ORIGINAL ARTICLE

Quantitative relations between exposure to respirable quartz and risk of silicosis

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Occup Environ Med 2003;**60**:159–164

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Accepted 5 June 2002

Aims: To reanalyse exposure-response data from a Scottish colliery to gain a more detailed knowledge of the relations between exposure to quartz and risks of silicosis in coal miners, and hence inform the debate on an appropriate occupational standard for respirable quartz.
Methods: Detailed data on working times at different quartz concentrations were combined to produce exposure profiles for miners who had provided a full chest radiograph at a follow up survey. Logistic regression methods were used to model profusion of radiographic abnormalities category 2/1+, and a general exposure index was used to compare different quartz exposure measures in these models.
Results: Results in 371 men aged 50–74 indicated that cumulative quartz exposure at higher concentrations resulted in proportionally greater risks of abnormalities. One g.h.m^{-3} of cumulative exposure at quartz concentrations greater than 2 mg.m^{-3} was estimated to have equivalent risks to 3 g.h.m^{-3} at lower concentrations. The timing of exposure relative to follow up appeared less important, although the study had limited power to compare different lag periods between exposure and effect.
Conclusions: Quantification of the risks of silicosis should take account of variations in quartz exposure intensity, particularly for exposure to concentrations of greater than 1 or 2 mg.m^{-3}, even if exposure is for relatively short periods. The risks of silicosis over a working lifetime can rise dramatically with even brief exposure to such high quartz concentrations. Risk estimates are given, to inform choice of control limits.

The British coal industry's Pneumoconiosis Field Research (PFR) was an extensive programme, over more than 30 years, of research into coal workers' lung disease. In general, early reports established relations with exposures to respirable coalmine dust, but did not show any consistent evidence that the quartz component of the dust was an important determinant of risk.[1–3]

Coal workers' pneumoconiosis (CWP) was historically relatively rare at Scottish pits in comparison with pits in other areas of Britain. However, in one Scottish colliery, exposure to unusually high levels of quartz occurred in the 1970s, due to the incursion of coal getting machinery into the sandstone seam roof and floor. Rapid radiological changes were observed in some men within several years. Access to the detailed exposure data from the PFR showed a clear relation between this progression and exposure to quartz.[4 5] The colliery closed in 1981.

In 1990–91, a follow up study of these miners was carried out.[6 7] Logistic regression analyses of the relation between cumulative exposure to dust and the prevalence of radiographic abnormality at follow up showed that the association was strongest for exposures during the period 1970 to 1978, followed by the period from 1964 to 1970, and was stronger in relation to estimated quartz exposure than to the non-quartz component. The association with quartz exposures during the 1970s was most marked for the prevalence of more serious abnormalities. A miner aged 60 at follow up, with 15 years exposure to quartz at an average airborne concentration of 0.3 mg.m^{-3}, was predicted to have a risk of 22% of showing the degree of abnormality usually required for eligibility for workers' compensation.

In some fitted regression models, a significant positive effect of age remained after adjusting for quartz exposure.[7] This was believed to be acting as a surrogate for some unmeasured exposure effect. The logistic regression analysis was based on a simple dependence on estimated cumulative quartz exposure. Given the magnitude of the risks predicted, particularly in relation to current occupational exposure limits for quartz, it was necessary to widen the analysis of exposure-response relations to include alternative and, possibly, more realistic dose measures. Dose measures that took account of factors affecting the deposition, clearance, and potency of quartz particles in the lung were envisaged to be more influential in causing lung damage during periods of high exposure intensity, which was a feature of some occupations at this colliery in the 1970s.

We report here on further detailed statistical analyses of these data, designed to explore the shape of the relation between exposure to respirable silica and risk of silicosis, by considering a range of exposure metrics other than simple cumulative exposure. The results should inform the debate on a level that is appropriate as an occupational standard for respirable quartz.

