Table 2.1. Cohort studies of silica and lung cancer

Reference, location, name of study	Cohort description	Exposure assessment	Organ site (ICD code)	Exposure categories	No. of cases/ deaths	Relative risk (95% CI)*	Adjustment for potential confounders	Comments
Diatomaceous earth								
Checkoway *et al*. (1997) United States	Further analysis of Checkoway *et al*. (1993) with 7 more years of follow up and quantitative silica exposures. 2342 WM workers exposed to crystalline silica, predominantly cristobalite, in a diatomaceous earth mining and processing facility in California. Study period 1942–1994.	Quantitative estimates of cumulative respirable silica dust exposure; mean (sd) = 2.16 (3.51) mg-yr/m^3	Lung	**Cumulative silica dust exposure:**		RR	Age, calendar year, duration of follow-up, ethnicity and with and without asbestos	Borderline significant test for trend (1.05: 0.99 – 1.14) and (1.06: 1.01 – 1.11) for unlagged exposure per mg-yr/m^3
				Unadjusted for asbestos				
				< 1.9 (mg-yr/m^3)	17	1.00		
				1.9–< 4.0	14	1.07 (0.53 – 2.18)		
				4.0–< 7.4	7	0.55 (0.23 – 1.32)		
				7.4–< 18.3	15	1.19 (0.59 – 2.41)		
				≥ 18.3	24	2.11 (1.07 – 4.11)		
				Continuous	77	1.06 (1.01 – 1.11)		
				Adjusted for asbestos				
				Continuous	77	1.06 (1.01 – 1.11)		
Rice *et al*. (2001) United States	Further analysis of Checkoway *et al*. (1996) including risk assessment modeling. 2 342 WM workers exposed to crystalline silica, predominantly cristobalite, in a diatomaceous earth mining and processing facility in California. Study period 1942 – 1994.	Quantitative estimates of respirable cumulative respirable silica dust exposure (mg-yr/m^3)	Lung	**Cumulative silica dust exposure:**		RR	Time since first observation, calendar time, age, and Hispanic ethnicity	Results shown for best fitting model. Respirable crystalline silica dust was a significant predictor ($P < 0.05$) in a variety of models except additive excess rate $P = 0.09$).
				Lagged 10 years				
				Linear relative rate				
				0 (mg-yr/m^3)		1.0		
				7.31 (mean cumulative respirable dust exposure)		1.64 (trend $P < 0.006$)		
Ore mining								
Hnizdo & Sluis-Cremer (1991) South Africa	2 209 gold miners (WM); mortality follow-up 1968–1986; internal proportional hazards analysis	Quantitative estimates of cumulative respirable surface area years.	Lung	**Cumulative mixed dust exposure:**		RR	Smoking	No arsenic present in the dust. Uranium was mined in some gold mines. Radon levels 0.1 – 3.0 WL
				≤ 15	4	1.0		
				16–30	30	1.54 (0.6–4.3)		
				31–40	20	2.07 (0.7–6.0)		
				≥ 41	23	2.92 (1.02–8.4)		
				Continuous	77	1.02 (1.01–1.04)		

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Steenland & Brown (1995) United States	Further follow-up of cohort studied by Brown *et al*. (1986). 3 328 South Dakota gold WM miners who worked underground for ≥ 1 year 1940–1965 followed-up to 1990. National and county referent population.	Quantitative estimates of cumulative respirable silica dust exposure (mppcf-days)	Lung	**Cumulative silica dust exposures:**		SMR	No adjustment for low exposures to radon, arsenic, and asbestos	Tuberculosis and silicosis were significantly increased (SMR = 3.44 and 2.61) and exhibited clear exposure-response trends. Cohort smoked slightly less than national figures.
				< 8000 (mppcf-days)	44	1.17 (0.84 – 1.55)		
				8000–32 000	35	1.01 (0.71 – 1.41)		
				32 000–48 000	8	0.97 (0.41 – 1.85)		
				≥ 48 000	28	1.31 (0.87 – 1.89)		
Carta *et al*. (2001) Italy	724 Sardinian miners and quarrymen with radiologically-defined silicosis between 1964 and 1970. Vital status to 1997, 98% traced, cause of death for 100%	Quantitative estimates of respirable mixed dust exposure derived from personal measurements; mean = 7.3–8.6 g-hr/m^3 [~4 mg-yr/m^3]. Radon exposures derived similarly	Lung	**Cumulative silica dust exposures:** ***No latency***		SMR	No adjustment for radon exposures	More evidence of a trend in data with 20-year latency but still NS trend. Small study
				<5.0 (g-hr/m^3)	11	1.55 (0.59 – 2.57)		
				5.1–10.0	13	1.25 (0.73 – 2.15)		
				>10.0	10	1.35 (0.73 – 2.51) (trend NS)		
Chen *et al*. (2006) China	7 837 workers registered in the employment records in 4 Chinese tin mines between 1972 and 1974 followed-up through 1994. Cause of death ascertained for 97% of the 1 094 deaths	Quantitative estimates of cumulative mixed total dust; mean (sd) = 64 (64) mg-yr/m^3	Lung	**Cumulative mixed total dust exposure:** *All workers*		SMR		Unresolved confounding from arsenic
				< 0.1 (mg-yr/m^3)	22	1.29		
				0.1 – 29.99	20	2.65		
				30 – 69.99	25	2.66		
				≥ 70	71	3.33 (Lower 95%CI > 1.0 for 3 higher exposure groups)		

