Longitudinal and cross sectional analyses of exposure to coal mine dust and pulmonary function in new miners

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Abstract

The association between exposure to dust and pulmonary function was studied by longitudinal and cross sectional analyses in a group of United States underground coal miners beginning work in or after 1970. Quantitative estimates of exposure to respirable coal mine dust were derived from air samples taken periodically over the entire study period. The cohort included 977 miners examined both in round 2 (R2) (1972–5) and round 4 (R4) (1985–8) of the National Study of Coal Workers' Pneumoconiosis. Multiple linear regression models were developed for both cross sectional (pulmonary function at R2 and R4) and longitudinal (change in pulmonary function between R2 and R4) analyses with exposure partitioned into pre-R2 and post-R2 periods and controlled for covariates including smoking history. The results indicate a rapid initial (at R2) loss of FVC and FEV_1 in association with cumulative exposure of the order of 30 ml per mg/m^3-years. Between R2 and R4 (about 13 years) no additional loss of function related to dust exposure was detected although the percentage of predicted FVC and FEV_1 did decline over the period. After some 15 years since first exposure (at R4), a statistically significant association of cumulative exposure with FEV_1 of about $-5{\cdot}9$ ml per mg/m^3-years was found. These results indicate a significant non-linear effect of exposure to dust on pulmonary function at dust concentrations present after regulations took effect. The initial responses in both the FVC and FEV_1 are consistent with inflammation of the small airways in response to exposure to dust.

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Cross sectional analyses of respiratory disease in coal miners have provided strong evidence for an exposure-response relation between cumulative exposure to dust and decrements in pulmonary function[1–6] and increased prevalence of symptoms of chronic bronchitis.[7,8] None the less, longitudinal studies may provide a more sensitive design for the detection of low level effects and for examination of temporal aspects of the exposure-disease relation.

Two among several longitudinal analyses of pulmonary function in coal miners are of particular interest. Love and Miller[9] studied the change in forced expiratory volume in one second (FEV_1) between two surveys about 11 years apart in 1677 long term (average age 45) British coal miners. Results of this analysis showed a loss of around 0·6 ml per mg/m^3-year exposure before the first survey. A relation between cumulative exposure between the two surveys and change in (FEV_1) was also found but only if the effect of coal mine was left out of the models. Attfield[10] completed a comparable study in 1072 United States miners over nine years. Exposure estimates relied on years worked for the period before the study (average nine years) and on personal dust measurements between the two surveys. Results of this analysis indicated a weak association ($p = 0{\cdot}12$) of average dust concentrations with decrements in FEV_1 and a statistically significant ($p < 0{\cdot}05$) decline of 7·3 ml in FEV_1 for each year worked at the face between the surveys. Although these studies generally confirm a relation between exposure to coal dust and a fall in FEV_1, their design limits the interpretation of

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the reported outcomes. The United States study used relatively unstable quantitative estimates only for the concurrent exposure period and used years underground as a surrogate for earlier exposures. Neither of these studies considered the relation of dust exposure to loss of forced vital capacity (FVC). Most importantly, both studies included only miners with long histories of mining work, limiting their ability to examine the effects of initial exposure on respiratory health.

This study considers the effect of exposures to coal dust on pulmonary function through both longitudinal and cross sectional analyses. The subjects included participants in round 4 (R4) (1985–8) of the National Study of Coal Workers' Pneumoconiosis (NSCWP) who started work during or after 1970, the year in which national exposure standards came into effect in the United States. The initial exposure limit was set at 3·0 mg/m^3 of respirable dust on 31 December 1969 and this was lowered to 2·0 mg/m^3 three years later.[11] The same miners had also been studied in round 2 (R2) (1972–5) of the NSCWP; thus each participant had been given at least two pulmonary function tests 11 to 18 years apart. Also, quantitative estimates of exposure were available for the cohort based on federal government sampling data over the entire study period. Thus with these quantitative historical exposure data and two sets of pulmonary function studies, the current study considers the exposure-response relations with time in a group of new miners.

Methods

The cohort for this analysis was similar to one previously described.[12 13] That cohort was defined by the criteria: (1) they were men; (2) they were surveyed by the NSCWP at R4, (3) their first mining job was reported in their R4 work history in 1970 or later and their R2 work history did not suggest more than one year of pre-1970 mining work; (4) they had at least three pulmonary function test manoeuvres meeting the American Thoracic Society (ATS) acceptability requirements[14] at R4. For this analysis, the only other requirement was that the miner had also completed acceptable pulmonary function tests at R2. Hence, each participant had begun work as a coal miner from one to five years before testing at R2 and 15 to 18 years before testing at R4.