METHODS

The follow up procedures, and the extensive exposure data already available from the PFR studies, have been described in detail elsewhere.[6 7] Briefly, over 1400 men worked at this colliery and attended at least one of the routine medical surveys that took place in 1970, 1974, and 1978. Of these, almost 400 were known to be deceased, and over 100 untraced or abroad by the time of the follow up study. The remaining 921 survivors were traced and invited to attend a follow up health survey in the winter of 1990–91. In total 547 men attended the survey and provided full sized posterior-anterior chest radiographs together with a smoking history questionnaire.

Radiographs were read by three physicians according to the ILO (1980) scheme.[8] This is a scheme whereby standardised

Abbreviations: CWP, coal workers' pneumoconiosis; GEI, general exposure index; ISP, intersurvey period; OG, occupational group; PFR, Pneumoconiosis Field Research

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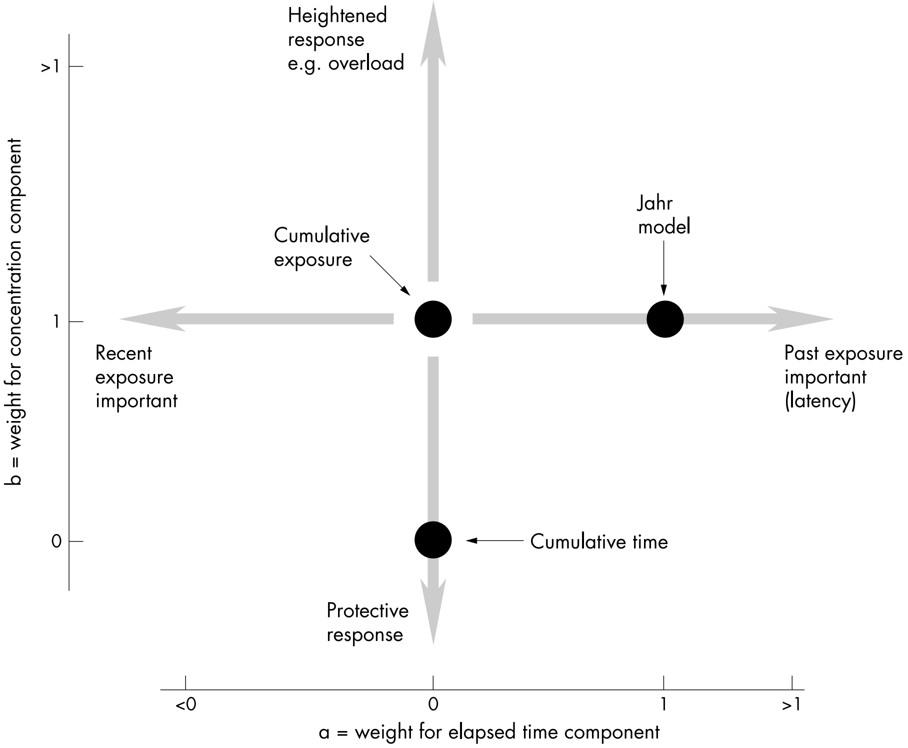

Figure 1 Interpretation of the parameters *a* and *b* within the general exposure index. Adapted from fig 1 in Seixas *et al.*[10]

descriptions are recorded of the visual appearance on a chest radiograph of the small opaque markings typical of pneumoconiotic lesions in the lung. Profusion of these opacities is described in terms of their similarity to standard films showing typical profusions described as 0 (normal) and 1, 2, and 3 in increasing severity. The scale allows minor gradations: an assigned category 2/1 indicates that the film was classified as being most like the category 2 standard, but that category 1 was also considered. Category 2/1 is usually treated as the minimum level of abnormality for eligibility in workers' compensation schemes for pneumoconiosis. The three independent readings were summarised by the median profusion of small opacities.

