Mortality in Vermont granite workers and its association with silica exposure

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ABSTRACT

Objectives To assess mortality in Vermont granite workers and examine relationships between silica exposure and mortality from lung cancer, kidney cancer, non-malignant kidney disease, silicosis and other non-malignant respiratory disease.

Methods Workers employed between 1947 and 1998 were identified. Exposures were estimated using a job–exposure matrix. Mortality was assessed through 2004 and standardised mortality ratios (SMRs) were computed. Associations between mortality and exposure to silica were assessed by nested case–control analyses using conditional logistic regression.

Results 7052 workers had sufficient data for statistical analysis. SMRs were significantly elevated for lung cancer (SMR 1.37, 95% CI 1.23 to 1.52), silicosis (SMR 59.13, 95% CI 44.55 to 76.97), tuberculosis (SMR 21.74, 95% CI 18.37 to 25.56) and other non-malignant respiratory disease (SMR 1.74, 95% CI 1.50 to 2.02) but not for kidney cancer or non-malignant kidney disease. In nested case–control analyses, significant associations with cumulative exposure to respirable free silica were observed for silicosis (OR 1.13, 95% CI 1.05 to 1.21 for each 1 mg/m^3-year increase in cumulative exposure) and other non-malignant respiratory disease (OR 1.10, 95% CI 1.03 to 1.16) but not for lung cancer (OR 0.99, 95% CI 0.94 to 1.03), kidney cancer (OR 0.96, 95% CI 0.84 to 1.09) or non-malignant kidney disease (OR 0.95, 95% CI 0.84 to 1.08).

Conclusions Exposure to crystalline silica in Vermont granite workers was associated with increased mortality from silicosis and other non-malignant respiratory disease, but there was no evidence that increased lung cancer mortality in the cohort was due to exposure. Mortality from malignant and non-malignant kidney disease was not significantly increased or associated with exposure.

What this paper adds

- Although crystalline silica was classified as a known human carcinogen by the International Agency for Research on Cancer (IARC) in 1997, epidemiological evidence for this is inconsistent.
- The Vermont granite industry has played an important role in US regulation of exposures to silica because of its long history of exposure and health monitoring and a general absence of occupational co-contaminants.
- The current study is the most comprehensive mortality assessment of Vermont granite workers conducted to date.
- Mortality from lung cancer was higher than previously observed in this industry, but there was no evidence of a relationship with silica exposure.
- The results of this study do not provide support for proposed changes to the US exposure limit for silica on the basis of lung cancer risk.

The Vermont granite industry has been closely scrutinised since the 1920s, when a high prevalence of respiratory morbidity and mortality among workers was first documented.[1] This led the Vermont Department of Health Division of Industrial Hygiene (DIH) to conduct a series of environmental surveys to assess exposure levels, adopt a standard to keep dust exposure levels below 10 million particles per cubic foot (mppcf) and begin a medical surveillance program.[2] As a consequence, the Vermont granite workers have played an important role in the development of US standards for occupational exposure to crystalline silica.

The US Occupational Safety and Health Administration (OSHA) and the US Mine Safety Health Administration currently have an occupational exposure limit (OEL) for respirable silica of essentially 0.1 mg/m^3. However, the National Institute for Occupational Safety and Health (NIOSH) has promoted a recommended exposure limit of 0.05 mg/m^3 and the American Conference of Governmental Industrial Hygienists has a current threshold limit of 0.025 mg/m^3, based primarily on concerns about lung cancer risk.[3 4] In light of this, OSHA has given notice of its intention to revise its OEL for silica in the near future.

Previous mortality studies of the Vermont granite industry have not provided consistent evidence of a relationship between silica exposure and lung cancer. Davis *et al* carried out a proportionate mortality analysis of 969 deaths occurring between 1952 and 1978 and found an excess of deaths from silicosis and tuberculosis, but no proportionate excess from lung cancer.[5] Costello and Graham studied 5414 men employed in the granite industry from 1950 to 1982 and found that, in addition to mortality from silicosis and tuberculosis, overall lung cancer mortality was significantly increased compared to the rates for white males in the USA (standardised mortality ratio (SMR) 1.18).[6 7] They also found that men hired after the implementation of dust controls in 1940 had lung cancer mortality rates similar to those for men with comparable tenure and latency who were hired before that time. Because exposures are known to have been much higher prior to 1940, they concluded that the

increased lung cancer mortality was not due to silica exposure. Data from that study were subsequently analysed by Attfield and Costello, using exposure estimates derived by Davis *et al* to examine the exposure–response relationship for lung cancer.[5 8] Their results indicated an increase in the SMR for lung cancer with increasing cumulative exposure to silica.