The methods of data collection used at R2 were similar to those used at R4 and included a chest radiograph, a British Medical Research Council respiratory symptom questionnaire, work history, and pulmonary function tests. Spirometry was conducted according to the ATS guidelines in effect at the time by technicians trained by a highly qualified National Institute of Occupational Safety and Health pulmonary physiologist. The testing equipment used was the same (dry rolling seal volume displacement spirometers) in both R2 and R4. The FVC and FEV_1 were obtained from the largest value found regardless of the exhalation from which it derived. Two procedures used in R2 were different from those adopted at R4. Firstly, a maximum of five manoeuvres were elicited in R2 to obtain three acceptable values whereas up to 10 were obtained in R4. This is unlikely to lead to any substantial bias as most subjects will obtain three acceptable values within five attempts.[15] Secondly, timed volumes, for example, FEV_1, were originally obtained by the flow threshold method at R2 and according to the 1979 ATS recommendations[14] by back extrapolation at R4. To ensure comparability with R2 results for this analysis, R4 results were recalculated from flow threshold methods. Consistent with the ATS guidelines, no reproducibility criteria were applied to the cohort. Results from an analysis of the effect of reproducibility on the R4 results were presented in a previous paper.[13]

Variables of pulmonary function considered in this analysis were the FVC, FEV_1, and their ratio FEV_1/FVC. Cross sectional analyses used the absolute value of the measures and the longitudinal analysis used the change in function from R2 to R4 divided by the time interval between the two surveys $((FVC_{R4}-FVC_{R2})/(date_{R4}-date_{R2}) = l/year)$. Some analyses also used the per cent predicted based on Crapo *et al.*[16]

Methods by which cumulative exposure to respirable coal mine dust were estimated for the cohort have been described in detail elsewhere.[12 17 18] Briefly, exposure data collected for legal compliance purposes under the auspices of the Mine Safety and Health Administration were used. The data for the analysis included only personal samples collected on miners for the period 1970 to the end of 1987 in the 36 mines from which the R4 cohort was originally selected. Several potential biases in the data were identified and where possible, corrections were made to account for them.[17] Arithmetic mean exposures were estimated within strata defined by mine, occupation, and year and for decreasingly specific stratifications: occupation/year, mine/year (within occupation group), and year (within occupation group). To minimise the variance of means for occupation/mine/year strata with very few samples, the three way means were combined with two way (occupation/year) means in a manner that minimised the mean squared error.[18] Cumulative exposure was estimated for each cohort member by matching each occupation/mine/year specific job identified in the oral work histories obtained at R4 and the estimated mean exposures.