The PFR had accumulated over 30 years worth of dust concentration and composition measurements at this and other research collieries. These had been classified by occupational groups (OGs), where an OG represented an occupation covering a group of miners performing similar work under similar working conditions. Average respirable dust concentrations within OGs were available from 1954 to late 1980. Compositional analysis of the dust samples had been carried out using infrared spectrophotometry, although dust samples from prior to 1965, when a standard thermal precipitator had been used to count dust particles, had been analysed later by interference microscopy. For the calculation of individual workers' exposures, records of number of hours worked in each OG had been extracted from the colliery payroll system and from interviews. Times within OGs prior to October 1974 were available, grouped into intersurvey period (ISP) (the approximate five year period between medical surveys in 1954, 1958, 1964, 1970, 1974, and 1978). Later times were available by quarter year within OGs. Times worked were extracted and combined with concentrations to construct an exposure profile for each individual, consisting of a series of exposure history lines, each representing a quarter year within an occupational group (1974–81), or an occupational group within ISP (1954–74), with start and end dates, mean respirable dust and quartz concentrations, and time worked. Each mean concentration was based on many daily samples, with higher numbers of samples in the dustier OGs.

Earlier analyses[7] had been in terms of cumulative exposure, without regard to varying levels of intensity (concentration). Alternative indices of exposure can be constructed,[9–11] which assign different weightings to a particular component of exposure, depending on its intensity and the time elapsed since it was experienced (residence time). We constructed a number of alternative quartz exposure indices within the framework of a general exposure index (GEI), with weighting parameters that moderated the influence of lung residence time (a) and concentration (b) of exposures, as follows:

$$GEI(a,b) = \sum_i \sum_j w_i^a C_{ij}^b T_{ij} \qquad (1)$$

where C_{ij} is the mean quartz concentration for OG j during period i, T_{ij} the corresponding number of hours worked, and w_i the time from period i to follow up survey. Times since exposure, w_i, were calculated from midway between the start and end date of each exposure period.

The exposure model in (1) does not attempt to capture all the subtleties that might be built into a dynamic model of deposition and clearance for the human lung, but it is capable of mimicking many of the principal behaviours that such a model might exhibit. The different exposures that can be created by varying the combinations of parameters a and b on a two way grid can allow for differential response with intensity of exposure and with length of residence time. Figure 1 shows some of the variants possible. For example, GEI(a=0, b=1) corresponds to simple cumulative exposure while GEI(a=1, b=1) corresponds to the model proposed by Jahr,[9] which assumes no clearance of deposited dust and that the potency of the deposited dust persists at its initial strength for the whole of the residence time. Further variants can model thresholds in concentration or latency periods for disease development.

Table 1 Distribution of hours worked by quartz concentration, % quartz, and dust concentration

	Profusion category						All	
	0 (n=389)		1 (n=111)		2+ (n=47)			
	Mean	%	Mean	%	Mean	%	Mean	%
Exposure history time								
Pre-1954	9.58		14.69		12.00		10.83	
Post-1954	4.36		4.46		5.02		4.44	
Attendance record time (post-1954)	25.76	100	30.94	100	34.61	100	27.57	100
By quartz conc.								
0–0.01	5.15	20	2.80	9.0	2.37	6.8	4.43	16
0.01–0.1	14.51	56	17.84	58	18.68	54	15.55	56
0.1–0.3	3.60	14	5.95	19	8.07	23	4.46	16
0.3–1.0	2.37	9.2	4.08	13	4.63	13	2.91	11
>1.0	0.13	0.5	0.27	0.9	0.87	2.5	0.22	0.8
By % quartz								
0–5	16.66	65	17.34	56	18.76	54	16.98	62
5–10	5.49	21	8.55	28	9.47	27	6.45	23
10–15	2.67	10	3.33	11	3.28	9.5	2.86	10
15–20	0.61	2.4	0.93	3.0	1.51	4.4	0.75	2.7
>20	0.33	1.3	0.78	2.5	1.60	4.6	0.53	1.9
By dust conc. (mg.m^{-3})								
0–1	12.51	49	11.36	37	10.92	32	12.14	44
1–2	7.65	30	9.47	31	9.12	26	8.15	30
2–3	3.52	14	5.90	19	7.40	21	4.34	16
3–5	1.86	7.2	3.58	12	5.83	17	2.55	9.3
>5	0.22	0.8	0.64	2.1	1.34	3.9	0.40	1.4
Missing concentrations	0.24		0.27		0.40		0.26	

Results expressed as the mean numbers of thousand hours per subject within each profusion category.

