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Assessment of silicosis risk for occupational exposure to crystalline silica

by Faye L Rice, MPH,[1] Leslie T Stayner, PhD[1]

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Epidemiologic studies of workers exposed to silica were reviewed to identify data on airborne concentrations of quartz that are not associated with an increased risk of silicosis, the lowest concentrations associated with silicosis, and studies that used statistical models to quantitate the risk of silicosis as a function of silica exposure. The no observed adverse effect levels varied from 7 to 100 $\mu g \cdot m^{-3}$, and the lowest observed adverse effect levels ranged from 8 to 252 $\mu g \cdot m^{-3}$ in five different cohorts. Studies using quantitative exposure-response models revealed a wide difference in the cumulative risk estimates for silicosis. The differences in the risk estimates and the no observed and lowest observed effect levels may have been the result of errors in exposure estimates, physicochemical characteristics of silica and quartz content of the dust, cohort differences, and reader variability. Further research is needed to define the dose-response relationship between silica exposure and silicosis.

Key terms epidemiology, LOAEL, lowest observed adverse effect level, NOAEL, no observed adverse effect level, quartz, risk assessment.

Silica is the designation given to minerals that contain silicon dioxide (1). It occurs naturally in crystalline and amorphous forms. The most common crystalline forms of silica encountered in industry (quartz, tridymite, and cristobalite) have been associated with the development of silicosis in workers (2, 3). However, quartz is by far the most common natural form of silica (1, 3).

Approximately 1 600 000 workers were exposed in the United States to respirable crystalline silica dust in mining and nonmining industries in 1986 (4, 5).

Based on information from death certificates, the reported number of deaths involving silicosis in the United States has decreased gradually from more than 1000 in 1970 to fewer than 400 in 1987 (4). The New Jersey Department of Health reported 121 confirmed cases of silicosis for 1979—1987 (6), and there were 562 cases detected in Ohio in 1989—1994 (7), but the true number of new cases is unknown because of underreporting by employers (8) or misdiagnosis by physicians on death certificates.

Many epidemiologic studies have addressed the relationship between occupational exposure to crystalline silica and silicosis, but few have provided information for quantifying this relationship. Such studies are needed to estimate risks from occupational exposures to crystalline silica and to evaluate the adequacy of current occupational health standards.

The current permissible exposure limit (PEL) set by the Occupational Safety and Health Administration in the United States for respirable crystalline silica (quartz) is 10 $mg \cdot m^{-3}/(\%SiO_2+2)$ for general industry [29 CFR 1910.1000 (CFR = Code of Federal Regulations; see reference 9)]. The current recommended exposure limit for respirable crystalline silica (all types) set by the National Institute for Occupational Safety and Health (NIOSH) is 0.05 $mg \cdot m^{-3}$ (2, 10).

Identifying an exposure limit that will prevent silicosis may also reduce the risk of lung cancer among silica-exposed workers. In 1987, the International Agency for Research on Cancer (IARC) (1) concluded that there is "sufficient evidence" for the carcinogenicity of crystalline silica in experimental animals but only "limited evidence" for the carcinogenicity of crystalline silica in humans. Subsequently, Simonato & Saracci (11) and Pairon et al (12) have reviewed the epidemiologic studies on the relationship of lung cancer to silica dust and concluded that the risk of lung cancer appears to be limited primarily to workers who develop silicosis. One study that controlled for environmental exposure concentrations reported a direct relationship between silica exposure and lung cancer independent of silicosis (13). The hypothesis that the risk of lung cancer is limited to individuals with silicosis is still debatable (14).

Methods

Study objectives. Our review was restricted to epidemiologic studies that have provided quantitative information about the relationship between silica exposure and the risk of silicosis. Two objectives of this review were to identify airborne concentrations of quartz that have not been associated with an increased risk of silicosis [ie, the no observed adverse effect level (NOAEL)] and to identify the lowest concentrations associated with silicosis [ie, the lowest observed adverse effect level (LOAEL)]. The LOAEL and NOAEL values were not determined on the basis of statistical significance, but rather on the basis of biologically meaningful evi-

1 National Institute for Occupational Safety and Health, Education and Information Division, Cincinnati, Ohio, United States.

Reprint requests to: Ms Faye L Rice, National Institute for Occupational Safety and Health, Education and Information Division, 4676 Columbia Parkway, M/S C-15, Cincinnati, OH 45226—1998, USA.

