMR = 5.7, 1.2–16.7) and in smokers diagnosed while employed in the dusty trades (SMR = 3.1, 1.7–5.2). There were no

TABLE V. Number of White NC Silicotics and Person-Years (PY) by Status of Silicosis Determination and Job Type or Cigarette Smoking Habit*

	Status of silicosis determination							
	Silicosis determined after leaving employment[a]		Silicosis determined while employed[a]		Status unknown		Total	
	No.	PY	No.	PY	No.	PY	No.	PY
Type of jobs ever held								
Silica exposure only	89	833	483	6,707	5	72	577	7,611
Silica and other exposures[b]	7	78	71	914	0	0	78	992
Cigarette smoking habit[c]								
Ever smoked	33	273	245	3,169	1	0	279	3,442
Never smoked	12	172	123	1,678	2	37	137	1,887
Unknown	51	466	186	2,774	2	35	239	3,274
Total	96	911	554	7,620	5	72	655	8,603

*Person-years were tallied from date of silicosis diagnosis to date of death or end of study. Person-years were rounded-off and may not sum exactly to column and row totals.
[a]Employment in NC dusty trades industry.
[b]Exposure to silica and other known occupational carcinogens (asbestos manufacturing, insulation, olivine mining, talc mining, and foundry work).
[c]Smoking history data were only available on workers examined after 1964.

lung-cancer cases in non-smokers whose silicosis was diagnosed after leaving employment. Lung-cancer mortality was increased but did not reach significance in non-smokers diagnosed while employed (SMR = 2.0, .6–4.6) and in non-smokers diagnosed while employed who had no other occupational carcinogenic exposures (SMR = 2.3, .6–5.8).

In workers who were diagnosed as having silicosis while still employed, lung-cancer SMRs were 3.8 (1.5–7.8) within 5 years after diagnosis of silicosis, 1.3 (.3–3.9) at 5–9 years, 2.4 (1.2–4.5) at 10–19, and 2.8 (1.2–5.6) at 20 or more years after diagnosis. In subjects diagnosed as having silicosis after leaving employment, SMRs were significantly increased only within 10 years after silicosis diagnosis and not at 10 or more years.

The number of lung-cancer deaths and person-years by age, smoking, and study group are presented in Table VII, and rate ratios for silicosis and lung-cancer mortality are presented in Table VIII. The age-adjusted lung-cancer risk for cigarette smokers with no exposure to other known occupational carcinogens was 1.8 (.8–4.2) times that of smoking, active coal miners, 1.7 (.8–3.7) times that of smoking ex-coal miners, 1.8 (.9–3.8) times that of all smoking coal miners, and 3.2 (1.8–5.8) times that of smoking metal miners, but figures reached significance only in metal-miner comparisons. However, rates were significantly higher (RR = 2.6, 1.1–6.1) in smokers age 60–69 than in smoking coal miners age 60–69. Although there were only 4 non-smoking silicotics and 5 non-smoking metal miners who had died of lung cancer, the age-adjusted lung-cancer risk for non-smokers was 8.6 (3.6–20.5) times that of non-smoking metal miners.

The age- and smoking-adjusted lung cancer rate in silicotics was 3.9 (2.4–6.4) times that of metal miners based on data for smokers and non-smokers tabulated

TABLE VI. Observed (O) and Expected (E) Number of Lung Cancer Deaths, and SMR for White NC Silicotics by Status of Silicosis Determination and Job Type, Cigarette Smoking Habit, or Years After Silicosis Diagnosis*