GEIs were calculated for quartz exposure after 1954 and adjusted for exposure due to working time collected by exposure history questionnaire (which lacked the detail to be incorporated directly).

The risk of showing radiographic abnormalities of category 2/1 or higher (2/1+) was analysed in relation to quartz exposure using logistic regressions.[12] Data were from 371 men aged 50–74 at follow up, including 35 with opacities of category 2/1+. Some analyses used polychotomous logistic regression models,[13] essentially simultaneous regressions for risks of category 2/1+ and the less severe stage 1/0+, parallel on the logistic scale. The improvement in the fit for each exposure index was compared by observing the changes in the model deviance (analogous to the sum of squares for fitted terms in simple least squares regression). Models were fitted using Genstat for Windows.[14]

RESULTS

Table 1 summarises the patterns of exposure data available for the 547 men who attended the follow up survey. The table provides a breakdown of the number of hours worked at different quartz, dust, and percent quartz concentrations separately for miners classified into profusion categories 0, 1, and 2+ at follow-up. On average the miners in this study group spent almost 8000 hours at quartz concentrations greater than 0.1 mg.m^{-3}. Category 2+ miners were exposed to higher levels of quartz, dust, and per cent quartz. On average miners spent 11 000 hours working in this and other collieries prior to the start of dust sampling at this colliery.

Table 2 shows the results of fitting simple logistic regression models to men aged 50–74 at follow up, with cumulative dust and quartz exposures covering different periods. The 95% confidence interval for the odds ratio was furthest from 1.0 (and the contribution therefore most statistically significant) for the quartz exposures accumulated after 1964; with this variable in the model, there was no significant model improvement from earlier exposures, from time spent in uncharacterised conditions before 1954, from age, or from smoking habits. This was consistent with earlier analyses.[7] The next stage, of modelling with GEIs, therefore omitted consideration of all variables except quartz exposures from 1964 onwards.

Table 2 Odds ratios for risk of 2/1+ within age group 50–74, showing the individual effect of a number of cumulative exposure indices, plus the effect of confounders individually after adjusting for cumulative post-1964 quartz exposure

Predictor variable	Estimated odds ratio	95% CI
Dust (g.h.m^{-3})		
All periods	1.030	(1.018 to 1.043)
Pre-1964	0.995	(0.977 to 1.014)
Post-1964	1.101	(1.068 to 1.135)
Quartz (g.h.m^{-3})		
All periods	1.702	(1.456 to 1.990)
Pre-1964	0.884	(0.633 to 1.236)
Post-1964	1.811	(1.536 to 2.136)
After quartz (post-1964)		
Quartz pre-1964	0.854	(0.534 to 1.365)
Dust pre-1964	0.996	(0.971 to 1.022)
Dust post-1964	1.025	(0.974 to 1.079)
Age	0.990	(0.925 to 1.059)
Ex-smoker*	0.453	(0.140 to 1.467)
Smoker*	0.556	(0.176 to 1.757)
Pre-1954 h×10^{-3}	0.987	(0.944 to 1.032)

*Relative to non-smokers.

Polychotomous logistic regression was used to compare the predictive ability of each of a series of GEIs in the range $-4 \leqslant a \leqslant 2$ and $0 \leqslant b \leqslant 3$ for the prevalence of the three main profusion categories 0, 1, and 2+. For each model, the reduction in