These previous studies had potential limitations arising from their use of records from the DIH medical surveillance program to identify cohort members and determine work histories. There was the potential for selection bias because the DIH program was voluntary and the employment information in the DIH records was often incomplete. The availability of additional sources of employment data provided us with an opportunity to conduct a new mortality study with a more inclusive cohort and more accurate work histories. We independently assessed mortality and used raw data and unpublished reports from all previous environmental surveys to estimate exposure levels.

METHODS

Cohort assembly

The target population was all men who had worked in the Vermont granite industry at any time between 1 January 1947, when all workers were enrolled in a group insurance program, and 31 December 1998. In addition to insurance records, we used the following resources to identify workers: date abstracted from DIH records,[6] pension records, data from a study of workers employed from 1979 to 1987,[9 10] and data from a study of retired workers.[11] Data from all sources were linked and compared to eliminate duplications and resolve discrepancies in identifying information.

Mortality ascertainment

We determined vital status through 2004 by searching the US National Death Index (NDI), US Social Security Administration vital status records and Vermont State Records Office. Additional information sources included a commercially available Social Security death index, obituary and genealogy websites, and websites for locating individuals who are currently alive. We requested death certificates from relevant state record offices to evaluate questionable NDI matches and to obtain cause of death information for deceased individuals without a valid NDI match. Workers whose vital status remained unknown and workers who were known to have died in Canada were included in a search of Quebec vital records. We used coded cause of death information from the NDI when available and an experienced nosologist coded cause of death information from death certificates. All causes were coded to the 9th Revision of the International Classification of Diseases (ICD-9). Underlying cause of death was determined by either the nosologist or the NDI's automated algorithm, based on the ICD-9 selection and modification rules.

Exposure assessment

We used three primary sources of data to determine employment in the Vermont granite industry: work history information obtained from DIH surveillance program participants, self-reported work histories from a pulmonary function study conducted during 1979–1987,[10] and pension records for individuals who worked during or after 1957 and left work prior to 1999. The source that provided the earliest evidence of employment in the industry was used to determine a subject's initial year of work, which defined their date of entry into the cohort. To compile detailed work histories for subjects included in the exposure–response analyses described below, we carefully reviewed data from all sources while blinded to the subject's vital status and cause of death. To resolve discrepancies between data sources, we used additional employment information in obituaries, autopsy reports and death certificates whenever available.

We used 5204 exposure measurements made in the Vermont granite industry between 1924 and 2004 to construct a job–exposure matrix (JEM). Details of the methodology are described in a separate paper (Verma *et al*, *J Occup Environ Hyg*, submitted 2010). Briefly, jobs were classified into 22 categories reflecting their exposure potential and the concentration of respirable free silica for each category was estimated for three time periods: before 1940, 1940–1949 and 1950–2004 (table 1). Estimates for the middle time period, when dust controls were being implemented, are averages of the earlier and later time periods. Impinger counts (mppcf) were converted to gravimetric respirable free silica (mg/m^3) using 10 mppcf=0.1 mg/m^3, based on earlier studies and NIOSH recommendations.[12 13] A worker's exposure level for each year of employment was determined by classifying his job into one of the 22 categories and assigning the silica concentration for that category and year as specified in the JEM. We then computed summary exposure metrics by accumulating yearly exposure over the relevant time period for each case and control.

Statistical analysis

We used a modified life table approach as implemented by OCMAP statistical software[14] to compute SMRs, adjusted for 5-year age and calendar year groupings. Confidence intervals and significance tests were based on the Poisson distribution and an SMR was considered to be statistically different from 1.00 if the p value was <0.05. Both US and Vermont white males were used as reference populations.