*Table 1 Description of the study cohort by smoking state**

	Whole cohort	*Smoking state (at R4)*		
		Current	*Ex*	*Never*
No	977	385	319	273
Age (y)	39·9 (6·3)	39·5 (6·1)	41·0 (6·6)	39·0 (6·2)
Cumulative exposure (mg/m³-years)	15·4 (6·2)	15·9 (6·2)	15·1 (6·1)	15·2 (6·4)
Pre-R2 cumulative exposure	3·8 (2·9)	4·0 (3·0)	3·8 (2·8)	3·5 (2·8)
Post-R2 mean exposure (mg/m³)	0·92 (0·38)	0·94 (0·38)	0·89 (0·38)	0·93 (0·39)
Race (% white)	94·8 (926)	94·8 (365)	95·9 (306)	93·4 (255)
Pack-years	12·3 (14·1)	19·0 (13·0)	14·7 (14·8)	0·0
FVC:				
R2 (l)	5·47 (0·78)	5·41 (0·76)	5·56 (0·76)	5·47 (0·83)
R2 (% predicted)	103·7 (12·2)	102·9 (12·0)	105·0 (12·4)	103·1 (12·4)
R4 (l)	4·98 (0·83)	4·89 (0·80)	5·06 (0·83)	5·02 (0·86)
R4 (% predicted)	97·0 (13·2)	95·6 (12·7)	98·4 (13·7)	97·2 (13·3)
R4-R2 (l/y)	−0·039 (0·039)	−0·041 (0·036)	−0·039 (0·041)	−0·036 (0·042)
FEV_1:				
R2 (l)	4·33 (0·67)	4·23 (0·67)	4·39 (0·67)	4·40 (0·65)
R2 (% predicted)	98·3 (12·7)	96·3 (12·7)	99·8 (13·0)	99·4 (12·0)
R4 (l)	3·87 (0·71)	3·70 (0·72)	3·97 (0·71)	3·98 (0·67)
R4 (% predicted)	92·4 (14·3)	88·7 (14·3)	94·9 (14·5)	94·6 (12·8)
R4-R2 (l/y)	−0·037 (0·032)	−0·041 (0·032)	−0·034 (0·033)	−0·033 (0·029)
FEV_1 FVC:				
R2 (%)	79·3 (7·4)	78·0 (8·0)	79·0 (8·0)	81·0 (7·0)
R2 (% predicted)	94·8 (8·5)	93·6 (8·8)	95·0 (8·6)	96·5 (7·8)
R4 (%)	77·7 (7·3)	75·7 (7·8)	78·4 (7·0)	79·6 (6·4)
R4 (% predicted)	95·4 (8·8)	92·9 (9·3)	96·6 (8·4)	97·6 (7·6)
R4-R2 (%/y)	−0·12 (0·43)	−0·20 (0·42)	−0·05 (0·43)	−0·09 (0·40)

*Variables given as measured at R4.
Values are means (SD); pulmonary function based on Crapo *et al.*[16]

When estimates for the three way stratification exposures were unavailable, estimates based on decreasingly specific stratifications were used. Cumulative exposure to respirable coal mine dust was also partitioned for each miner into the pre-R2 and post-R2 periods. For longitudinal analyses that examined the change per year in pulmonary function between R2 and R4, the post-R2 cumulative exposure was standardised to the time between surveys and presented as the average exposure over the interval in mg/m³.

Multiple regression analyses were conducted to simultaneously control for age, height, cigarette smoking (current, ex, never), pack-years of cigarette smoking, race/ethnicity (White, Black, Hispanic), mining state at R4 (current, ex) and years worked in non-mining dusty occupations. Age, height, pack-years, non-mining dust exposure and cumulative exposure to respirable coal mine dust were entered into the models as continuous variables; current and ex-smoker, mining state, and race/ethnicity were represented by dummy variables. For the longitudinal analysis of changes from R2 to R4, variables such as age and smoking history were obtained from the R4 results. For cross sectional analysis of R2, data from that survey were used. Cumulative exposure up to R2 or R4 were always included in the respective cross sectional analyses. For the longitudinal analyses, pre-R2 cumulative exposure and post-R2 average exposure were used. All variables other than exposure to dust were selected first by a simple forward stepwise procedure (p for inclusion <0·2). All selected variables with p between 0·1 and 0·2 were then evaluated to determine their effect on the cumulative exposure coefficient. If removal of the variable resulted in a change in the coefficient for cumulative exposure greater than 10%, the covariate remained in the model. A previous cross sectional analysis of R4 found that the use of the log of cumulative exposure and interactions between age, smoking state, and exposure improved the fit of the model.[13] No such improvement was found for the R2 or change from R2 to R4 analyses presented here, so only the simple linear models are presented to allow comparability across time frames of analysis. After we identified the model, further improvements were tested through the addition of age² and interaction terms between exposure and age and exposure and smoking variables. The fit for each primary model was evaluated by examining residual plots for outliers and non-random patterns. No evidence of systematic poor fit was found.

Results

Of the 1185 miners meeting the cohort definition for the earlier analysis,[13] 977 had pulmonary function tests at R2. Table 1 gives the characteristics and pulmonary function results for this population, stratified by R4 smoking state. The average age at R4 was about 40 and cumulative exposure was

*Table 2 Linear regression models for change per year of pulmonary function varables between R2 and R4 (n = 977)**