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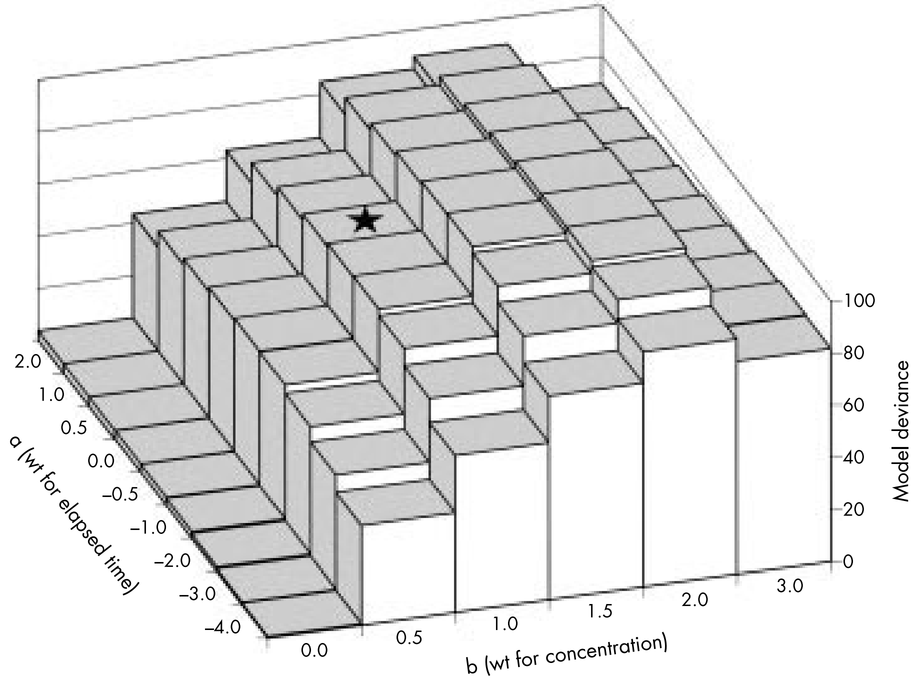

Figure 2 Model deviance associated with including, in a polychotomous regression model of profusion categories, each GEI formed from the combination of powers of time since exposure (*a*) and concentration (*b*). Age groups 50–74, post-1964 exposure.

deviance (−2 × log likelihood) from the null model is a measure of strength of the model in describing the data. We call this "model deviance". Figure 2 compares model deviances for the different combinations, with larger deviances indicating better fit. A star marks GEI(a=0, b=1)—that is, cumulative quartz exposure—and the graph shows that many other GEIs gave higher deviances. The model deviance peaked for the GEI with a=−2, b=2, although this index was similar to all the other indices with b=2. This suggested that cumulative exposure to higher concentrations had greater effect in regression models than exposure to lower concentrations. There was little power in this study to compare the effect of the timing of exposure since the very high quartz exposure increments were experienced over a relatively short period of time and elapsed time at follow up was therefore nearly constant for those increments.

The relative importance of exposure to high concentrations was further investigated by adding separately variables quantifying the numbers of hours worked at concentrations higher than a range of lower limits to a polychotomous regression model that included simple cumulative exposure (table 3). The model deviance increased to a maximum at a lower limit of 2 mg.m^{-3} before falling again. Relatively few subjects experienced any concentrations exceeding 3 mg.m^{-3}.

A further model was fitted that included, simultaneously, cumulative exposure since 1964 within two quartz concentration bands, defined by the cut point 2.0 mg.m^{-3}. This confirmed the high importance of cumulative exposure to quartz greater than 2 mg.m^{-3} in relation to exposure at concentrations lower than this, giving the following prediction equation:

$$\log(p_2/(1-p_2)) = -4.83 + 0.443 \times CE_{<2} + 1.323 \times CE_{>2} \qquad (2)$$

where p_2 is the probability of profusion category 2/1 or higher at follow up respectively, and $CE_{<2}$ and $CE_{>2}$ represent cumulative quartz exposure at concentrations less than and greater than 2 mg.m^{-3} respectively. Although the two exposures are in the same units, the coefficient for the higher concentrations was three times that for the lower, and each was highly statistically significant in the presence of the other.

Table 3 Improvement in model deviance with the addition of variables quantifying number of working hours at quartz concentrations exceeding various lower limits, in polychotomous regression models that also include cumulative exposure

Model	Model deviance	Improvement (1 df)
Cumulative exposure	74.9	
Add hours above concentration (mg.m^{-3})		
0.05	75.1	0.2
0.1	79.9	5.0
0.5	76.7	1.8
1.0	87.8	12.9
1.5	89.6	14.7
2.0	96.4	21.5
2.5	87.1	12.2
3.0	87.1	12.2

Age group 50–74, exposures from 1964.