Table 1 Estimated exposure concentrations of respirable free silica by time period

		<1940		1940–1949*	≥1950	
Job class	Location	N	mg/m^3	mg/m^3	N	mg/m^3
Bit grinder†	Quarry	1	0.17			
Blacksmith†	Quarry	4	0.03			
Boxer	Shed	14	0.08	0.06	103	0.04
Carver	Shed	19	0.37	0.22	149	0.07
Channel bar	Quarry	3	0.15	0.08		0.01‡
Crane	Shed	9	0.16	0.11	32	0.05
Cutter	Shed	331	0.39	0.23	1569	0.07
Draftsman	Shed	12	0.01	0.01		0.01
Driller	Quarry	120	1.07	0.54	7	0.01
Foreman	Shed		0.12	0.09	9	0.05
Grinder	Shed	31	0.19	0.13	5	0.07
Jackhammer	Quarry	10	1.05	0.56	7	0.06
Labourer	Shed		0.24	0.17	8	0.10
Lumper	Shed	5	0.30	0.18	138	0.06
Maintenance	Shed	12	0.24	0.16	28	0.07
Quarry (general)	Quarry	22	0.13	0.07		0.01‡
Office worker	Shed	29	0.04	0.04		0.04
Polisher	Shed	35	0.12	0.10	570	0.07
Sandblaster	Shed	43	0.24	0.16	337	0.07
Sawyer	Shed	13	0.13	0.10	634	0.06
Shed (general)	Shed	153	0.12	0.09	491	0.05
Surfacer	Shed	150	0.28	0.18	101	0.08

*Estimates are averages of those for the earlier and later periods because few measurements were available from 1940 to 1949.
†Job not performed after 1939.
‡Trend applied using jackhammer and driller data.

We assessed exposure–response relationships by performing nested case–control analyses. For each disease of interest, cases were grouped into risk sets based on year of birth and year of death. Three controls for each risk set were randomly selected from among all cohort members who were born in the same year and survived through the case's year of death. We used conditional logistic regression to model the relationships between mortality and net exposure duration, cumulative exposure and average exposure. Net exposure duration was computed as the number of years employed in the granite industry (excluding gaps in employment), while cumulative exposure was computed by summing average annual exposures for the relevant years. All analyses were performed both by accumulating exposures up to the year of death for the case or cases in a particular risk set, as well by excluding exposures occurring within 10 years before the time of death of the case to reflect a lag between exposure and mortality. We analysed cumulative exposure as both a continuous and a categorical variable, with category cut points based on the quintiles of the combined distribution for cases and controls. Multivariate models were used to examine the effect of exposure after adjustment for the number of years since the start and end of exposure. All models were fitted by maximum likelihood using EGRET statistical software.[15]

The research methods used in this study were approved by the University of Vermont Committees on Human Research.

RESULTS

Description of the cohort

Of 7661 men indentified as eligible for the study, 609 were excluded because of missing birth date or date of hire. Missing data occurred most often for men who were hired after the last survey of the industry in 1987 and who were still working in 1999, when pension records for current employees became unavailable. The 7052 workers remaining in the cohort contributed 269 253 person-years of follow-up for computation of SMRs. The birth year, year of first employment and vital status of these workers are given in table 2. More than half (54.5%) were deceased by 31 December 2004, but the date of death was unknown for 14. All 74 workers with unknown vital status were born before 1920, so presumably many of these men had also died before the end of 2004. The 74 men with unknown vital status and 14 deceased men with unknown date of death were included in computation of SMRs, but follow-up on these workers was censored at the time their employment ended, when they were last known to be alive. They were eligible for selection as a control in the case–control analyses if the censoring date was not before the year of death of the case.

Table 2 Characteristics of the final cohort

	N	%
Date of birth		
<1900	781	11.1
1900–1909	933	13.2
1910–1919	1003	14.2
1920–1929	1177	16.7
1930–1939	1093	15.5
1940–1949	997	14.1
≥1950	1068	15.1
Date began employment		
<1930	1170	16.6
1930–1939	544	7.7
1940–1949	1137	16.1
1950–1959	1350	19.1
1960–1969	1455	20.6
≥1970	1396	19.8
Vital status through 31 December 2004		
Alive	3133	44.4
Deceased	3845	54.5
Unknown	74	1.0
Total	7052	

Standardised mortality ratios

Information about cause of death was unavailable for 207 (5.4%) of the 3831 deceased workers with known date of death. Overall mortality, including unknown cause, was significantly elevated in the cohort compared to US white males (SMR 1.08, 95% CI 1.05 to 1.12). This is attributable to significantly increased mortality from tuberculosis, malignant neoplasms and non-malignant respiratory disease (table 3). Mortality from all heart disease and from all external causes was significantly lower in the cohort than in the reference population. The increased mortality from malignant neoplasms reflects the significantly elevated SMR for cancers of the bronchus, trachea or lung (SMR 1.37). No other cancers were significantly elevated.