	FVC	FEV_1	$FEV_1/FVC\%$
r^2	0·109	0·065	0·044
Constant	−0·2368	0·0858	−1·8863
	0·0452	0·0377	0·5079
	(<0·001)	(0·023)	(<0·001)
Age (y)	−0·0116	−0·0049	0·0823
	0·0022	0·0018	0·0242
	(<0·001)	(0·007)	(<0·001)
Age^2	0·00011	0·00004	−0·00092
	0·00003	0·00002	−0·00028
	(<0·001)	(0·032)	(0·001)
Current smoker	−0·0044	−0·0087	−0·1305
(0 = no, 1 = yes)	0·0024	0·0020	0·0274
	(0·073)	(<0·001)	(<0·001)
Current miner		−0·0033	
(0 = no, 1 = yes)		0·0021	
		(0·107)	
Black			0·1554
(0 = no, 1 = yes)			0·0678
			(0·022)
Pre-R2			
Cumulative			
exposure†	0·0012	0·0007	−0·0059
	0·0004	0·0004	0·0049
	(0·006)	(0·066)	(0·232)
Post-R2 mean			
exposure	−0·0018	0·0028	0·0472
	0·0032	0·0028	0·0361
	(>0·2)	(>0·2)	(0·0191)

*Calculations from pulmonary function values in l per year (FVC, FEV_1) and % per year ($FEV_1/FVC\%$).
†Cumulative exposure (mg/m^3-years) up to R2 (pre-R2) and mean exposure (mg/m^3) between R2 and R4 (post-R2).
Results are coefficient, standard error, (p value).

*Table 3 Linear regression models for pulmonary function outcomes at R4 (n = 977)**

	FVC	FEV_1	$FEV_1/FVC\%$
r^2	0·407	0·439	0·157
constant	−5·4734	−3·0636	92·819
	0·6387	0·5370	1·5328
	(<0·001)	(<0·001)	(<0·001)
Age (y)	−0·0379	−0·0423	−0·3120
	0·0033	0·0030	0·0370
	(<0·001)	(<0·001)	(<0·001)
Height (cm)	0·0682	0·0497	
	0·0034	0·0029	
	(<0·001)	(<0·001)	
Current smoker	−0·1138	−0·1182	−2·7668
(0 = no, 1 = yes)	0·0422	0·0518	0·4895
	(0·007)	(0·023)	(<0·001)
Ex-smoker		0·1167	
(0 = no, 1 = yes)		0·0493	
		(0·018)	
Pack-years		−0·0056	−0·0499
		0·0016	0·0180
		(<0·001)	(0·006)
Black	−0·8851	−0·5392	3·2682
(0 = no, 1 = yes)	0·1040	0·0872	1·0950
	(<0·001)	(<0·001)	(0·003)
Hispanic			4·1205
(0 = no, 1 = yes)			2·0604
			(0·046)
Cumulative			
exposure†	−0·0020	−0·0059	−0·0775
	0·0033	0·0028	0·0350
	(>0·2)	(0·033)	(0·027)

*Calculations from pulmonary function values in l(FVC, FEVM) and $\%(FEV_1/FVC\%)$
†Cumulative exposure (mg/m^3-years).
Results are coefficient, standard error, (p value).

about 15 mg/m^3-years. More than one third of the group were current smokers at R4. The FEV_1 and FVC as a per cent of predicted declined between R2 and R4. The average changes in FVC and FEV_1 over the interval were 39 and 37 ml per year respectively.

Linear regression models were developed for the change per year in each of the pulmonary function test measures (table 2). Inclusion of a quadratic age term to the models improved the model fit but none of the interactions considered were significant ($p > 0·05$). No statistically significant associations were found between post-R2 average exposure and pulmonary function changes. There was a small but statistically significant increase in FVC and FEV_1 with higher pre-R2 cumulative exposures. The low r^2 values for these models are similar to other longitudinal pulmonary function studies of coal miners with two time points.[9 10]

Because these findings on exposure to dust and ventilatory function seem to contradict those from an earlier cross sectional study of R4 miners,[13] further analyses were undertaken. Firstly, to confirm that the previously detected trend of decline in ventilatory function with increasing dust exposure was still evident in the subset of R4 data examined here, a cross sectional analysis of the R4 pulmonary

