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Mortality Study of Gold Miners Exposed to Silica and Nonasbestiform Amphibole Minerals: An Update With 14 More Years of Follow-Up

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We have updated a study of 3,328 gold miners who worked underground for at least 1 year between 1940–1965 in South Dakota, extending the follow-up from 1977 to 1990. The exposures of concern were silica and nonasbestiform amphibole minerals. The lung cancer standardized mortality ratio (SMR) was 1.13 (95% confidence interval [CI] 0.94–1.36, 115 observed) when the U.S. population was used as the referent group, increasing to 1.25 (95% CI 1.03–1.51) when the county was used as the referent, and to 1.27 (1.02–1.55) for person-time with more than 30 years potential latency. However, lung cancer mortality did not show a positive exposure–response trend with estimated cumulative dust exposure. Data on smoking habits suggested that the miners smoked slightly more than the U.S. population in a 1960 cross-sectional survey. In contrast to lung cancer, other diseases known to be associated with silica exposure (tuberculosis and silicosis) were significantly increased (SMR = 3.44 and 2.61) and exhibited clear exposure–response trends. Nonmalignant renal disease, also associated with silica exposure, was elevated for those hired in early years and showed a significant positive exposure–response trend. Multiple-cause analysis revealed significant excesses of arthritis, musculoskeletal diseases (including systemic lupus and sclerosis), and skin conditions (including scleroderma and lupus), diseases of autoimmune origin which have been associated with silica exposure in other studies. Multiple cause analysis also showed a significant excess of diseases of the blood and blood-forming organs.

Key words: silica, silicosis, lung cancer, asbestos, gold miners

INTRODUCTION

We have studied 3,328 gold miners who were exposed to several potential lung carcinogens. Of primary interest was exposure to silica and to nonasbestiform amphibole fibers (primarily cummingtonite-grunerite [CG] fibers). Silica has been shown to cause lymphomas after pleural injection and lung cancer after inhalation in rats [IARC, 1987]. Data from humans exposed to silica have been inconclusive for lung cancer, although cohorts of men with silicosis have shown consistent excesses of lung cancer [see reviews by Pairon et al., 1991; Goldsmith, 1994]. Nonasbestiform

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amphibole fibers have not been shown to cause lung cancer, but are suspect because of their similarity to asbestiform fibers.

Subcohorts of the cohort studied here have been studied previously. Gillam et al. [1976] studied 440 white males employed as of 1960 who had at least 5 years underground, while McDonald et al. [1978] studied 1,321 miners who were retirees in 1973, all with at least 21 years underground. Follow-up for these studies ended in 1973. Gillam et al. [1976] reported a lung cancer excess, while McDonald et al. [1978] found no excess and no indication of a positive trend with increasing exposure. The current cohort was identified and first studied by Brown et al. [1986], with follow-up through June 1977, partly to resolve this discrepancy. Brown et al. [1986] found a standardized mortality ratio (SMR) of 1.00 for lung cancer with no apparent trends with increased estimated cumulative exposure or latency. There were significant excesses of tuberculosis (largely silico-tuberculosis) and nonmalignant respiratory disease (largely silicosis) which exhibited a positive trend with increasing estimated cumulative dust exposure. Accidental deaths were significantly elevated, and there was an indication of an increasing trend in nonmalignant renal disease with increasing exposure.

The analysis by Brown et al. [1986] was based on follow-up through June 1977 with 861 total deaths observed (43 lung cancer deaths). We have extended follow-up of this cohort through 1990 and now have observed a total of 1,551 deaths (115 lung cancer deaths).

MATERIALS AND METHODS

Exposure Estimates

Most of the cohort (58%) was first employed before 1950. The silica content of respirable dust was estimated at 13% in a survey in the mid-1970s, while the silica content of settled dust was estimated to be 39% [Zumwalde et al., 1981]. The American Conference of Governmental Industrial Hygienists' [ACGIH, 1983] threshold limit value (TLV) in terms of millions of particles per cubic foot (mppcf) of dust ($300/[\%SiO_2$ in settled dust $+ 10]$) is 6.1 mppcf. Estimated dust levels were such that silica exposures exceeded this level prior to 1950 but were below this level after dust controls were implemented in 1950 [Zumwalde et al., 1981]. Based on average dust levels, prior to 1950 silica exposures would have ranged from approximately 10 to 30 mppcf. These are substantial levels (approximately one to three times current standards) although still somewhat less than other occupational cohorts of the time, such as granite cutters whose exposures prior to dust controls in the 1940s ranged from 20 to 50 mppcf [Steenland and Beaumont, 1986].