Silicosis mortality was very high in the cohort (SMR 59.13) and contributed to the significantly increased mortality from non-malignant respiratory disease. However, mortality from other respiratory diseases, which excludes silicosis, influenza, pneumonia, bronchitis, emphysema and asthma, was also significantly increased (SMR 1.74). Of the 174 deaths in this category, chronic airway obstruction was listed as the cause for 122 (70%).

Most deaths from tuberculosis and silicosis occurred in men who began work before 1940, prior to the implementation of dust controls in the industry. No deaths from tuberculosis occurred in men who began work in 1950 or later. Only six of the 55 men who died of silicosis began work after 1940. Three of these began work after 1949 and worked for less than 10 years in the Vermont granite industry. However, one was known to have previously worked for 40 years as a stone cutter in Canada. Information about previous employment was unavailable for the other two, but they began working in the Vermont granite industry at 43 and 52 years of age, so may also have been exposed to silica elsewhere. All deaths from silicosis occurred in workers born before 1925.

For most diseases we obtained similar results when white Vermont males were used as the reference population. As expected for a rare disease in a small population, the SMR for silicosis (SMR 15.85, 95% CI 11.96 to 20.66) was lower than the estimate based on US mortality rates because silicosis deaths in the cohort elevated the Vermont mortality rate.

Exposure–response analyses

To examine exposure–response relationships, we performed nested case–control analyses for silicosis, other non-malignant respiratory disease, lung cancer, kidney cancer and non-malignant kidney disease. We did not examine tuberculosis because reductions in silica exposure levels coincided with the introduction of effective treatment for the disease, making it impossible to estimate their independent effects on mortality. The results presented for kidney cancer include a 10-year lag, while those for non-malignant diseases do not. For lung cancer the results from both analyses are presented. For all diseases the results based on the two computations of exposure were very similar. We also performed the analyses both with and without adjustment for the number of years since first and/or last employment. These adjustments had little effect on the results, so the unadjusted results are presented.

Table 3 Causes of death through 2004: SMRs and CIs based on US white male rates

Cause of death (ICD-9 codes)	Observed	Expected	SMR	95% Confidence limits	
				Lower	Upper
Tuberculosis	147	6.8	21.75†	18.37	25.56
All malignant neoplasms	896	795.4	1.13†	1.05	1.20
Buccal cavity and pharynx	20	19.9	1.01	0.62	1.55
Digestive organs and peritoneum	218	209.9	1.04	0.91	1.19
Larynx	10	10.1	0.99	0.48	1.82
Bronchus, trachea, lung	359	261.5	1.37†	1.23	1.52
Cancer of prostate	61	68.5	0.89	0.68	1.14
Kidney	28	19.8	1.41	0.94	2.04
Bladder and other urinary organs	34	23.8	1.43	0.99	2.00
All lymphatic, haematopoietic tissue	73	78.8	0.93	0.73	1.16
All other malignant neoplasms	93	105.1	0.88	0.71	1.08
Cerebrovascular disease	217	213.0	1.02	0.89	1.16
All heart disease	1219	1372.4	0.89†	0.84	0.94
Non-malignant respiratory disease	377	272.5	1.38†	1.25	1.53
Influenza and pneumonia	71	88.1	0.81	0.63	1.02
Bronchitis, emphysema, asthma	77	81.6	0.94	0.75	1.18
Silicosis	55	0.9	59.13†	44.55	76.97
Other non-malignant respiratory disease	174	100.0	1.74†	1.50	2.02
Diabetes mellitus	67	61.2	1.09	0.85	1.39
Cirrhosis of liver	63	77.3	0.82	0.63	1.04
Nephritis and nephrosis	34	34.4	0.99	0.68	1.38
All external causes of death	264	304.7	0.87*	0.77	0.98
All other causes of death	326	410.7	0.79†	0.71	0.89

ICD-9, 9th Revision of the International Classification of Diseases; SMR, standardised mortality ratio.
*Significant at the 5% level.
†Significant at the 1% level.