Table 4 Linear regression models for pulmonary function variable at R2

	FVC	FEV_1	$FEV_1/FVC\%$
r^2	0·379	0·393	0·140
Constant	−7·8990	−4·9735	101·44
	0·7102	0·6018	6·559
	(<0·001)	(<0·001)	(<0·001)
Age (y)	0·0794	0·0445	−0·3020
	0·0260	0·0220	0·0402
	(0·002)	(0·044)	(<0·001)
Age^2	−0·0015	−0·0012	
	0·0004	0·0004	
	(<0·001)	(0·001)	
Height (cm)	0·0708	0·0517	−0·0719
	0·0033	0·0028	0·0362
	(<0·001)	(<0·001)	(0·047)
Ex-smoker		0·0910	
(0 = no, 1 = yes)		0·0447	
		(0·042)	
Pack-years		−0·0094	−0·1452
		0·0023	0·0299
		(<0·001)	(<0·001)
Black	−0·8586	−0·5925	
(0 = no, 1 = yes)	0·1003	0·0853	
	(<0·001)	(<0·001)	
Cumulative			
exposure			
Pre-R2†	−0·0304	−0·0275	−0·0816
	0·0071	0·0060	0·0766
	(<0·001)	(<0·001)	(>0·2)

*Calculations from pulmonary function values in l(FVC, FEV_1) and $\%(FEV_1/FVC\%)$.
†Cumulative exposure (mg/m^3-years) up to R2.
Results are coefficient, standard error, (p value).

*Table 5 Linear regression models for FVC and FEV_1 at R2 by age category**

	FVC		*FEV_1*	
	< 25	*⩾ 25*	*< 25*	*⩾ 25*
No	415	562	415	562
r^2	0·326	0·410	0·263	0·412
Constant	−13·4910	−7·7660	−7·6878	−4·8043
	4·4648	1·1562	4·0503	0·9858
	(0·005)	(<0·001)	(0·058)	(<0·001)
Age	0·6041	0·0562	0·3285	0·0108
	0·4313	0·0521	0·3662	0·0445
	(0·162)	(>0·2)	(>0·2)	(>0·2)
Age^2	−0·0135	−0·0012	−0·0075	−0·0007
	0·0100	0·0008	0·0085	0·0007
	(0·178)	(0·134)	(>0·2)	(>0·2)
Height (cm)	0·0699	0·0724	0·0490	0·0540
	0·0051	0·0042	0·0044	0·0036
	(<0·001)	(<0·001)	(<0·001)	(<0·001)
Ex-smoker			0·0577	0·1058
(0 = no, 1 = yes)			0·0759	0·0557
			(>0·2)	(0·058)
Pack-years			−0·0076	−0·0096
			0·0071	0·0024
			(>0·2)	(<0·001)
Black	−0·5483	−1·0212	−0·5104	−0·6399
(0 = no, 1 = yes)	0·1709	0·1238	0·1458	0·1058
	(0·001)	(<0·001)	(<0·001)	(<0·001)
Cumulative exposure				
Pre-R2†	−0·0134	−0·0416	−0·0163	−0·0358
	0·0120	0·0089	0·0102	0·0076
	(>0·2)	(<0·001)	(0·111)	(<0·001)

* Calculations from pulmonary function values in l (FVC, FEV_1).
† Cumulative exposure (mg/m^3-years) up to R2.
Results are coefficient, standard error, p value.

function data was repeated with cumulative exposure before R4. The results (table 3) were similar to those found previously.[13] The FEV_1 and FEV_1/FVC were associated with cumulative exposure and the estimated effect of exposure on FEV_1 was −5·9 ml per mg/m^3-years.

*Table 6 Regression coefficients for cumulative exposure (pre-R2) from previously developed models (table 4) for pulmonary function variables stratified by R2 smoking state**

Smoking State	*FVC*	*FEV_1*	*FEV_1/FVC%*
Current (n = 557)	−0·0254	−0·0237	−0·1089
	0·0089	0·0078	0·0990
	(0·004)	(0·002)	(>0·2)
Ex (n = 169)	−0·0449	−0·0524	−0·2476
	0·0186	0·0160	0·1999
	(0·017)	(0·001)	(>0·2)
Never (n = 251)	−0·0335	−0·0179	0·0888
	0·0148	0·0117	0·1525
	(0·025)	(0·128)	(>0·2)

Calculations from pulmonary function values in l (FVC, FEV_1) and FEV1/FVC%). Results are coefficient, standard error, (p value).
Each coefficient was derived from a separate multivariate linear regression model. Covariates included (not shown) age, age^2, height, race, and smoking history as in table 4.