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Stone Quarries								
Attfield and Costello (2004) United States	5 414 Vermont granite quarry and shed workers employed 1950 – 82 and X-rayed at least once in a medical surveillance programme. Participation reported to be 98%. National referent rates. Extended follow-up of Costello & Graham (1988), and including quantitative estimates of silica exposure	Quantitative estimates of cumulative respirable silica exposure based on multiple environmental surveys and work histories; mean = 2.1 mg-yr/m^3	Lung	**Cumulative silica dust exposures:** ***Lagged 15 years*** 0 (mg-y/m^3) - 0.25 - 0.5 - 1.0 – 1.5 – 2.0 – 3.0 – 6.0 –	 35 18 32 22 17 27 23 27	SRR 1.00 1.24 2.14 1.93 1.68 2.60 1.90 1.18 (trend *P* = 0.003 without highest exposure group; *P* = 0.46 with highest exposure group)		All models (Poisson lagged and unlagged, internal and external rates, and un- or log-transformed) without ultimate exposure group showed strong statistical significance, but, except in one case, not when highest exposure group included
Ulm *et al.*(2004) Germany	440 stone and quarry workers compensated for silicosis between 1988 and 2000. Silicosis defined by ILO cateogory 1/1 or greater. Lung function had to be reduced for compensation to be awarded. Mortality followed up to 2001	Quantitative estimates of a variety of silica exposure indices based on measurement data and expert opinion. Median cumulative silica exposure = 19.8 mg-yr/m^3.	Lung	Modelled using cumulative, average, and peak exposures.	16	No relationships detected	Smoking	Very small study and restricted exposure range because of focus on silicotics

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Sand and gravel								
Steenland and Sanderson (2001) United States	4 626 industrial sand workers from 18plants with ≥ 1 week employment from 1960 – 1988 with follow-up to 1996	Quantitative estimates of cumulative respirable silica exposure (mg-yr/m^3) based on company work histories and industrial hygiene data	Lung	**Cumulative silica dust exposure:** ***Lagged 15 years*** > 0 – 0.10 (mg-yr/m^3) > 0.10 – 0.51 > 0.51 – 1.28 > 1.28	 17 21 20 16	SRR 1.00 0.78 1.51 1.57 (trend *P* = 0.07		9 yr mean duration of employment. Reported that smoking might account for 10 – 20% of the lung cancer excess
Brown & Rushton (2005) United Kingdom	2 703 silica sand industry workers with ≥ 1 yr employment at one of seven silica sand quarries 1950 – 1986 followed up to 2001. 764 deaths	Quantitative estimates of cumulative respirable silica exposure based on company work histories and industrial hygiene data. Exposures before 1978 back-extrapolated to 1950; geometric mean (sd) = 0.31 (5) mg-yr/m^3	Lung	**Cumulative silica dust exposure:** < 0.13 (mg-yr/m^3) 0.13–<0.40 0.40–<1.00 ≥1.00	 20 21 22 19	RR 1.0 1.24 (0.66–2.34) 1.42 (0.76–2.67) 0.88 (0.45–1.73)	Age. No adjustment for potential exposure to PAHs at one quarry.	Large lung cancer deficit at second largest quarry. Somewhat smaller RRs in middle two exposure groups when time from first employment, employment status, year of starting employment, and quarry in model. Low silica exposures compared to other studies

* specify *p*-value if no confidence interval indicated
• Include preferably the most informative/up-to-date study. Previous publications may be briefly mentioned in the corresponding text, where more details on cohort description and exposure assessment can be given.
• Cohort characteristics: size (men, women) – inclusion criteria, employment period if occupational cohort– age range – mortality/incidence, duration and completeness of follow-up.
• Exposure assessment: mailed questionnaire – structured interview – job–exposure matrix – biomarker.
• ICD codes to be given only for some cancers, incl. upper aerodigestive tract, colorectal, uro-genitary, leukaemia, lymphoma. ICD-9, unless otherwise specified.
• RR: consider the most valid point estimate (e.g. adjusted)
• Comments, if relevant for the interpretation of the study, such as: type of reference used for SMR calculation (national/local rates) – stratified results/interaction

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