# ORIGINAL ARTICLE

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# Differential respirable dust related lung function effects between current and former South African coal miners

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Abstract Dust-related dose-response decrements in lung function among coal miners have been reported in several studies, with varying magnitudes across populations. Few studies have compared differences between current and former coal miners. No studies on dose response relationships with lung function have been conducted in South African coal mines, one of the top three producers of coal internationally. The objectives of this study were (1) to describe the relationship between respirable dust exposure and lung function among current and former South African coal miners and to determine whether differential dust related effects were present between these employment categories; (2) to examine dust related dose response relationships, controlling for potential confounding by smoking and a history of tuberculosis (TB). Six hundred and eightyfour current and 188 ex-miners from three bituminous

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McGill University/Respiratory Epidemiology Unit, Montreal Chest Institute, 3650 St-Urbain Street, Montreal, Quebec, H2X 2P4, Canada coal mines in Mpumalanga Province were studied. Interviews assessing work histories, smoking profiles and other risk factors were conducted. Work histories were also obtained from company records. Standardised spirometry was performed by trained technicians. Cumulative respirable dust exposure (CDE) estimates were constructed from company-collected sampling and measurements conducted by the researchers. Regression models examined the associations of CDE with per cent predicted FEV<sub>1</sub> and FVC, controlling for smoking, past history of TB and employment status. A statistically significant decline in FEV<sub>1</sub> of 1.1 and 2.2 ml/mg-year/m<sup>3</sup> was found in representative 40-year-old, 1.7-m tall current and former miners, respectively. Significant differences were found between the highest and medium exposure categories. Ex-miners had a lower mean per cent predicted lung function than current miners for each cumulative exposure category, suggesting a "healthy worker" effect. Past history of TB contributed to 21 and 14% declines in per cent predicted FEV<sub>1</sub> and FVC, respectively. Thus, in this cohort, a dose-related decline in lung function was associated with respirable dust exposure, with a magnitude of effect similar to that seen in other studies and important differences between current and former employees. A "healthy worker" effect may have attenuated the magnitude of this relationship. TB was a significant contributor to lung function loss.

**Keywords** Coal dust · Lung function · Cumulative dust exposure · Dose response relationship

# Introduction

Accelerated declines in lung function associated with exposure to respirable dust among coal miners have been documented since the 1960s. However, scientific debate on declines in lung function still continues on the role of confounders such as smoking, time of entry into the industry, the "healthy worker" effect, specific dose response relationships and vulnerable subpopulations of miners. Few studies have specifically compared the differences in dust related lung function outcomes in currently employed and former coal miners. In one such study, British ex-miners were found to have a non-statistically significant 0.21 ml/g h/m<sup>3</sup> (equivalent to 0.36 ml/mg-year/m<sup>3</sup>) greater declines in FEV<sub>1</sub> than current miners (Soutar and Hurley 1986). In a further evaluation of this cohort, the researchers found among 199 ex-miners with chronic bronchitis, who had left the industry voluntarily, a dust related effect in FEV<sub>1</sub> of 2.4 ml/g h/m<sup>3</sup> (4.17 ml/mg-year/m<sup>3</sup>) (Hurley and Soutar 1986).

Other researchers have considered other potential confounders to describe variation in the magnitude of effects. Seixas et al. (1992) found losses in FEV<sub>1</sub> of up to 27.5 ml/mg-year/m<sup>3</sup>, among a group of new miners and a 15-year cumulative exposure related declines of 5.9 ml in FEV<sub>1</sub> per mg-year/m<sup>3</sup>. The greater effect among new miners compared with old miners found in cross sectional studies has been attributed to differences in cumulative exposures and to "healthy worker" effect (Henneberger and Attfield 1996). Such steep dose response relationships have been attributed to population effects, characterisation of exposure, and non-linearity of the dose response curve (Seixas et al. 1992).

Cross-sectional and longitudinal studies have demonstrated dust-related effects on lung function of varying magnitude, independent of the effects of smoking. Several of these studies have been either part of the British Pneumoconiosis Field Research (PFR) or the United States National Study of Coal Workers' Pneumoconiosis (NSCWP). The early cross-sectional studies, not controlling for employment status, have shown mean losses in FEV<sub>1</sub> ranging from 1.0 to 1.6 ml/mgyear/m<sup>3</sup> (Soutar and Hurley 1986; Henneberger and Attfield 1996; Rogan et al. 1973; Attfield and Hodous 1992).