As the previously noted cross sectional relations between ventilatory function and exposure to dust were not clearly echoed in the longitudinal analysis, it seems that much of the dust related decline in ventilatory function evident at R4 must have occurred before the start of the longitudinal follow up period—that is, before R2. Hence, further cross sectional analyses were undertaken modelling R2 ventilatory function with cumulative dust exposure before R2. These results (table 4) indicated a strong association of cumulative exposure with reduced pulmonary function (FVC and FEV_1 were some 30 ml lower for each additional mg/m^3-years worked). This association was found over an average exposure time of about 2·5 years, with a maximum mining experience of about five years.

Because pulmonary function is expected to peak at about age 25 before beginning its age related decline, separate regressions were run for miners less than age 25 and greater than or equal to 25 years at R2 (table 5). Miners less than 25 years old did not have statistically significant declines in FVC or FEV_1 associated with exposure, although the point estimates of −13·4 and −16·3 ml per mg/m^3-years are substantial. Miners older than 25

years had striking dust related decrements of the order of −40 ml per mg/m³-years.

To further examine the effect of smoking at R2, the regressions presented in table 4 were rerun stratified by R2 smoking state (table 6). Exposure related decrements were present for both FVC and FEV_1 in all smoking categories. The largest coefficients were ex-smokers. Never smokers had a statistically significant loss of FVC in relation to dust exposure and the exposure-related loss of FEV_1 for never smokers was somewhat smaller (about 16 ml per mg/m³-year) than for the other two smoking groups and was not statistically significant ($p > 0.1$).

Discussion

This study suggests that coal miners beginning their mining tenure at the same time that the federal government instituted comprehensive exposure regulations have experienced exposure related losses of lung function but that the losses were not linearly related to exposure over time. During the first few years of mining (less than five), the miners seem to have had a rapid initial loss of lung function associated with their cumulative exposure to respirable coal mine dust. There was a comparable effect on both the FVC and FEV_1 of about 30 ml for each mg/m³-year of exposure and the effect was more pronounced (−40 ml per mg/m³-year) in miners over the age of 25 at R2. Over the next 10 to 14 years, although the mean FEV_1 and FVC as a per cent of predicted declined (table 1), no additional loss associated with continued exposure was detected.

The models presented in this analysis were simple linear regressions. In a previous cross sectional analysis at R4, stronger associations were found from the log of cumulative exposure and interactions between smoking state, age, and log cumulative exposure.[13] In the analysis of R2 or the change from R2 to R4, no improvement was found by substituting the log of exposure. To keep the analyses consistent and more easily interpretable, only the simple linear models were presented for the R4 cross sectional analysis. The stronger association of pulmonary function with the log of cumulative exposure at R4 may, in fact, be related to the large effect of early exposures in this analysis.

The changes in pulmonary function (especially FVC) between R2 and R4 were associated with the earlier exposures (the pre-R2 cumulative exposure), but in the opposite direction from that expected. It seems plausible that this result stems from a recovery after the initial exposure related decrements. That is, miners with heavy initial dust exposure and pulmonary function decrements may have a subsequent recovery or slowing of loss and seem to have a positive pre-R2 exposure to post-R2 change in pulmonary function relations.

The apparent lack of association between the exposure between R2 and R4 and decrements in FVC and FEV_1 in the longitudinal analysis (table 2) should be considered carefully. In a study of 418 non-occupationally exposed non-smoking adults followed up in up to seven surveys over 11 years, Burrows, *et al*[19] were able to generate estimates of decline in FEV_1 with time. They found that the mean FEV_1 in different surveys deviated from the predicted values by as much as ±30 ml. Such survey effects were not explained by any changes in personnel, equipment, or methodology. Furthermore, Berry[20] used an estimate of between occasion (between survey) standard deviation in FEV_1 of 120 ml/year derived from five longitudinal studies of working populations to calculate the standard deviation of estimates of annual declines. His results indicate that in a study comparable with this one (two measurements 10 years apart), a standard deviation of annual decline of 43 ml per year would be expected. The standard deviation of annual decline was 32 ml per year in our current study. In view of this, the power to detect an exposure related effect on FEV_1 less than 2 or 3 ml per mg/m³ is probably limited in the current longitudinal analysis.