	Status of silicosis determination											
	Silicosis determined after leaving employment[a]				Silicosis determined while employed[a]				Total			
	O	E	SMR	95% CI	O	E	SMR	95% CI	O	E	SMR	95% CI
Type of jobs ever held												
Silica exposure only	3	1.6	1.9	.4–5.5	23	9.6	2.4	1.5–3.6	26	11.3	2.3	1.5–3.4
Silica and other exposures[b]	2	.1	14.0	1.7–50.4	5	1.4	3.5	1.1–8.2	7	1.6	4.5	1.8–9.2
Cigarette smoking habit												
Ever smoked[c]	3	.5	5.7	1.2–16.7	15	4.8	3.1	1.7–5.2	18	5.3	3.4	2.0–5.3
Never smoked[c]	0	.4	0	—	5	2.6	2.0[d]	.6–4.6	5	3.0	1.7	.5–3.9
Unknown[c]	2	.8	2.5	.3–9.0	8	3.7	2.2	.9–4.3	10	4.5	2.2	1.1–4.1
Years after silicosis diagnosis												
<5	1	.5	2.2	.1–12.2	7	1.9	3.8	1.5–7.8	8	2.4	3.4	1.5–6.7
5–9	3	.4	7.0	1.5–20.6	3	2.2	1.3	.3–3.9	6	2.7	2.2	.8–4.9
10–19	1	.6	1.6	.0–9.2	10	4.1	2.4	1.2–4.5	11	4.8	2.3	1.2–4.1
≥20	0	.2	—	—	8	2.8	2.8	1.2–5.6	8	3.0	2.7	1.1–5.1
Total	5	1.7	2.9	.9–6.8	28	11.0	2.5	1.7–3.7	33	12.9	2.6	1.8–3.6

*US white male rates.
[a]Employment in NC dusty trades industry.
[b]Exposure to silica and other known occupational carcinogens (asbestos manufacturing, insulation, olivine mining, talc mining, and foundry work).
[c]US population rates consisting of a mix of smokers and non-smokers were used for calculating expected deaths for these SMRs. See cautionary note in text.
[d]There were 4 lung cases (SMR = 2.3, .6–5.8) in non-smokers whose silicosis was determined while employed and who had no other known occupational carcinogenic exposures.

(Table VII) by 5 age groups (<40, 40–49, 50–59, 60–69, and ≥70). The age- and smoking -adjusted MH rate ratio (RR = 4.5, 2.9–7.0) was also significantly increased after the data were re-grouped by age (<50, 50–59, 60–69, and ≥70) to minimize the number of age and smoking groups with no lung-cancer cases.

DISCUSSION

Lung-cancer mortality was higher in white silicotics than in US and NC white males, metal miners, and possibly coal miners. These increased risks were not explained by confounding from age or cigarette smoking, or from bias introduced by workers whose silicosis was diagnosed after leaving employment. The association does not appear to be explained by confounding from exposure to other known carcinogens, because while the lung-cancer risk was higher among silicotic workers potentially exposed to asbestos, fibrous minerals, and carcinogens in foundry work, lung-cancer risk nonetheless was significantly elevated among workers whose jobs in the dusty trades entailed silica- and nuisance-dust exposures only.

Although findings were consistent with a silicosis–lung-cancer association, several caveats must be noted. Whether metal and Appalachian coal miners are comparable to NC silicotics is questionable because of possible differences in selection

TABLE VII. Number of Lung Cancer Deaths (LC) and Person-Years (PY) by Age at Follow-Up and Cigarette Smoking Habit for White NC Silicotics With No Exposure to Other Known Occupational Carcinogens and for Coal- and Metal-Miner Referent Groups

	Age at follow-up									
	<40		40–49		50–59		60–69		≥70	
	LC	PY	LC	PY	LC	PY	LC	PY	LC	PY
Ever smoked										
Active coal miners[a]	0	42	0	306	3	919	6	780	0	56
Ex-coal miners[a]	0	7	0	38	1	228	6	905	2	251
All coal miners[a]	0	49	0	344	4	1,147	12	1,685	2	307
NC silicotics[a]	0	3	0	5	0	382	8	434	0	137
Metal miners[b]	1	31,246	16	33,484	46	28,362	37	12,697	13	1,986
NC silicotics[b]	0	7	0	115	1	555	9	508	0	168
Never smoked										
Metal miners[b]	0	7,729	0	6,279	1	5,771	2	3,734	2	949
NC silicotics[b]	0	3	1	26	1	167	1	328	0	133
Total group[c]										
Active coal miners[a]	0	42	0	327	3	1,020	6	1,123	0	146
Ex-coal miners[a]	0	20	0	127	1	318	6	999	2	329
All coal miners[a]	0	62	0	454	4	1,338	12	2,122	2	475
NC silicotics[a]	0	25	1	199	0	723	11	1,043	2	470
Metal miners[b]	1	38,975	16	39,763	47	34,133	39	16,431	15	2,935
NC silicotics[b]	0	52	1	342	2	1,125	13	1,344	2	573