Table 1. Summary of six epidemiologic studies of silicosis with environmental data. (ILO = International Labour Office)

Reference	Study design*	Study population	Adverse health effect	Silica (quartz) content of dust (%)
Davis et al (20)	Proportionate mortality study	Vermont (US) granite workers who died between 1952 and 1978 and were employed ≥ 1 years (N = 969)	Silicosis mortality (28 deaths)	9—14 (years 1965—1966)
Hnizdo & Sluis-Cremer (15)	Retrospective cohort study	South African underground gold miners who started working after 1938, worked ≥ 10 years, and were followed until 1991 (N = 2235)	Silicosis (ILO ≥ 1/1, 313 cases)	30
McDonald & Oakes (19)	Retrospective cohort mortality study	South Dakota (US) underground gold miners employed ≥ 21 years (N = 1321)	Pneumoconiosis mortality	39 (settled dust samples)
McDonald & Oakes (19)	Cross-sectional study	Underground gypsum miners employed ≥ 20 years in the United Kingdom (N = 64)	Silicosis (ILO ≥ 1/0, number of cases for ≥ 20 years was not reported, total silicosis cases = 16)	Not reported
Muir et al (16, 17, 21, 22)	Retrospective cohort study	Ontario (Canada) gold and uranium miners who started between 1940 and 1959 and were followed to 1982 or to the end of their dust exposure, whichever came first (N = 2109)	Silicosis (ILO ≥ 1/1, 32 cases)	6.0 for gold mines and 8.4 for uranium mines
Rice et al (18)	Case-referent study	North Carolina (US) dusty trades workers diagnosed with silicosis between 1935 and 1980	Silicosis; radiographic classification not reported for 216 silicosis cases; 672 referents consisted of disease-free dusty trades workers	1—50

dence that the risk for silicosis was above that posed by some background concentrations of silica. The studies that provided information about effect levels (NOAEL and LOAEL) analyzed various categories of silica exposure. When the authors defined these categories as a range of exposures, the midpoint of the range was used for estimating the effect levels. A third objective of this paper was to review studies that present statistical models of the quantitative relationship between silica exposure and the risk of silicosis.

Descriptions of reviewed studies. Table 1 describes the populations and designs of six epidemiologic studies that reported evidence of an exposure-response relationship for silicosis. The study outcomes varied greatly. In four studies concerning South African gold miners, Ontario hardrock miners, North Carolina dusty trades workers, and British gypsum miners, silicosis was defined on the basis of chest X-ray classification (15—19). These studies used different classification systems for diagnosing silicosis from X rays. The other two studies of Vermont granite workers and South Dakota gold miners were based on the diagnosis of silicosis or pneumoconiosis on death certificates (19, 20).

The six studies also differed in the quality of available exposure information. Several studies presented results in millions of particles per cubic foot (mppcf) or as total dust exposure. Exposure estimates were converted by the authors to micrograms of respirable silica per cubic meter ($\mu g \cdot m^{-3}$). These conversions were made using the conversion factors and percentages of silica in published studies. When the findings were expressed as cumulative exposures, the results were converted to the NOAEL and LOAEL values corresponding to 45 years of occupational exposure (a maximum worklife assuming employment from ages 20 to 65 years).

Finally, these studies differed in the statistical methods used to examine the relationship between silica exposure and silicosis. Several studies analyzed their results through categories of exposures that could be used to determine the NOAEL or LOAEL values. Some of the studies (15—17, 21, 22) used statistical models to describe the relationship between silica exposure and the risk of silicosis. These models could not be used to determine the NOAEL since they produce risk estimates at any nonzero concentration of silica exposure. An exception was the study by McDonald & Oakes (19), which examined models with and without a "threshold" parameter. These models were used to identify a NOAEL.

Table 2. Summary of the no observed and lowest observed adverse effect levels (NOAEL and LOAEL, respectively) in six studies of silicosis. ($\mu g \cdot m^{-3}$ = micrograms of respirable silica per cubic meter, mppcf = millions of particles per cubic foot)

Reference	NOAEL		LOAEL	
	$\mu g \cdot m^{-3}$	mppcf	$\mu g \cdot m^{-3}$	mppcf
Davis et al (20)	67.5	9	.	.
Hnizdo & Sluis-Cremer (15)	7	.	20	.
McDonald & Oakes (19)				
Gold miners	.	.	8	0.5[a]
Gypsum miners	35[a]	.	49[a]	.
Muir et al (16, 17, 21)	..[b]	..[b]	..[b]	..[b]
Rice et al (18)	80—100	1	200—252	2.5

[a] Derived from a subcohort of workers with > 20 years of employment; does not reflect a 45-year lifetime of work.
[b] Effect levels could not be derived from this study because the results were only presented in terms of a dose-response model that implied risk at any level of exposure.