Selection effects might be invoked to provide an explanation for the large exposure-response relation at R2. If miners with lower initial pulmonary function were selected into jobs with high exposures, a falsely positive exposure-response analysis at R2 with no subsequent change might be found. Such a selection process, however, seems implausible. The apparent lack of any exposure-response during the R2-R4 interval could conceivably be explained by selection effects if ill members of the cohort were less likely to participate at R4. Although such an effect cannot be ruled out entirely, R4 participants and non-participants were found to be similar at R2 in a previous analysis.[13] In that analysis, the R4 participants and non-participants did not differ significantly in age (27·6 and 26·4), pack-years (6·2 and 6·0), per cent predicted FVC (103·8 and 103·0), FEV_1 (98·6 and 98·9), and FEV_1/FVC (95·0 and 95·9).

Selection bias could account for the minimal effect of dust from R2 to R4 if miners who were more susceptible to the dust were less likely to participate in both R2 and R4. This is unlikely to be operative given that the effect in the pre-R2 period was so pronounced, suggesting that susceptible miners were included in the group.

One possible explanation for the difference in dust effect at R2 and from R2 to R4 is raised by the finding of Mannino *et al*, that miners with airways hyper-responsiveness were more likely to work in

low exposure jobs.[21] If the young cohort in the current analysis at R2 included a sub-group of miners with hyper-reactive airways, who later migrated to lower exposure jobs, this could result in high initial dust-related effects and lower effects subsequently. Given the fact, that R2 participants also participating in R4 were not substantially different from eligible non-participants in R4, however, selective migration to low exposure jobs by miners with airways hyper-reactivity seems unlikely to solely explain the differences seen between R2 and R4.

It is also conceivable that differential errors in measurements explained the results. For instance, if the pre-R2 exposure estimates were highly accurate and precise, and the post R2 estimates contained substantial random misclassification resulting in a bias toward the null hypothesis, then the exposure-response analysis might behave as found. This phenomenon is unlikely, however, because the dust estimates were obtained in the same manner in both periods. In fact, dust concentration measurements in the first few years of the programme are somewhat less reliable than in later years[22] and the occupational histories recalled for the more distant time periods are more likely to be misclassified.[23] Thus greater misclassification may exist in the exposure estimates for the pre-R2 years.

Given that exposure levels were higher (1·5 to two times) during the pre-R2 period than during the subsequent years,[18] another possible explanation of the rapid initial loss of function is that intensity of exposure to dust is responsible for the effects. We might hypothesise that a threshold value exists, below which dust exposure has no effect on the airways and above which, a strong dose-dependent effect occurs. An analysis of the exposure-response relation at R4 on miners who had never worked in jobs with exposures exceeding 2·0 mg/m^3 (n = 344) indicated that a significant exposure-response relation was present even for these miners with the lower maximum exposures (coefficient for cumulative exposure: −0·0213 FEV_1 per mg/m^3-years, p = 0·002). A similar analysis with a threshold cutoff of 1·5 mg/m^3 was not informative because so few miners had worked in jobs with these lower exposures.

The per cent predicted FVC and FEV_1 were lower in R4 than in R2 in all smoking categories (table 1) although no exposure-related decrements for this time were found. One plausible interpretation of this finding is that exposure did affect pulmonary function and that random variability in the exposure and pulmonary function data was too great to permit its detection. It is also possible that ethnic, climatic, or other unspecified factors led to more rapid age related declines than expected on the basis of the prediction formulas of Crapo *et al*[16]

The differences in response to dust in miners younger and older than age 25 (table 5) are unexplained. Although the cumulative exposures of the two groups were different (mean 3·1 and 4·3 mg/m^3-years respectively) the difference was not sufficiently large to suggest a threshold phenomenon to explain the result. Further stratification by age into four groups did not change the pattern substantially (for FEV_1 the coefficients for cumulative exposure were −0·021, −0·011, −0·040 and −0·026 ml per mg/m^3-years, for age groups <23, 23–25, 25–30, and ⩾30 years respectively). Given these findings, physiological differences between younger and older miners may account for the disparate responses to exposure to dust.