Asbestos refers to a variety of hydroxylated silicate minerals. These minerals are said to exist in an asbestiform or fibrous "habit" when the mineral has grown in one dimension to form long thin crystals. Nonasbestiform varieties of these minerals have crystallized in two or three dimensions and are generally composed of shorter fibers. When nonasbestiform minerals are broken up or crushed during mining operations, the fibers or cleavage fragments of nonasbestiform minerals are almost indistinguishable from asbestiform fibers under the light microscope. While the division between asbestiform and nonasbestiform minerals is not clear-cut, for the purpose of regulation the Occupational Safety and Health Administration (OSHA) has restricted its definition of asbestos to asbestiform fibers greater than 5 μm with aspect

(length to width) ratios of at least 3:1 [Code of Federal Regulations 29, 1990]. In general it is believed that the long thin fibers are more pathogenic [Stanton et al., 1981].

Asbestos minerals are also divided into two broad groups, serpentine and amphibole. The amphibole family includes CG (commercially called amosite), tremolite, and actinolite, all of which can exist in asbestiform or nonasbestiform varieties. The gold miners in this study were exposed to nonasbestiform CG (69% of all fibers) and tremolite–actinolite (15%), as well as other nonasbestiform varieties (16%) [Zumwalde et al., 1981]. The percentages of airborne fibers greater than 5 μm for CG and tremolite–actinolite fibers were 24% and 32%, respectively. The geometric mean of personal exposures to fibers greater than 5 μm in length in the mid-1970s was 0.44 fibers/cm^3, below the then-current OSHA standard (time-weighted average [TWA]) of two fibers greater than 5 μm in length/cm^3 [now reduced to 0.2 fibers, Code of Federal Regulations, 1990]. OSHA has recently exempted nonasbestiform amphiboles (tremolite, actinolite, and anthophyllite) from the asbestos standard [Code of Federal Regulations 30, 1992]. Levels of exposures to fibers in years prior to the 1970s were not measured, but presumably would have been somewhat higher, based on known higher levels of respirable dust.

Exposures also occurred to the potential lung carcinogens arsenic and radon. However, these exposures were below OSHA standards when measured in the mid-1970s (earlier measurements are not available). Radon daughters in the 1970s ranged from 0 to 0.17 working levels [Zumwalde et al., 1981; 0–2 working level months (WLM) per year]. The current Mine Safety and Health Administration (MSHA) standard is 4 WLM per year [Code of Federal Regulations 30, 1992]. With an average of 9 years exposure, these miners would have been exposed to average cumulative levels ranging from 0 to 18 WLMs, considerably below any levels associated with lung cancer in epidemiologic studies of uranium miners. Arsenic exposures in 1970s averaged under 5 μg/m^3 [Zumwalde et al., 1981]. The current OSHA standard is 10 μg/m^3. However, 16 of 51 samples exceeded the National Institute for Occupational Safety and Health (NIOSH) recommended 15-min standard of 2 μg/m^3.

Methods

A job–exposure matrix was created to estimate dust exposures for each job in the mine over time. Details are available in Brown et al. [1985, 1986] and Zumwalde et al. [1981]. Briefly, all full-time underground jobs were assembled into five major groups based on similarity in job function and dust exposures (laborers, miners, motormen, supervisors, and skip loaders). A sixth category grouped all jobs not considered full-time underground jobs (these jobs were considered nonexposed). Average dust exposures for the job categories were then calculated using existing measurements for each year from 1937 to 1975. The gold mine operated from the early 1900s, and prior to 1937 exposures had to be estimated. No job history data were collected after 1975. The mine continued to operate after that year, but with reduced numbers of miners and with low levels of exposure, so that there is little underestimation of cumulative exposure in our cohort by ignoring exposures after 1975 (only 15% of our cohort were still employed as of 1975).

The estimated daily dust exposures (constant over yearly intervals) for each of the five job categories were weighted (multiplied) by a factor estimating how much daily time was spent underground by miners in these jobs, with a factor of 1 assigned

to work done in the earliest years, decreasing in later years [Zumwalde et al., 1981]. For each miner, estimated daily dust levels were summed over time and this measure (dust-days, each dust-day is one day exposed to 1 mppcf of dust) was used as the estimate of cumulative exposure. Because this quantitative measure refers to total dust, it is not specific to either silica exposure or exposure to nonasbestiform minerals.