[a]Person-years and deaths tabulated from Jan. 1, 1963, to Dec. 31, 1975.
[b]Person-years and deaths tabulated from Jan. 1, 1959, to Dec. 31, 1975.
[c]The number of lung cancer deaths and person-years for silicotics whose smoking history was not collected are included in the total group figures, and thus, figures for smokers and non-smokers do not necessarily sum to those in the total group.

factors. Silicotics and referent groups were enumerated from the roles of those who participated in voluntary examination studies. Whether participants in the NC program were more likely to have died of lung cancer than non-participants and whether this selection probability was greater than in the coal and metal miner groups seem unlikely but could not be determined.

However, there is little likelihood that major confounding factors were unaccounted for in this study. The rate ratio for silicosis and lung cancer may have been underestimated based on the coal-miner referent group because some of the coal miners may have had silicosis. Additionally, the rate ratios may have been underestimated based on the metal-miner referent group because some may have developed silicosis during the follow-up period and because of radon exposures.

It is possible that cigarette smoking enhanced the increased risk in silicotics, but this could not be fully determined due to the small number of lung-cancer cases in non-smokers. Part of the increased lung-cancer risk among silicotics could have been due to differences in amount and duration of cigarettes smoked between silicotics and referent groups. However, confounding from smoking would not likely have increased the lung-cancer SMR by more than a factor of .3 [Finkelstein et al., 1987] and thus would have explained only part of the increased SMR (2.3) in workers who were not exposed to other known occupational carcinogens.

Misclassification of silicosis due to use of small chest films or due to reader

TABLE VIII. Age-Adjusted Mantel-Haenzel Lung Cancer Rate Ratios (RR) by Cigarette-Smoking Habit and Referent Group for White NC Silicotics With No Exposure to Known Occupational Carcinogens*

Cigarette smoking status	Referent group	RR	95% confidence interval	
			Lower	Upper
Ever smoked	Active coal miners	1.8	.8	4.2
	Ex-coal miners	1.7	.8	3.7
	All coal miners	1.8	.9	3.8
	All coal miners (age 60–69 only)	2.6	1.1	6.1
	Metal miners	3.2	1.8	5.8
	Metal miners (age 50–69 only)	4.2	2.3	7.7
Never smoked	Metal miners	8.6	3.6	20.5
	Metal miners (age 50–69 only)	10.0	2.5	40.3
Total group	Active coal miners	1.5	.7	3.4
	Ex-miners	1.2	.6	2.6
	All coal miners	1.5	.8	2.9
	All coal miners (age 60–69 only)	1.9	.8	4.2
	Metal miners	2.4	1.5	3.9
	Metal miners (age 40–69 only)	2.4	1.5	3.8
Total group metal miners[a]		3.9	2.4	6.4

*Statistics were calculated from figures in Table VII by employing a continuity correction for cells with no lung-cancer deaths and 10 year age strata. Smoking and non-smoking silicotics were compared to smoking-specific referent groups. Comparisons could not be made to non-smoking coal miners because there were no lung cancer cases in this group.
[a]RR adjusted for age and smoking (all other figures in table only age-adjusted).

error was not evaluated, but if present, would likely be non-differential between silicotics who did and did not develop lung cancer, and thus would cause us to underestimate the true effect of silicosis on lung-cancer risk. Future work includes re-evaluating radiographs on NC silicotics according to the 1980 ILO Classification of Radiographs of the Pneumoconiosis [ILO, 1981] in order to substantiate the diagnoses.