When analysed as continuous variables, cumulative exposure, exposure duration and average exposure concentration were not significantly related to lung cancer mortality, regardless of whether or not exposures included a 10-year lag (table 4). Lags of 15 and 20 years were also examined and led to reductions in the ORs. To examine whether deaths from silicosis and tuberculosis might have biased the results by eliminating men with high exposures who died before they had an opportunity to develop lung cancer, we performed separate analyses for men born before 1920 (189 cases) and during or after 1920 (169 cases). All tuberculosis deaths and all but three silicosis deaths occurred in men born before 1920. A third of the deaths from other non-malignant respiratory diseases occurred in men born since 1920, but these are of less concern as a competing cause of death because their average age at death was 74.0 years, compared to 67.3 years for the lung cancer cases. There were no statistically significant associations between exposure and lung cancer mortality in either subcohort (table 4).

In contrast, cumulative exposure was significantly related to both silicosis and other non-malignant respiratory disease. The

Table 4 Associations between lung cancer risk and exposure measured as continuous variables

	No lag				10-Year lag			
	Coefficient	OR*	95% CI	p Value	Coefficient	OR	95% CI	p Value
All workers (356 cases, 941 controls)								
Cumulative exposure: 1 mg/m^3-year	−0.0100	0.99	0.95 to 1.03	0.641	−0.0120	0.99	0.94 to 1.03	0.598
Log transformed cumulative exposure: 1 ln(mg/m^3-years)	0.0518	1.05	0.97 to 1.14	0.208	0.0319	1.03	0.96 to 1.11	0.388
Net duration of employment: 10 years	0.0123	1.01	0.93 to 1.10	0.771	0.0203	1.02	0.93 to 1.12	0.671
Average exposure: 0.10 mg/m^3	−0.0207	0.98	0.83 to 1.16	0.809	−0.0092	0.99	0.85 to 1.16	0.907
Workers born before 1920 (189 cases, 497 controls)								
Cumulative exposure: 1 mg/m^3-year	−0.0176	0.98	0.94 to 1.03	0.450	−0.0182	0.98	0.94 to 1.03	0.444
Log transformed cumulative exposure: 1 ln(mg/m^3-years)	0.0407	1.04	0.93 to 1.16	0.466	0.0246	1.03	0.94 to 1.12	0.591
Net duration of employment: 10 years	−0.0648	0.94	0.84 to 1.05	0.266	−0.0062	0.94	0.83 to 1.06	0.331
Average exposure: 0.10 mg/m^3	−0.0159	0.98	0.82 to 1.18	0.860	0.0062	1.01	0.86 to 1.18	0.939
Workers born in or after 1920 (167 cases, 444 controls)								
Cumulative exposure: 1 mg/m^3-year	0.0420	1.04	0.93 to 1.17	0.484	0.0838	1.09	0.91 to 1.30	0.362
Log transformed cumulative exposure: 1 ln(mg/m^3-years)	0.0646	1.07	0.95 to 1.20	0.285	0.0433	1.04	0.93 to 1.17	0.456
Net duration of employment: 10 years	0.0962	1.10	0.98 to 1.24	0.114	0.1260	1.13	0.98 to 1.30	0.082
Average exposure: 0.10 mg/m^3	−0.0566	0.95	0.58 to 1.54	0.821	−0.2220	0.80	0.44 to 1.45	0.465

*OR per specified units of increase in exposure.

ORs indicate that for each 1 mg/m^3-year increase in cumulative exposure, the risk of silicosis mortality increased by 13% (OR 1.13, 95% CI 1.05 to 1.21) and the risk of mortality from other non-malignant respiratory disease increased by 10% (OR 1.10, 95% CI 1.03 to 1.16). Cumulative exposure was not significantly related to mortality from kidney cancer (OR 0.96, 95% CI 0.84 to 1.09) or non-malignant kidney disease (OR 0.95, 95% CI 0.84 to 1.08).

Silicosis mortality was also significantly associated with the net duration of exposure, analysed as a continuous variable (OR 1.36 per 10 years of work, 95% CI 1.06 to 1.76). No significant associations were observed between exposure duration and other non-malignant respiratory disease (OR 1.02, 95% CI 0.90 to 1.15), kidney cancer (OR 0.80, 95% CI 0.58 to 1.11) or non-malignant kidney disease (OR 0.91, 95% CI 0.69 to 1.20). Average exposure concentration was significantly related to both silicosis (OR 1.50 per 0.10 mg/m^3, 95% CI 1.13 to 1.98) and other non-malignant respiratory disease (OR 1.35, 95% CI 1.08 to 1.68). However, many men worked both before and after the large reduction in exposure levels due to dust controls, so average exposure does not reflect their actual work environment.