Mortality analyses were conducted using the Life Table Analysis System (LTAS) of NIOSH for [Steenland et al., 1990b]. Due to the cohort entry criteria, person-time for each miner did not begin to accumulate until he had spent 12 months in an underground job or in 1940, whichever came first. Person-time continued until date-last-observed or December 31, 1990, whichever was earlier. Follow-up for vital status was done via Social Security and the National Death Index (NDI), with the latter source searched through December 31, 1990. Men known to be alive after the beginning of NDI in 1979 were considered alive as of December 31, 1990 if not found via NDI.

Life-table analyses were conducted for 92 categories of death, using as the referent group either the U.S. population, the population of Lawrence County, South Dakota, where the mine was located, or the population of the entire state of South Dakota. Analyses using the Lawrence County or South Dakota referent population only consider person-time and deaths occurring after 1960, when county and state rates are first available (69% of the person-time and 82% of the deaths occurred after 1960). Analyses were also conducted by duration, time-of-hire, time-since-first-employment, and estimated cumulative exposure (dust-days). Categories of dust-days for cohort analysis were chosen a priori to conform to those used in the prior publication of these data.

Further analyses were conducted using only person-time after the end of employment ('inactive') person-years, which represented 74% of the person-time and 92% of the deaths). Such analyses may sometime reveal trends with cumulative exposure which are obscured when active and inactive person-years are combined [Steenland and Stayner, 1991]. Chi-square tests for trend in SMRs were done according to Breslow et al. [1983].

Analyses were also conducted using national rates for multiple causes of death, which include all causes of death listed on the death certificate and are particularly useful for diseases which are usually contributory rather than underlying causes. These analyses were restricted to post-1960 because U.S. referent rates are only available after 1960 [Steenland et al., 1992].

In addition, a nested case–control analysis of lung cancer, in which estimated cumulative exposure could be treated as a continuous variable, was also conducted. In this analysis, five controls were randomly selected from the risk set of all those who had achieved the age of the case at the time the case failed [incidence–density sampling, see Beaumont et al., 1989]. Work history and cumulative exposure were truncated for controls at the failure time of their index case. Analyses were conducted via conditional logistic regression using PHREG procedure of the Statistical Analysis System [SAS, 1991].

Smoking data for 602 men (volunteers) in the cohort were available from a 1960 Public Health Service silicosis survey [see Gillam et al., 1976], when these men were aged 35–64. Cigarette smoking categories included never/occasional (including smokers of only pipe or cigar), current, and former. Data were also available on

amount smoked for current cigarette smokers, never/occasional. Compatible age and race-specific data for U.S. white males were available from a 1955 survey of approximately 40,000 subjects, done as a supplement to the February 1955 Current Population Survey [Haenszel et al., 1956]. Age-adjusted smoking prevalences for the U.S. and the miners by smoking category were then compared, and the effect of smoking differences upon observed lung cancer rate ratios was estimated according to the technique of Axelson [Axelson and Steenland, 1988]. The assumed rate ratios for cigarette smokers vs. never smokers, used for this estimation, were 5 for former smokers and current smokers of less than 10 cigarettes, 10 for current smokers of 10–20 cigarettes, and 20 for current smokers of more than 20 cigarettes a day. These rate ratios were chosen to reflect average values from large prospective studies of smokers.

RESULTS

We observed 1,551 deaths among the 3,328 miners during 106,000 person-years of observation. Only 2% of the cohort were lost to follow-up. The average year of first exposure was 1945, the average length of follow-up was 37 years, and the average length of employment underground was 9 years. The median cumulative dust-days was 8,376, the mean was 23,569, and the range was 2,193–225,774. Seventy-five percent of the cohort had fewer than 26,823 dust-days. Based on data from Vermont where the silica content of respirable dust was similar, 10 mppcf of respirable dust would be approximately equivalent to 0.1 mg silica/m^3 of air. Using this conversion, the median average exposure level of these miners was 0.05 mg/m^3 (the current OSHA standard is 0.1 mg). However, this varied considerably by time period, with exposures being much higher in earlier years. The median average exposure for men hired prior to 1930, 1930–1950, and after 1950 was 0.15, 0.07, 0.02, respectively.