Table 4 presents examples of predicted risks based on the logistic regression model for profusion 2/1+ silicosis shown in equation (2). This shows the combined effect on risk of long term exposure to low quartz concentrations (for example, 0.1 mg.m^{-3}) and short term exposure to high concentrations (for example, 2 mg.m^{-3}). This shows very clearly the dramatic rise in predicted risk with relatively short periods of exposure to high quartz concentrations. For example, the model predicts a risk of 2.5% for 15 years exposure to 0.1 mg.m^{-3}, which rises to 10.6% with the addition of only four months exposure at 2 mg.m^{-3}, and 72% with a year at the higher exposure.

The results here, from a cohort of coal miners aged 50–74 at follow up, indicated that variation in exposure concentration was of great importance in predicting risk, and that exposures to higher concentrations increased risk at an exaggerated rate. It was estimated that 1 g.h.m^{-3} of exposure at greater than

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Table 4 Predictions of risk (%) of silicotic signs of profusion 2/1+, 15 years after exposure ends, as a function of 15 years spent in low concentrations and additional months in high (2 mg.m^{-3}) concentrations

		Extra months at 2.0 mg.m^{-3} (SEM in italics)							
Silica conc. (mg.m^{-3})	Equivalent cum. exp. (g.h.m^{-3})*	0		4		8		12	
0.30	7.83	20.52	*4.95*	54.51	*8.74*	84.76	*7.83*	96.27	*3.25*
0.20	5.22	7.50	*1.77*	27.36	*5.96*	63.61	*13.22*	89.03	*8.59*
0.10	2.61	2.49	*0.89*	10.58	*3.72*	35.46	*14.18*	71.84	*18.37*
0.08	2.09	1.98	*0.78*	8.59	*3.32*	30.36	*13.49*	66.93	*20.36*
0.06	1.57	1.58	*0.68*	6.93	*2.94*	25.70	*12.58*	61.62	*22.08*
0.04	1.04	1.26	*0.59*	5.58	*2.58*	21.53	*11.53*	56.02	*23.40*
0.02	0.52	1.00	*0.51*	4.48	*2.25*	17.88	*10.39*	50.26	*24.18*
0.00	0.00	0.80	*0.44*	3.59	*1.95*	14.73	*9.23*	44.50	*24.37*

Population aged 50–74, post-1964 exposures. $\ln(p_2/(1-p_2)) = -4.83 + 0.44 \times CE_{<2} + 1.32 \times CE_{>2}$.
*Assumes a standard working year of 1740 hours.

2 mg.m^{-3} was equivalent in terms of predicted risk of radiographic abnormalities to about 3 g.h.m^{-3} at less than 2 mg.m^{-3}. Variation in the timing of exposure appeared to have less influence, but in this study there was limited power to detect the effect of the timing of exposure.

DISCUSSION

This paper describes a reanalysis of the exposure-response relation between exposure to quartz in coal mine dust and silicosis. Given the ongoing debate on a safe control limit for quartz, the reanalysis was motivated by the need to look at dose measures other than simple cumulative exposure, particularly among a cohort of miners exposed to unusually high levels of quartz for a part of their working lives. We have focused on risks of silicosis using category 2/1 or greater small opacities on the ILO scale. This is equivalent to well established silicosis, and in this population was associated with, on average, a lung function defect of about 250 ml of FEV$_1$, compared with those without opacities.[6]

The predicted risks per g.h.m^{-3} reported here, if restricted to quartz concentrations less than 2 mg.m^{-3}, are slightly lower than those reported in the original analysis of these data,[7] which were based on men of all ages. It is likely that restriction to the ages most informative about the effects of the high quartz episode, and the modelling of differential effects by concentration, will have produced a more focused set of models. In addition, the usual cautions apply about predicting where the data are sparse, which here means the small number of cases at very low concentrations and exposures.