Most prior lung-cancer studies of silicotics (Table I) did not adequately control bias due to confounding, selection, and silicosis diagnosis error. Selection and detection biases in these studies were possible due to relying on registry, insurance fund, and compensation records to define silicosis. Confounding was possible in some studies due to a lack of individual cigarette-smoking data. The International Agency for Research on Cancer [IARC, 1987] indicated that these studies may have overestimated the silicosis–lung-cancer association.

In our study, the lung-cancer SMR was 2.3 and the age- and smoking-adjusted Mantel-Haenzel rate ratio based on the metal-miner referent group was 3.9 in those who had no exposures to other known occupational carcinogens. These findings were consistent with those from other studies in which lung cancer was defined from certified cause of death records (age-adjusted rate ratios ranged from 1.1 to 6.5, Table

I). SMRs ranged from 1.4 to 1.7 in silicotics enumerated from cross-sectional medical examination data [Neuberger et al., 1986; Amandus and Costello, 1990]. Age- and smoking-adjusted risk ratios ranged from 1.1 to 2.1 based on internal reference groups [Hessel and Sluis-Cremer 1986; Forastiere et al., 1986, 1987; Mastrangelo et al., 1988; Amandus and Costello, 1990].

One plausible explanation of bias in silicotic studies which have relied upon compensation, registry, insurance, or voluntary examination records is that it may have been due to ill-health from lung cancer before silicosis was detected [Infante-Rivard et al., 1989; McDonald, 1989]. If this were true, then lung-cancer mortality would be high within a short time after onset of clinical symptoms of lung cancer. Additionally, if such a bias occurred, then mortality would likely be increased from all cancers for which a radiographic examination of the chest is usually given.

In our study, this detection bias was more likely to have occurred in silicotics who were diagnosed as having silicosis after leaving employment on the basis of a self-initiated examination submitted for compensation than in those who were diagnosed while employed on the basis of a periodic examination administered by the NC Industrial Commission. In those diagnosed after leaving employment, lung-cancer mortality was increased only within 10 years and not at 10 or more years after diagnosis (Table VI), and their SMR for all cancers excluding lung cancer was 2.1. In those diagnosed while employed, lung-cancer mortality was increased within 5 years after diagnosis (SMR = 3.8) but was also increased at 10–19 (SMR = 2.4) and at 20 or more years (SMR = 2.8) since diagnosis, even in those who had no exposure to known occupational carcinogens (10–19 years: SMR = 2.2; 20 or more years: SMR = 2.8). Their SMR for all cancers excluding lung cancer was .9. Thus, this bias possibly explains the excess lung-cancer risk in those diagnosed after leaving employment, but although possibly operating in those who were diagnosed while employed, it does not appear to explain all of the excess in this group.

Competing causes of death from diseases related to silica and silicosis, if operating, may possibly result in an underestimate of the lung-cancer risk in silicotics [IARC, 1987]. However, competing causes did not negate the association between silicosis and lung-cancer mortality because lung-cancer rates were higher in NC silicotics than in the referent groups.

To evaluate the argument that the risk of lung cancer is elevated in silicotics not because of silica exposure but because of the presence of a chronic fibrotic disease of the lungs, we compared our silicosis cohort with selected referent groups. The age-adjusted lung-cancer rate in NC silicotics who had no exposures to other known occupational carcinogens was 1.5 times higher than that in coal miners with CWP, 2.4 times higher than that in non-silicotic metal miners, and 2.3 times higher than that in the US population. Additionally, the age- and smoking-adjusted lung-cancer rate in silicotics was 3.9 times higher than that in the metal miners. This analysis effectively controls for confounding by age, cigarette smoking, and exposure to other known occupational carcinogens. It is unlikely that other lung-cancer risk factors which are correlates of silica exposure can explain the excess lung-cancer mortality in silicotics.

In conclusion, our results are consistent with the hypothesis of an association between silicosis and cancer. Whether silica exposure explains our findings has not been determined. Future work includes estimating lifetime cumulative silica exposures for our cohort.

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