Table I presents SMRs for the entire cohort for a number of causes of a priori interest, as well as common causes and causes which showed marked elevations. Death from all causes was elevated 13%. Most of the excess overall death was accounted for by excess deaths from tuberculosis, nonmalignant respiratory disease, and accidents, causes which are associated with silica exposure and mining.

A review of death certificates showed that 21 of 39 tuberculosis deaths indicated silico-tuberculosis, while 40 of 92 deaths in the "other respiratory disease category" mentioned silicosis or unspecified pneumoconiosis (one death in this category was due to asbestosis). A review of all 1,551 death certificates for the entire cohort found that 140 men (9%) had some mention of silicosis on their death certificate, either as an underlying or contributing cause. The significant elevation for asthma may also have been the result of misdiagnosed silicosis, although silica also has pronounced effects on the immune system (see below).

Lung cancer was only marginally elevated for the cohort as a whole (SMR = 1.13). The SMR for person-time occurring more than 30 years since time of first exposure (first job underground) was 1.27 (95% CI 1.02–1.55, 90 observed), compared with an SMR of 0.82 (25 observed) for person-time with less than 30 years since first exposure. Trends with duration of exposure were inconsistent (SMRs of 1.02, 1.55, 1.01 for less than 10 years, 10–20 years, and 20+ years of exposure, based on 65, 35, and 15 observed deaths, respectively).

TABLE I. Overall Gold Miner Mortality Results (U.S. Referent Rates): Update of South Dakota Cohort to 1990

Cause (ICD9)[a]	Obs	SMR	(95%CI)
All deaths	1551	1.13	(1.07–1.19)
All cancers (140–208)	303	1.01	(0.90–1.13)
Ischemic heart disease (410–414)	431	0.94	(0.85–1.03)
Tuberculosis (010–012)	36	3.52	(2.47–4.87)
Cerebrovascular disease (430–438)	77	0.94	(0.75–1.18)
Cancers			
Digestive system (150–159)	69	0.85	(0.66–1.07)
Peritoneum, other (158–9)	4	2.81	(0.76–7.19)
Respiratory			
Larynx (161)	3	0.71	(0.15–2.07)
Lung (162)	115	1.13	(0.94–1.36)
Other respiratory (160, 3–5)	3	2.54	(0.52–7.43)
Urinary (188–189)	9	0.57	(0.26–1.08)
Hematopoietic (200–208)	35	1.29	(0.90–1.79)
Lymphosarcoma/reticulosarcoma (200)	8	1.72	(0.74–3.39)
Hodgkin's (201)	2	0.79	(0.09–2.85)
Leukemia/aleukemia (204–8)	14	1.24	(0.68–2.08)
Other (202–3)	11	1.26	(0.62–2.26)
Nonmalignant respiratory disease (460–519)	170	1.86	(1.58–2.16)
Emphysema (492)	23	1.39	(0.88–2.09)
Pneumonia (480–486)	40	1.27	(0.91–1.74)
Bronchitis (490–491)	6	1.66	(0.61–3.61)
Asthma (493)	7	2.61	(1.09–5.61)
Pneumoconioses and other respiratory (470–478, 494–519)[b]	92	2.61	(2.11–3.20)
Acute kidney disease (580–581, 584)	2	1.19	(0.14–4.29)
Chronic kidney disease (582–583, 585–587)	11	1.25	(0.62–2.23)
Accidents (E800–E949)	139	1.78	(1.49–2.09)
Falls (E880–888, E929.3)	15	1.55	(0.87–2.55)
Other accidents (E890–E928, E929.4–929.9)	67	2.98	(2.31–3.79)

[a]International Classification of Disease codes, 9th revision.
[b]includes chronic obstructive pulmonary disease and other disease besides pneumoconioses.

When local county rates were used as the referent rates, the SMR for lung cancer was 1.25 (1.03–1.51, 112 observed) and was 1.27 (1.02–1.57, 88 observed) for those with 30 or more years since first exposure. When South Dakota rates were used, the SMR for lung cancer was 1.59 (1.31–1.92), markedly increased from the SMRs using either U.S. or county rates. South Dakota has notably lower lung cancer rates than the rest of the United States, but is divided between the larger cities on the plains in the eastern portion and the mountainous western area where the gold mine is located. It may be that the county rates or the U.S. rates are preferable to the South Dakota rates for use as a referent population, although the county rates suffer from small numbers and instability. We have chosen to emphasize the U.S. rates throughout this discussion. Conclusions about the etiologic significance of findings are best based on biological plausibility and disease trends with calendar time or estimated exposure, rather than point estimates based on any set of referent rates.