Results and discussion

Identification of adverse effect levels. Table 2 lists the NOAEL and LOAEL for each of the six studies. The estimated NOAEL values ranged from 7 to 100 $\mu g \cdot m^{-3}$ and the LOAEL values were between 8 and 252 $\mu g \cdot m^{-3}$.

In the cohort of Vermont granite workers (20), only 1 of the 28 silicosis deaths occurred among the men who were hired after dust controls were implemented in the granite industry. However,

this death was discounted because it was believed to have been caused by emphysema — a diagnosis based on an X-ray reading done two months before the worker's death. During that postcontrol period, the highest concentration of granite dust was 9 mppcf (67.5 μg · m^{-3}); hence 67.5 μg · m^{-3} was chosen as the NOAEL.

A lifetable analysis of silicosis cases among South African underground gold miners (15) was used to derive a NOAEL of 7 μg · m^{-3} and a LOAEL of 20 μg · m^{-3} for a 45-year worklife. No cases of silicosis were observed among 2218 gold miners with cumulative dust exposures of 1 mg · m^{-3}-years (the midpoint of the cumulative dust exposure category), which is equal to 7 μg · m^{-3} for 45 years [1 × 0.3 (for 30% silica)/45 years]. Nine cases of silicosis were observed among 2014 miners in the exposure category of 3 mg · m^{-3}-years (the midpoint of the cumulative dust exposure category), which is equal to 20 μg · m^{-3} for 45 years (3 × 0.3/45).

McDonald & Oakes (19) analyzed two cohorts, underground South Dakota (United States) gold miners and British underground gypsum miners. In the mortality study of 1321 gold miners in the United States, 8 μg · m^{-3} was the lowest concentration at which deaths were observed. However, a NOAEL could not be identified from either the stratified analysis or the model. The study of 64 British gypsum miners used radiographic data from a cross-sectional study done in 1976 and 1977. The NOAEL for small radiographic opacities (≥ 1/0) was 35 μg · m^{-3} on the basis of the threshold model and 33 to 35 μg · m^{-3} on the basis of the stratified analyses of the prevalences in different mines. The LOAEL based on the stratified analysis was 49 μg · m^{-3}. A NOAEL or LOAEL for a 45-year worklife could not be calculated because the results were reported only for men who had worked for 20 or more years.

For workers in the North Carolina dusty trades (18), the NOAEL was 90 to 113 μg · m^{-3} and the LOAEL for silicosis was 225 to 283 μg · m^{-3} for a 40-year worklife (based on the silicosis odds ratios calculated by conditional logistic regression). Ranges exist for the NOAEL and LOAEL values because two methods were used to convert count data (mppcf) to mass concentration units (μg · m^{-3}). When mass was estimated for size fractions, the NOAEL was 1 mppcf (113 μg · m^{-3}). The LOAEL for silicosis using this conversion method was 2.5 mppcf (283 μg · m^{-3}). The second approach used a conversion factor translating cyclone data to count estimates. The count value was multiplied by 0.09 to arrive at mass in milligrams per cubic meter. When this method is used, the NOAEL is 1 mppcf (90 μg · m^{-3}) for a 40-year worklife. The LOAEL is 2.5 mppcf (225 μg · m^{-3}) over a 40-year worklife. For a 45-year worklife, the NOAEL is 80 to 100 μg · m^{-3} (90 × 0.889; 113 × 0.889), and the LOAEL is 200 to 252 μg · m^{-3} (225 × 0.889; 283 × 0.889). However, the NOAEL and LOAEL identified from this study may have been affected by errors in the classification of the silicosis cases. A review of the X-rays found that 104 of the 370 cases categorized as silicosis in this study were actually category 0 (23). Concern also existed that the use of cumulative exposure in this and other studies may ignore differences in risk resulting from different dose-rate patterns. In a reanalysis of the dusty trades cohort data, Checkoway & Rice (24) showed that peak exposures may predict silicosis risk better than cumulative exposures.

Exposure-response models. Only two studies (15, 17, 21, 22) used statistical models to assess the relationship between cumulative silica exposure and the risk of silicosis. Figure 1 shows the cumulative risk of silicosis with a five-year lag for the cohort of Ontario hardrock miners by each of the five readers used in the study by Muir et al (17, 22). This study used a Weibull statistical model (23, 17), which assumes some risk for any exposure. With this model, the current NIOSH recommended exposure limit (REL) of 50 μg · m^{-3} for a 45-year worklife would correspond with a cumulative exposure of 2.0 mg · m^{-3}-years [50 μg · m^{-3} × [45 minus the five-year lag)], and the risk at the NIOSH REL would range from 0.0009 for reader 5 to 0.0062 for reader 2. This nearly sevenfold difference in risk estimates reflects the great uncertainty related to different diagnoses made by individual readers.