Several studies of coal miners have reported either obstructive lung disease occurring as a chronic process requiring the accumulated insult of dust exposure over many years,[1 8] or restrictive lung disease among the subset of workers who evidence large opacities (progressive massive fibrosis) on chest *x* ray films.[24] Also, there is increasing evidence of a restrictive process among coal miners even in the absence of progressive massive fibrosis.[4 6]

For instance, Soutar and Hurley[4] found parallel losses of FEV_1 and FVC in relation to quantitative estimates of lifetime dust exposure in a study of 4059 British miners and ex-miners with no progressive massive fibrosis. The findings of this study, however, may not be comparable with the current analysis as cumulative exposures were significantly higher and there is little tendency in the current data toward a progression of the losses in FVC as would be expected in an ongoing fibrotic process. The long term losses found among the British miners may represent a combination of a classic restrictive (for example, loss due to irreversible interstitial fibrosis) and obstructive (airways narrowing and emphysematous) processes. By contrast, the rapid initial loss of function over a short period with relatively low dust concentrations and the parallel loss of FVC and FEV_1 we found, are unlikely to represent either an interstitial fibrotic process, or the more gradual obstructive changes usually seen in dust induced chronic obstructive disease.

It is also important to note that the effect estimates from the cross sectional British studies are considerably lower than those obtained cross sectionally here, even at R4. Estimates from British studies range from about 1·0 to 1·6 ml FEV_1 per mg/m^3-year[25] compared with the 5·9 ml at R4 or 27·5 ml decrement per mg/m^3-year in our current study. Possible reasons for the differences are discussed in detail in an earlier paper,[13] and include the differences in the cohort's ages (the British cohort was older), work histories (British workers had worked substantially longer in significantly higher dust concentrations), misestimation of either the British or American dust concentrations,

chance (the 95% confidence intervals at R4 include the British effect estimates), and finally, non-linearities in the effect of dust on the airways. Given the results in this paper, the non-linearity of effect may be an important reason for the apparent discrepancies.

Only one other study of lung function in miners during their initial years of mining has been reported. Hodous and Hankinson[26] studied a group of 65 new miners with measures of pulmonary function every six months for two years and once more five years later. The average age at the first examination was 29 y. During the first two years, the miners lost 134 and 200 ml of FVC and FEV_1 respectively, or an average loss of 67 and 100 ml per year. During the next five years, they lost an average of only a further 72 ml FEV_1, a rate of loss of 14·4 ml per year. Over the same five year period, the miners gained 107 ml of FVC for an average gain of 21·4 ml per year. No exposure measurements were made on these miners and no control group followed up for the same period. Although not conclusive, the results suggest that miners had an accelerated loss of function over the first two years of mining exposure with a substantial levelling off of decline in FEV_1 and a reversal of the initial losses reflected in the FVC. Given the surprising results obtained, the authors discounted their findings as a result of random variability. In view of the striking similarity of their results with the current analysis, Hodous and Hankinson's results deserve more consideration.

The apparently rapid onset of a dust-related effect that later moderates may be consistent with an inflammatory response to exposure to coal dust. A restrictive pattern of pulmonary function could be seen with an inflammatory process of the small airways. Dust depositing in the alveoli may be cleared by macrophages to the terminal bronchioles and, along with dust depositing there, elicit an inflammatory response[27] that may be reversible.[28] Although an inflammatory response of the small airways is usually associated with obstructive pulmonary function,[29] it may also be consistent with restrictive changes. For instance, Churg *et al*[30] have described a lesion of the small airways that resulted from exposure to mineral dust. Although the report of Chung *et al* considered primarily obstructive changes, the effect on the FVC was similar to the effect on the FEV_1 with little change in the FEV_1 to FVC ratio, suggesting a restrictive effect.

The relation of any such hypothesised sub-acute inflammatory changes to chronic lung disease in miners is unclear. It is possible that the initial postulated inflammatory response may begin the process of emphysematous changes associated with chronic obstruction in miners,[27] or the beginning of the formation of coal macules and fibrosis of the small airways associated with either *x* ray film changes or the restrictive pattern found in some long term miners without progressive massive fibrosis.

In summary, exposures to respirable coal mine dust at concentrations present in United States mines since 1970 seem to have a substantial effect on pulmonary function, as reflected in a parallel exposure related loss of FEV_1 and FVC over the first few years of exposure. Although the miners continue to lose function over subsequent years, as expressed as a per cent predicted, the loss was apparently not related to exposure. It seems that the subsequent loss of pulmonary function is less rapid. Nevertheless, over the period covered in this study (18 years), the loss of FEV_1 in relation to exposure to dust persists. Investigation of the significance of the initial reaction to exposure to coal mine dust and estimation of the effect of continued low level exposure on morbidity and mortality will require further follow up.

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