To explore potential non-linear exposure–response relationships, we used a logarithmic transformation of cumulative exposure and also fitted polynomial regression models and spline functions. The logarithmic transformation yielded an even stronger relationship with silicosis, but was not significantly related to mortality from the other diseases. Likelihood ratio tests indicated that the quadratic models significantly improved fit to the data for both silicosis (p=0.003) and other non-malignant respiratory disease (p=0.019). Neither higher order polynomials nor spline functions provided further improvements in fit. These analyses indicated that the linear models underestimated risk of silicosis mortality at high cumulative exposures and overestimated risk of non-malignant respiratory disease at all but very high cumulative exposures. We did not observe significant non-linear relationships with cumulative exposure for any of the other diseases. Exposure–response relationships were also examined using categories based on quintiles of cumulative exposure and a statistically significant trend was observed only for silicosis (table 5).

DISCUSSION

This study found a strong relationship between exposure to silica and mortality from silicosis. All silicosis deaths occurred in men born before 1925, consistent with earlier studies indicating that silicosis mortality was confined to workers with documented or probable exposure before the introduction of dust controls in 1938–1940.[5 7] We also found that mortality from non-malignant respiratory disease, other than silicosis, bronchitis, emphysema and asthma, was associated with high cumulative exposures. Our study does not provide exposure–response information about non-fatal silicosis, but a radiographic study in 1983 indicated a low prevalence of the disease.[9] Of 972 workers, 28 (3%) had films showing abnormalities that were consistent with pneumoconiosis, all with low grades of profusion, and only seven of these had the finding typically seen in uncomplicated silicosis.

Table 5 Associations between categories of cumulative exposure and mortality from selected disease

Quintiles of cumulative exposure	Cases	Controls	OR	95% CI	p Value	Trend test p value
Silicosis (55 cases)						
≤1.04 mg/m^3 years	4	40	1.00	–	–	<0.001
1.05–3.64 mg/m^3 years	5	38	2.02	0.45 to 9.09	0.358	
3.65–6.71 mg/m^3 years	13	30	8.62	1.86 to 39.95	0.006	
6.72–10.21 mg/m^3 years	17	27	12.36	2.67 to 57.2	0.001	
>10.21 mg/m^3 years	16	27	10.55	2.30 to 48.4	0.002	
Other non-malignant respiratory disease (172 cases)						
≤0.36 mg/m^3 years	38	92	1.00	–	–	0.318
0.37–1.18 mg/m^3 years	28	97	0.67	0.37 to 1.19	0.170	
1.19–2.57 mg/m^3 years	31	94	0.76	0.43 to 1.33	0.331	
2.58–5.41 mg/m^3 years	28	99	0.68	0.37 to 1.25	0.271	
>5.41 mg/m^3 years	47	79	1.39	0.76 to 2.54	0.279	
Lung cancer (356 cases)						
≤0.26 mg/m^3 years	84	241	1.00	—	—	0.316
0.26–0.82 mg/m^3 years	56	176	0.87	0.56 to 1.29	0.481	
0.82–2.09 mg/m^3 years	91	206	1.28	0.90 to 1.83	0.170	
2.09–4.10 mg/m^3 years	74	167	1.29	0.87 to 1.89	0.202	
> 4.10 mg/m^3 years	51	151	0.96	0.60 to 1.54	0.880	
Kidney cancer (28 cases)						
≤0.49 mg/m^3 years	9	14	1.00	–	–	0.967
0.50–1.42 mg/m^3 years	3	19	0.22	0.05 to 1.07	0.061	
1.43–2.54 mg/m^3 years	2	20	0.49	0.16 to 1.52	0.217	
2.55–4.41 mg/m^3 years	7	16	1.68	0.37 to 7.69	0.505	
>4.41 mg/m^3 years	7	15	0.90	0.20 to 3.97	0.886	
Non-malignant kidney disease (32 cases)						
≤0.68 mg/m^3 years	7	18	1.00	–	–	0.919
0.69–1.66 mg/m^3 years	5	20	0.61	0.17 to 2.17	0.446	
1.67–3.19 mg/m^3 years	7	18	1.04	0.32 to 3.34	0.945	
3.20–6.01 mg/m^3 years	7	18	1.09	0.26 to 4.52	0.904	
>6.01 mg/m^3 years	6	19	0.76	0.19 to 3.06	0.704	

We found no statistically significant increase in mortality from either malignant or non-malignant kidney disease and no evidence of an association between silica exposure and these diseases. These result differ somewhat from those of McDonald *et al* who found significantly elevated SMRs for both kidney cancer and nephritis/nephrosis, but did not find significant associations with silica exposure.[16] Another study of industrial sand workers did find a significant association between kidney disease and silica exposure,[17] while in a recent study of the German porcelain industry there was no increase in mortality from malignant or non-malignant kidney disease.[18] Although the numbers of deaths from kidney cancer (28) and nephritis/nephrosis (34) in our study were quite small, they were substantially larger than in any of these other studies.