Although there is consistent evidence to show that declines in FEV1 are associated in a dose-related manner to respirable coal-dust exposure, the magnitude of this association varies amongst different studies. Additionally, few studies have examined differential effects of exposure on lung function among current and ex-miners. No studies of lung function effects have been conducted among South African coal miners, despite the fact that the country is among the top three producers of coal internationally. The aim of the current study was to describe the relationship between occupational respirable dust exposure and lung function among a sample of current and former South African coal miners and specifically to determine whether differential dust-related lung function effects were present between these categories of employees. A further objective was to examine dust-related dose-response relationships while controlling for potential confounding by other risk factors, particularly smoking and a history of tuberculosis (TB).

# **Materials and methods**

The study was approved by the Institutional Review Boards of the Universities of Natal and Michigan. Informed consent was obtained in writing from each of the participants.

Selection of the mining operations

A sample of current and former Black coal miners from three bituminous mines in Mpumalanga Province, South Africa was selected for this study. All mines had coal of similar rank and carbon content and low quartz content. The mining operations selected were among those of the mining company, which agreed to participate in the research project, which had (1) reliable historical environmental monitoring data (i.e. data obtained by acceptable techniques and by trained personnel, with recorded sampling procedures) and (2) were located in a specified geographical region to facilitate study.

Selection of the study sample

A sample of 900 mineworkers was selected. For purposes of sampling, miners were stratified according to employment status (current vs. ex-miners), and according to exposure history: more than 10 years at the coalface, between 2 and 10 years at the coalface and those with less than 2 years at the coalface.

Information from several databases maintained by the mines was merged to form the sampling frame. Collectively, these databases contained information on employment date, current job title, age of worker, salary/wage, company number, date of entry and exit from specific job descriptions and shaft/seam. To diminish potential confounding related to socio-economic status, those in positions higher than or equal to grade 13 (junior management level, administrative positions, etc.) were excluded.

Our review of the ex-employee records at each of the mines failed to provide the total target number (n = 200)of employees because of inadequate mining company records. Therefore, an alternate strategy was used to identify ex-employees. Fieldworkers sought information from the local community about ex-miners in the townships around the mining operations. Those exminers who were so identified and who met the eligibility criteria (formerly employed at the mining operations under study and having left the employ of the mine more than 6 months ago) were invited to participate in the study. Although no ex-employee identified in this manner refused to participate in the study, 24 (out of 212) did not report to the assessment centre as per their appointment. Most of these missed appointments were because of reasons such as job seeking, failure to meet the taxi time etc, and not obviously due to reasons related to health status. This approach to identify exminers did not allow for calculations of participation rates based on a fully enumerated target population.

A total of 188 ex-employees and 684 current employees were assessed. All current employees selected agreed to participate in the project.

# Occupational histories and job descriptions

Occupational histories of the sample of workers employed in the participating mines were extracted from the mine records over the entire period of employment. This involved determining the job description, the seam and section worked, and the duration of work in that job on seam and section. During the interviews, a detailed job history was obtained, using the previously obtained records to aid participants' recall of past jobs.

#### Smoking history

A detailed smoking history included the year of starting, number of cigarettes smoked previously, years smoking this number, number smoked currently, current status (an ex-smoker was defined as having stopped smoking more than a month ago); if the habit was stopped for any period of time greater than 1 year, for how long. Smoking was represented in two ways for analytic purposes: smoking status (current, ex, never) and as pack-years.

#### Pulmonary function assessments

Lung function assessments were conducted following American Thoracic Society standardised criteria by two trained technicians (American Thoracic Society 1995). The same make of equipment (Jaeger Flowmate) was used at all sites. Equipment was volume calibrated every 4 h on the days of testing with a 3-l calibrated syringe. Failure to meet reproducibility criteria was not a basis for exclusion of the subject from the data analysis, as prior studies indicate that this can introduce substantial selection bias (Eisen et al. 1984).

The prediction equations used in this project were derived from a study conducted by Louw et al. (1996) based on a South African Black male population consisting of non-smoking healthy individuals, not involved in activities involving exposure to respiratory hazards. These prediction equations have recently been proposed as the standard for work entry and in service screening of Black South African male miners by Ehrlich et al. (2000). They have been applied previously to Black inservice mining populations and shown to have good statistical fit (Hnidzo et al. 2000). The Louw equations for predicted FEV<sub>1</sub> and forced vital capacity (FVC) are:

$$\begin{split} FEV_1(L) &= -0.535 + 0.029 (height(cm)) \\ &- 0.027 (age(years)) \end{split}$$

$$FVC(L) = -3.08 + 0.048(\text{height}(\text{cm})) \\ - 0.024(\text{age}(\text{years}))$$

Per cent predicted values were calculated and used in subsequent analyses. There was no need for race correction factors for White mineworkers as the study participants were exclusively Black.