Hematopoietic cancers were slightly elevated in the cohort as a whole, with the

TABLE II. Gold Miner SMRs for Selected Causes by Cumulative Dust Exposure: South Dakota Cohort Update to 1990

	Dust-days[a]				
Cause (ICD9)	<8,000 SMR(obs)	8,000–32,000 SMR(obs)	32,000–48,000 SMR(obs)	48,000+ SMR(obs)	Chi-square trend test
Respiratory tuberculosis	0.52 (1)	0.78 (2)	0.89 (1)	6.95[b] (32)	23.76[b]
Lung cancer	1.17 (44)	1.01 (35)	0.97 (8)	1.31 (28)	0.21
Pneumoconioses, other respiratory diseases	1.79[b] (19)	1.46 (18)	2.95[b] (10)	8.87[b] (45)	25.77[b]
Chronic renal disease	0.40 (1)	0.34 (1)	1.26 (1)	2.77[b] (8)	7.62[b]
Non-Hodgkin's lymphomas (ICD9 200, 202) (after 1960 only)	1.27 (4)	1.48 (4)	0.00 (0)	3.29[b] (5)	1.75

[a]One dust-day is one day with an exposure of 1 mppcf dust.
[b]Significant at the 0.05 level.

most pronounced excess (SMR 1.72, 0.74–3.39) occurring among the category lymphosarcoma/reticulosarcoma (ICD9 codes 200), which are non-Hodgkin's lymphomas. To explore this excess, we combined other non-Hodgkin's lymphomas (ICD9 code 202) from the category "other hematopoietic cancer" (composed of multiple myeloma, ICD9 203, and other lymphomas, ICD9 202) for the calendar time period after 1960 (the appropriate rates were available only after 1960). This combined category of non-Hodgkin's lymphomas had 13 observed deaths with an SMR of 1.63 (0.86–2.78).

Table I indicates nonsignificant excesses of cancers of the peritoneum (SMR 2.81, four observed) and of cancers included in the category "other respiratory cancers" (SMR 2.54, three observed), categories which might include mesothelioma. A review of these seven death certificates did not find any mention of mesothelioma. Furthermore, no mention of mesothelioma was found in a review of deaths from lung cancer or other nonspecified cancer, categories which at times include mesotheliomas [Lilienfeld and Gunderson, 1984].

Table II shows SMR analyses by cumulative exposure category for selected causes. Significant positive trends were observed for tuberculosis, pneumoconioses, and chronic renal disease, and a positive nonsignificant trend was observed for non-Hodgkin's lymphomas. All these causes were significantly elevated in the highest exposure category. Chronic renal disease has been associated with silica exposure in other epidemiologic studies [Steenland et al., 1990a] and some authors have suggested it may reflect an autoimmune process [Osorio et al., 1987]. There was little trend for lung cancer. Restriction of person-time to time after last employment ("inactive" person-time) did not alter the lack of a trend for lung cancer and cumulative dust exposure. Since dust exposure levels were estimated before 1937, we also conducted analyses restricted to the 76% of the cohort hired after that date, when actual dust levels were measured. These analyses also failed to exhibit any increased lung cancer with increased cumulative dust exposure.

A nested case–control analysis of the 115 lung cancers and a set of matched controls revealed a negative nonsignificant trend with either estimated cumulative dust exposure or the log of estimated dust exposure (the mean cumulative dust exposure for cases was 28,389 dust-days, while it was 31,060 dust-days for controls).