Lung cancer mortality was significantly elevated in the study cohort (SMR 1.37), but there was no evidence of an association with silica exposure. In the previous mortality study of the Vermont granite workers, a lower SMR for lung cancer (1.18) was observed and some results indicated a relationship with silica exposure, while others did not.[7 8] A number of key differences preclude direct comparison of results from the current and previous study. Most notably, our study had approximately 1700 more workers, 10 additional years of follow-up and more complete mortality ascertainment. In addition, although both studies used employment information collected as part of the DIH surveillance program, we re-examined this data and augmented it with information from other sources. This revealed that the DIH information was incomplete for many workers.

Our lung cancer results are of particular interest because of continuing debate about the risk associated with silica exposure. Although the International Agency for Research on Cancer (IARC) concluded in 1997 that "crystalline silica inhaled in the form of quartz or cristobalite from occupational sources is carcinogenic to humans", they recognised that not all of the 10 least confounded studies cited in their review demonstrated excess cancer risks.[19] The weakness and inconsistencies in the evidence on which IARC relied were pointed out by Hessel *et al*, who also noted inconsistencies in exposure–response relationships.[20] In a 2006 review, Peretz *et al* concluded that the determination that silica is carcinogenic was evidence based.[21] However, their table of the 10 least confounded epidemiological studies showed no consistent statistically significant trends in lung cancer risk with cumulative crystalline silica exposure.

More recent epidemiological studies continue to yield inconsistent results. A large study of German porcelain workers showed increased silicosis mortality, but an association between crystalline silica exposure and renal or lung cancers was not found.[18] In contrast, a study of a Dutch population with potential exposure to silica in a wide range of occupations showed a statistically significant association between lung cancer risk and duration of exposure.[22] There was also an increased risk of lung cancer in workers with over 3 mg/m^3-years of silica exposure compared to those unexposed that was statistically significant in the group of subjects included in analyses to adjust for probable co-exposure to asbestos.

A key question for many years has been whether those with silicosis are at increased risk of lung cancer. A recent study of workers with silicosis in Hong Kong found that after adjustment for smoking there was no consistent exposure–response relationship between silica dust or severity of silicosis and lung cancer mortality.[23] Erren *et al* conducted a meta-analysis to determine whether exposure to silica was associated with lung cancer risks in individuals without silicosis and concluded that there were insufficient data to answer this question.[24] As our study does not include chest radiographs, it cannot directly address this issue. The strong relationship that we observed between estimated silica exposure and mortality from silicosis implies an association with non-fatal silicosis as well. Thus, if silicosis contributed to lung cancer risk in the Vermont cohort, we would have expected lung cancer mortality to also increase with exposure, but there was no evidence of this. The low prevalence of silicosis in a 1983 radiographic study of Vermont granite workers has not been accompanied by a decline in lung cancer mortality, but interpretation of this is complicated by temporal changes in smoking prevalence.

We were unable to obtain information on smoking for most workers in the cohort because of data confidentiality protections, but it is likely that the elevated SMR for lung cancer is due, at least in part, to differences between the smoking habits of the cohort and those of the reference population. Smoking prevalence was 50% among the 1457 cohort members who were interviewed between 1979 and 1985 for a pulmonary function study.[10] In contrast, the estimated smoking prevalence for white males in the USA in 1980 was 37%,[25] giving a relative prevalence in the cohort of 1.35%. This difference is consistent with the differences seen among various occupational groups in the USA.[26] Smoking prevalence reliably predicts future lung cancer mortality,[27] so if the relative prevalence of smoking among the workers remained at about 1.35% over time, the expected number of lung cancer deaths in the cohort after adjusting the reference rates for smoking would be 353, yielding a SMR of 1.02 (95% CI 0.92 to 1.14).