Use of cumulative exposure as a dose measure in exposure-response analyses implies several simplifying assumptions. Principally, exposure-response models based on cumulative exposure assume that the internal biologically significant dose is a linear function of both concentration and exposure time. Each period of exposure contributes to the total effect additively and independently of every other period. Therefore, cumulative exposure does not distinguish between periods of differing exposure intensity provided that the increment in cumulative exposure is the same. Also, cumulative exposure does not differentiate exposures on the basis of when they were experienced relative to the effect. Smith[15] highlights the potential shortcomings of cumulative exposure and, using a pharmacokinetic model for inhaled dust, argues that cumulative exposure is a poor index of dose for insoluble particles without acute effects if exposure intensity exceeds 0.1 mg.m^{-3}. Several authors have proposed alternative dose measures to take account of residence time in the lung,[9] clearance,[16] and differing toxicity.[17]

Models can be constructed that characterise dose as a dynamic function of processes such as inhalation to, deposition in, and clearance from the lung, but such models usually require complex calculations with integrals. The methods used here are more empirical, but are flexible enough to allow the fitting of models representing a wide range of possible assumptions. The results can therefore provide criticism of the cumulative exposure assumption by looking for improvements on model fit, and specific values for *a* and *b* in equation (1) can create indices that mimic the doses implied by dynamic models.

The elapsed period between exposure and effect has been shown in the literature to have an important effect on quantitative exposure-response relations and has been shown to explain some of the differences in reported risks.[18] The present study has shown clearly that exposure to higher concentrations increased risk at an exaggerated rate, but has not shown a strong effect of elapsed time, because the men who experienced damaging exposures did so over the same relatively short period. However, the prevalence of serious abnormalities in the follow up study[7] was much greater than that at earlier surveys,[4] an important reminder of the progressive nature of the disease. For the subcohort analysed here, the minimum elapsed period since last examination was over 10 years, and more than 15 years had elapsed since the very highest concentrations[7]; this should be taken into account when comparing with predicted risks from other studies if they differ in elapsed time.

The variation observed in risk estimates from studies of different working populations[19] may be greater than can be caused by methodological differences or by differences in elapsed time. We have a high degree of confidence in our risk estimates, since they are based on a uniquely detailed programme of measurements. Our risk estimates are generally at the highest end of the range, comparable to those reported in South African gold miners.[20] Others have reported much lower risks. The low risks reported in the heavy clay industry[21] may have been attributable to the clay minerals containing the quartz. We wonder whether the low estimated risks in some other reports[22–24] may be a benign consequence of a lack of excursions of quartz concentrations to very high levels. In the Scottish coalminers, exposure to high levels of freshly created silica particles in the respirable aerosol has led to high risks, and risk predictions from the fitted models may be useful wherever similar aerosols might be generated.

CONCLUSIONS

Quantification of the risks of silicosis should take account of variations in exposure intensity. This is particularly the case for exposure to high quartz concentrations, even if exposure is for relatively short periods. The risks of silicosis over a working lifetime can rise dramatically with exposure to such high quartz concentrations over a timescale of merely a few months.

ACKNOWLEDGEMENTS

The authors would like to thank the Health and Safety Executive for funding this study.[25]

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Main messages

- In the epidemiology of mineral dusts, we should examine whether cumulative exposure is the best exposure metric.
- We can construct many alternative exposure metrics, if we have detailed enough data.
- In data from coal miners who had unusual exposure to silica, exposure to higher concentrations was proportionally more risky than at lower concentrations.
- Even quite short exposures to high concentrations can increase risk dramatically.

Policy implications

- It continues to be important to control silica exposures.
- It is particularly important to avoid even brief excursions over control limits.

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Answers to multiple choice questions on *Confounding and confounders* by R McNamee, on pages 227–234

(1) (a) true; (b) false; (c) false; (d) true
(2) (a) true; (b) false; (c) false; (d) true
(3) (a) true; (b) true; (c) true
(4) (a) true; (b) false; (c) true
(5) (a) true; (b) false; (c) true; (d) false
(6) (a) true; (b) true; (c) false

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