TABLE III. Gold Miner SMRs for Three Year-of-Hire Subcohorts: South Dakota Cohort

	Year of hire		
Cause (ICD9)	<1930 SMR(obs)	1930–1950 SMR(obs)	1951+ SMR(obs)
All cancers	1.11 (66)	0.95 (169)	1.12 (68)
Tuberculosis	7.72 (33)[a]	1.00 (6)	0.00 (0)
Cancer of peritoneum	6.09 (2)	1.20 (1)	3.92 (1)
Lung cancer	1.30 (21)	1.14 (71)	1.01 (23)
Pneumoconioses, other respiratory diseases	5.37 (36)[a]	2.12 (48)[a]	1.36 (8)
Chronic kidney disease	2.39 (7)[a]	0.80 (4)	0.00 (0)
Hematopoietic cancer	1.64 (8)	1.30 (21)	0.97 (6)
Lymphosarcoma and reticulosarcoma	3.24 (3)	1.45 (4)	1.04 (1)
Leukemia	1.72 (4)	1.36 (9)	0.43 (1)

[a]95% CI excludes 1.00.

Stratification by duration of exposure did not change these results. Duration of exposure itself was not a significant predictor of lung cancer. Neither year of first exposure nor year of birth differed between cases and controls, and these variables did not modify the relationship between estimated cumulative dust and lung cancer. Again, because dust levels had to be estimated prior to 1937, we also conducted the case–control analyses restricting cases and controls to those hired in 1937 or later (75 of the 115 cases were hired in 1937 or later). These analyses likewise failed to show any relationship between lung cancer and cumulative dust exposure.

Table III shows SMRs for selected causes after dividing the cohort by year of hire. Tuberculosis and chronic renal disease were significantly elevated only for those hired prior to 1930, and pneumoconiosis was significantly elevated only for men hired prior to 1930 and men hired from 1930 to 1950. These diseases are clearly related to cumulative exposure and exposures were known to be higher in earlier years. Lung cancer also shows the highest elevation in the earliest hire period, but is not significantly elevated.

Table IV shows SMRs by multiple cause mortality analysis, in which rates are calculated using any mention of a given disease on the death certificate. These analyses are particularly useful for diseases which may be prevalent at death but are not fatal. Categories which showed marked excesses here, but which were not revealed by underlying cause analysis, included arthritis, other musculoskeletal disease (including lupus and sclerosis), other diseases of the skin (including scleroderma and lupus), alcoholism, other diseases of the blood-forming organs, and other myocardial degeneration. Several of these disease (lupus, scleroderma, systemic sclerosis, rheumatoid arthritis) are autoimmune diseases, and are known to be associated with silica [Rustin et al., 1990; Haustein et al., 1990; Koskela et al., 1987; Sluis-Cremer et al., 1985; Klockars et al., 1987]. The cardiovascular disease elevations revealed by multiple cause analyses may have been due to the effects on the circulatory system of the pneumoconiotic lung disease which was so prevalent in this cohort.

A review of the multiple cause mortality data stratified by time-of-hire (<1930, 1930–1950, 1951+) showed that the excesses for chronic renal disease (10 observed, SMR 2.14, 1.05–4.04), myocardial degeneration (15 observed, SMR 9.20, 5.14–15.18), and other diseases of the blood (3 observed, SMR 4.71, 0.97–13.77) were

TABLE IV. Gold Miner SMRs for Multiple Cause Mortality (After 1960), Considering all Causes Listed on the Death Certificate: South Dakota Cohort

Cause (ICD9)[a]	Obs	SMR	(95%CI)
All causes listed	3038	1.05	(1.02–1.09)
All cancers (140–208)	465	1.08	(0.98–1.18)
Ischemic heart disease (410–414)	527	0.88	(0.80–0.95)
Tuberculosis (010–012)	27	4.72	(3.11–6.87)
Cerebrovascular disease (430–438)	128	0.95	(0.75–1.18)
Diseases of arteries, veins, circulation (415–7,440–59)	180	1.19	(1.02–1.38)
Other myocardial degeneration (429.0,429.1)	20	3.03	(1.85–4.68)
Cancers			
Lung (162)	121	1.16	(0.96–1.38)
Lymphosarcoma/reticulosarcoma (200)	6	1.37	(0.50–2.98)
Hodgkin's (201)	2	0.87	(0.10–3.14)
Leukemia/aleukemia (204–8)	10	0.82	(0.39–1.50)
Other (202–3)	15	1.43	(0.80–2.36)
Nonmalignant respiratory disease (460–519)	454	1.62	(1.47–1.78)
Emphysema (492)	61	1.42	(1.08–1.82)
Pneumonia (480–486)	119	1.20	(1.00–1.44)
Bronchitis (490–491)	11	1.41	(0.70–2.52)
Asthma (493)	8	1.70	(0.73–3.35)
Pneumoconioses and other respiratory (470–478, 494–519)	251	2.08	(1.82–2.35)
Acute kidney disease (580–581, 584)	8	1.03	(0.44–2.02)
Chronic kidney disease (582–583, 585–587)	34	1.27	(0.88–1.77)
Arthritis (711–6, 720–1)	17	2.19	(1.27–3.50)
Other musculoskeletal (710, 717–9, 722–9, 731–9)	10	2.14	(1.03–3.94)
Alcoholism (303)	22	1.79	(1.12–2.71)
Other disease of blood-forming organs (288–289)	9	2.31	(1.05–4.39)
Other diseases of skin (690–709)	10	2.45	(1.17–4.51)