The study of South African underground gold miners (15) used the category of ≥ 1/1 of the International Labour Office to define silicosis. This study used an accelerated failure time model, which also assumes some risk for any exposure. Fourteen percent of this cohort (313 cases) met the definition for silicosis compared with 1.5% of the Canadian cohort that included gold miners (16, 17, 22). The silica content of the respirable dust in South African gold mines (after heat and acid treatment) is about 30% (15, 25). In the hardrock mines studied by Muir et al (17), the silica content of the respirable dust was 13 to 17% in the early years of the study when the concentrations were highest. Figure 2 shows that 2.25 mg · m^{-3}-years of exposure (which is equivalent to the NIOSH REL of 50 μg · m^{-3} for a 45-year worklife), the cumulative risk was 0.127. The risk estimates for the South African miners were

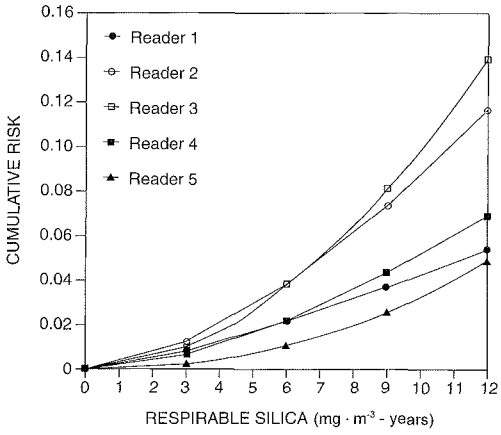

Figure 1. Estimates of silicosis risk based on the Ontario study of hardrock miners (adapted from reference 17).

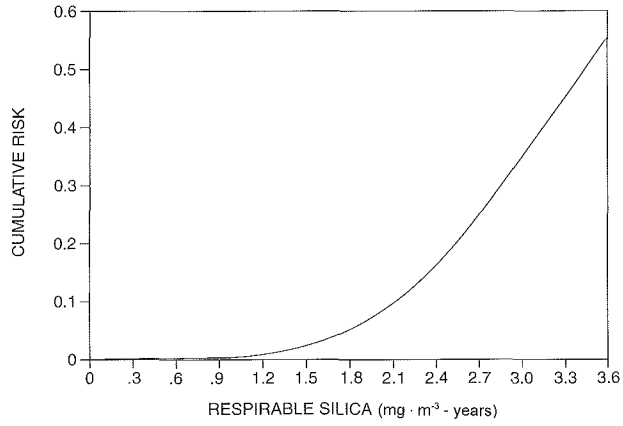

Figure 2. Estimates of silicosis risk based on the South African study of underground gold miners (adapted from reference 15).

clearly higher than those for the Canadian hardrock miners at higher exposure concentrations. Some of the risk differences may have been due to physicochemical differences between the silica particulates (Fubini et al, this volume) and the fact that the Canadian investigators only evaluated currently employed miners while the South African researchers included active and retired miners.

Concluding remarks

The epidemiologic studies of silicosis indicate that the NOAEL varies from 7 to 100 $\mu g \cdot m^{-3}$ and the LOAEL ranges from 8 to 252 $\mu g \cdot m^{-3}$. These wide ranges probably reflect differences in (i) the surface properties and particle sizes of crystalline silica from different mines, (ii) the definition and radiological classification of silicosis cases, (iii) the methods used to estimate exposures and risks, (iv) the background concentrations of airborne crystalline silica, (v) the sample sizes, and (vi) the methods used to convert particle counts to mass concentration units.

The two studies that used quantitative exposure-response models revealed a difference in the cumulative risk estimates for silicosis. For South African gold miners, the cumulative risk estimate for silicosis (0.127) was at least 20 times higher than that for the Ontario hardrock miners (0.0009 to 0.0062). This considerable difference may have resulted from (i) differences in the definition of radiographic silicosis used in the two studies, (ii) possible errors in exposure estimates, (iii) possible underestimation of the quartz content of the dust in the Canadian study (26), (iv) inhalation of aluminum dust as a protective measure by many of the Canadian miners (16), (v) reader variability, or (vi) the use of cumulative exposures to estimate risk. In addition, Muir (27) has hypothesized that exposure to higher concentrations of nonquartz dusts may have reduced the risk of silicosis observed in his study population; this hypothesis may also explain the discrepancy between his results and those of Hnizdo et al (27).

The results from our review raise concerns about the adequacy of current silica standards for preventing silicosis in the United States. However, the large variability between studies reflects a high degree of uncertainty and makes it difficult to draw firm conclusions about safe exposure concentrations. Further research is therefore needed to define the dose-response relationship between silica exposure and silicosis.

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