Another limitation of this study is the potential for errors in the exposure estimates due to inaccuracies in both the job histories and the JEM. Use of multiple sources of employment data likely reduced but did not eliminate errors in work histories, and construction of the JEM involved a number of assumptions and extrapolations. Estimation of exposure levels for quarry jobs prior to dust controls was particularly difficult because of the wide variation between measurements made near specific operations and those of general quarry air. Short-term samples obtained during drilling, jackhammering and blowing out channels indicated extremely high particle counts, but these do not reflect time-weighted daily exposures because men only spent a portion of the workday doing these jobs. It is also possible that the per cent of respirable free silica in the dust generated from these activities differed from that for other jobs. We were also concerned that our pre-1940 estimate of 0.15 mg/m^3 for channel bar operators, which was based on measurements made during the 1930s at two quarries using wet processes for this activity, was much lower than the estimate of 1.07 mg/m^3 used previously for both channel bar operators and drillers.[8]

To examine the impact of potential errors in the exposure estimates for quarry jobs, we conducted sensitivity analyses using four different modifications to the pre-1940 estimates: (1) 1.07 mg/m^3 for channel bar operators and drillers, 1.05 mg/m^3 for jackhammer operators; (2) 0.53 mg/m^3 for channel bar operators and drillers, 0.52 mg/m^3 for jackhammer operators; (3) 0.15 mg/m^3 for channel bar operators, 0.53 mg/m^3 for drillers, 0.52 mg/m^3 for jackhammer operators; and (4) 0.15 mg/m^3 for all three jobs. Corresponding changes were made to the extrapolated 1940–1949 estimates. The relationship between silicosis and cumulative exposure remained statistically significant under all four modifications, with ORs ranging from 1.06 to 1.17 per unit increase in cumulative exposure. Assigning 1.07 mg/m^3 to channel bar operators gave the poorest fit to the data, while

assigning 0.15 mg/m^3 to drillers, jackhammer operators and channel bar operators provided the best fit. The modifications had little effect on the lung cancer results, with ORs ranging from 0.98 to 1.01 per unit increase in cumulative exposure, and there were no significant exposure–response relationships.

It should be emphasised that despite the uncertainties in the exposure estimates, which are an inherent part of most epidemiological studies, we found an unequivocal, quantitative relationship between respirable free silica and mortality from silicosis. This provides evidence of the validity of the exposure estimates, making it unlikely that the absence of a relationship between silica exposure and lung cancer or kidney diseases is due to error in the exposure estimates.

Although our study was more inclusive than previous mortality studies of Vermont granite workers, 609 (8%) eligible men were excluded from the cohort because of missing data and an additional 99 were excluded from the case–control analyses because of insufficient work history information. However, most of those excluded were younger workers with short, recent exposures and hence they would not have been selected for the exposure–response analyses. Only 170 of the excluded workers were born in or before 1947, the latest birth year in the lung cancer case–control analysis, and just 11 would have been selected as controls. It is therefore unlikely that their inclusion would have substantially altered the results. There were eight lung cancer cases among all the excluded workers, six of whom were born between 1886 and 1910 and had left work before 1957, when pension records began. Available information indicated lengthy employment in the granite industry for one of these workers, but short employment for the others. One of the other two excluded cases was born in 1929 and stopped working in the granite industry at age 25, while the other was born in 1955 and began working in 1986, so both would have low cumulative exposure. The implications of excluding these eight cases are unclear, but we would not expect a substantial impact given the apparent variability in their exposures and the large number of cases in the analysis.

Despite its limitations, our study has many strengths. It is the largest and most complete cohort of Vermont granite workers studied to date. The study also had a lengthy follow-up (on average 38 years) and exhaustive investigation ensured that mortality ascertainment was as complete as possible. Our study encompassed 100 years of employment in the Vermont granite industry, and the changes in work conditions occurring over this time ensured ample variation in exposure, which facilitates detection of exposure–response relationships. Finally, we used multiple sources of information to estimate exposure levels for specific jobs and reconstruct work histories.

CONCLUSIONS

This study found that silica exposure was related to mortality from silicosis and other non-malignant respiratory disease. There was no evidence of an association between silica exposure and lung cancer mortality, indicating that the increased mortality from this disease among cohort members is most likely attributable to cigarette smoking or other exposures unrelated to employment in the Vermont granite industry. The study also found no evidence of an increased risk of mortality from malignant or non-malignant kidney disease associated with employment in this industry.

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