[a]International Classification of Disease codes, 9th revision.

concentrated in those hired prior to 1930. The excesses for arthritis (12 observed, SMR 2.63, 1.36–4.59), other musculoskeletal disease (6 observed, SMR 2.14, 0.78–4.46), and other skin conditions (8 observed, SMR 3.28, 1.41–6.45) were concentrated in those hired between 1930 and 1950. The excess for alcoholism was concentrated in those hired after 1950 (11 observed, SMR 2.56, 1.28–4.58).

Among 602 miners participating in a 1960 U.S. Public Health Service survey, 23.4% had never smoked cigarettes or smoked only occasionally, 64.6% were current smokers, and 12.0% were former smokers. Among current smokers, 4.9% smoked less than 10 cigarettes a day, 76.6% smoked 10–20 per day, and 18.4% smoked 20 or more per day. Among white U.S. males surveyed in 1955, the age-adjusted prevalence of never/occasional cigarette smokers, current cigarette smokers, and former cigarette smokers was 32.8%, 56.6%, and 10.6%, respectively. Among U.S. current smokers, the percent smoking less than 10 cigarettes, 10–19 cigarettes, and 20+ cigarettes per day was 13.5%, 58.0%, and 28.5%, respectively. These data indicate that in 1960 more gold miners smoked cigarettes than U.S. white males of

TABLE V. Four Cohort Mortality Studies of Gold Miners*

Authors (year) (lung cancers)	Exposure–response for dust, comments	SMR or OR (95% CI)	Smoking control	Radon and arsenic
Hnizdo and Sluis-Cremer [1991; 77 lung cancers]	Positive and significant, good historical estimates, 30% respirable-free silica, silicosis generally not related to lung cancer	OR = 3.2(1.3–3.5) for highest exposed vs. lowest, nested case–control study	Yes, good data	Cumulative WLM average = 70, no data on arsenic
Kusiak et al. [1991; 378 lung cancers]	Positive and significant for duration, no detailed dose data, 6–12% respirable-free silica	SMR = 1.29 (1.2–1.5), risk only for mining <1946 (SMR = 1.40), Poisson regression used for exposure–response	Some, for a sample, not thought to explain excess	+ dose–response for both, not easy to separate effects from silica, average cumulative WLM ranges from 2 to 23 for 90% of cohort but some men had more than 50 WLM
Wyndham et al. [1986; 39 lung cancers]	Positive, p = .06, good historical estimates, exposure better predictor than duration	SMR = 1.61 (1.1–2.2), nested case–control used for exposure–response	Yes, good data	average WLMs (cumulative) = 36, no data on arsenic
Armstrong et al. [1979; 59 lung cancers]	No trend with years underground, no data on exposures, no risk for silicotics	SMR = 1.45, p<.01, internal comparison SMR = 1.40 (0.7–3.0)	Yes, good data	about 20 WLMs (cumulative average), arsenic levels about 50 ppm

*Excludes some autopsy case–control studies of gold miners, as well as some other publications referring to these same cohorts.

the same age, but that among smokers fewer were heavy smokers. Using these data and the technique described by Axelson and Steenland [1988], the estimated lung cancer rate ratio due to smoking alone, for the cohort vs. the U.S. population, would have been 1.07.

DISCUSSION

There have been four other cohorts of gold miners which have been studied (Table V). All these cohorts have been exposed to silica. In two [Wyndham et al., 1986; Hnizdo and Sluis-Cremer, 1991], positive trends between estimated cumulative dust and lung cancer were observed, another one [Armstrong et al., 1979] showed no such trend but had no data on exposure beyond duration of years underground, and the fourth [Kusiak et al., 1991] showed a positive trend but the effect was difficult to distinguish from the effects of radon and arsenic exposures.

The gold miners studied here exhibited excess mortality from silicosis and

silico-tuberculosis, which showed positive exposure–response trends. Chronic renal disease was nonsignificantly elevated, but also showed a significant positive exposure–response trend.

We found an excess of lung cancer in this cohort, the magnitude of which varied depending on which referent group was used. However, this excess was not related to estimated exposure to dust. The fact that silicosis and silico-tuberculosis showed clear positive exposure–response trends suggests that the estimated dust exposures used here were reasonably accurate. This would suggest that neither exposure to nonasbestiform amphiboles nor silica was likely to be responsible for the observed excess of lung cancer, at least not in a way related to quantitative exposure to dust.

There was only one death from asbestosis in this cohort (which could have been the result of asbestos exposure outside the mine). Assuming the overall lack of asbestosis is real, however, it would therefore appear that the nonasbestiform fibers in this mine did not cause any marked excess of either asbestosis or lung cancer.

There is strong evidence from numerous studies that silicotics suffer from high rates of lung cancer [see for example, Amandus et al., 1991]. Evidence that exposure to silica itself causes lung cancer has been less consistent to date, although the majority of the studies are positive, and two have shown a positive dose–response [Checkoway et al., 1993; Hnizdo and Sluis-Cremer, 1991]. In this cohort there was considerable mortality and morbidity from silicosis. Those who did have silicosis may have contributed to the observed moderate lung cancer excess. We did examine the presence or absence of a listing for silicosis (or silico-tuberculosis or pneumoconiosis) on the death certificate, although this may not be a very precise measure of which men had silicosis. There was no evidence that lung cancer deaths had more silicosis listed on their death certificates than other deaths. Only 3 of the 115 lung cancer deaths indicated silicosis (or silico-tuberculosis or pneumoconiosis) on their death certificates, while 140 of the 1,551 total death certificates indicated silicosis.

Levels of exposure to crystalline silica in our study were high, especially prior to the lowering of dust levels in the early 1950s, although they were not as high as some occupational cohorts, such as Vermont granite cutters. Vermont granite cutters were exposed to 20–50 mppcf of dust from granite which was composed of 10–30% silica prior to the installation of dust controls in the 1940s [Steenland and Beaumont, 1986]. The gold miners studied here were exposed to approximately 10–30 mppcf of dust prior to 1950, dust composed of approximately 13% free silica, and to under 10 mppcf thereafter. It is of interest to note that an analysis of lung cancer risk and the presence of silicosis on the death certificate was strongly positive in the granite cutters, while no such relationship was apparent in this study for gold miners.

The exposure to silica did lead to a variety of diseases besides the expected silico-tuberculosis and pneumoconiosis. Silica exposure has been associated with autoimmune disease, and the excesses found here for arthritis and musculoskeletal disease (the latter category included several deaths mentioning systemic sclerosis and systemic lupus) have been noted elsewhere in the literature for silica-exposed workers [Steenland et al., 1992; Koskela et al., 1987; Sluis-Cremer et al., 1985; Klockars et al., 1987]. The category "other skin disease," which was also significantly elevated, included several deaths with mention of lupus erythematosus and scleroderma on the death certificate. Renal disease also showed associations with high silica exposure, and this association may also reflect an autoimmune mechanism.

The elevation of "other diseases of the blood-forming organs" is interesting in light of the excess also observed for non-Hodgkin's lymphomas and the evidence from animal studies that injected silica can cause lymphoma [IARC, 1987]. Listings on the death certificates for this category included bone marrow depression, myelodysplasia, blood dyscrasia, and myeloid metaplasia.

In summary, the present cohort with substantial silica exposure exhibited large excess mortality from several causes of death known to be related to silica. Lung cancer, of interest because of a possible association with either silica, silicosis, or nonasbestiform amphibole minerals, showed some elevation but did not exhibit a positive exposure–response trend using estimated quantitative cumulative dust exposures. This cohort represents one of the principal cohorts in which the association between cumulative silica exposure and lung cancer was generally negative. The reasons for the discrepancy between our findings and the positive findings in other gold miner studies and in the silica literature in general remain unexplained. One possibility is that not all silica is alike, and different mineralogic varieties may have different effects. Another possibility is that the positive dose–responses for dust in other gold miner studies reflect to some degree uncontrolled confounding by radon or arsenic.

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