# Evaluation of exposure

The exposure evaluation has been described in detail elsewhere (Naidoo 2002). Briefly, several sources of exposure data were used to develop exposure profiles for current and ex-workers in the study. These included the review of all historic dust sampling data that was available at the mining operation and the study of detailed job histories of each worker described above.

The research team did additional sampling over three sampling cycles per mine at each of the three mines. Each cycle was separated in time by intervals ranging from 2 to 4 weeks to allow for better characterisation of variability in dust levels. In each sampling cycle, the same 50 workers per mine were requested to wear personal samplers. Researcher collected data were done using the Mine Services Appliance (MSA) pumps and nylon cyclones according to the National Institute of Occupational Safety and Health (NIOSH) prescribed method 0600 (Department of Health and Human Sciences 1994).

Preliminary regression models of the historic data indicated that variables such as section and job description were not consistent across time and there was no definite trend in exposure measures noted over the years of sampling. The historic and investigator collected data were then combined into a single set. Regression models, using the log of exposure concentration as the dependent variable, were developed using mine, zone (face, backbye or surface), and sampler type, with section, job description and year being excluded.

This regression model allowed for the calculation of the arithmetic mean dust level by the following formula:

$$\chi_{ij} = \{ \exp \left( \beta_0 + \beta_1 \text{mine}_1 + \beta_2 \text{mine}_2 + \beta_3 \text{zone}_1 + \beta_4 \text{zone}_2 + \beta_5 \text{sampler}_1 + (\text{MSE}/2) \right) \}$$

where x = the arithmetic mean, with subscript i = mine and subscript j= zone, with zone<sub>1</sub> = surface and zone<sub>2</sub> = face (backbye used as baseline in the model), MSE = the mean square error of the regression model (the residual variance). Using this information, a mine/ zone exposure matrix allowed for the estimation of exposure for each particular mine, and the particular exposure zone (face, backbye or surface) in which the worker was employed. These estimates were used to calculate a cumulative exposure for each participating worker in mg-year/m<sup>3</sup>: Cumulative dust exposure (CDE<sub>s</sub>) =  $\sum_{ij} x_{ij}$  years<sub>ijs</sub>

where  $x_{ij}$  = arithmetic mean concentration of respirable dust (mg/m<sup>3</sup>) calculated for mine *i* and zone *j* (surface, backbye or face) and *years*<sub>ijs</sub> = years spent in a mine *i* within zone *j* by subject *s*.

#### Analysis

The primary outcome variables of interest were the lung function parameters per cent predicted  $FEV_1$  and FVC. Results of other important outcomes measures, radiographic findings and symptoms will be presented elsewhere. The primary exposure variable was cumulative dust exposure. Covariates examined were: smoking status, previous dusty occupations and history of tuberculosis. All analysis was done using the Statistical Analysis Software (SAS) Version 8.1.

Lung function statistics were calculated for each category of currently employed and ex-miner, further stratified according to exposure zone and for lifetime surface and ever underground workers. Trends were examined by categorising the cumulative dust exposure (CDE) variable approximately into tertiles: low exposure (0.6–20.1 mg-years/m<sup>3</sup>; n = 278); medium exposure  $(20.1-72.8 \text{ mg-years/m}^3; n = 285)$  and high exposure (72. 8–258.7 mg-years/m<sup>3</sup>; n = 294). Analysis of variance was used to test for differences in the mean lung function parameters in the different categories. Simple linear models were first developed using per cent predicted lung function outcomes (FEV<sub>1</sub> and FVC) regressed on cumulative dust exposure and then against pack-years of smoking. The multivariable models examined used per cent predicted FEV1 or FVC as the outcome variable and all included CDE. They also included various combinations of the following covariates and interaction terms:

Covariates	Job status (current vs ex) History of TB Smoking: smoking status (current and ex smoker, never smoker as baseline)
Interaction terms	Pack-years Job status × CDE CDE × smoking status CDE × pack-years Packyears × smoking statu

Standard tests were conducted to assess the fit for these multivariable linear models. Transformations, such as natural logarithm, of the cumulative dust exposure variable and interaction terms between CDE and employment status; CDE and pack-years; packyears and smoking status were considered in the modelling. The criteria used to select the best model were based on the model selection techniques, biological plausibility and objectives of the study (i.e. relationship to cumulative dust exposure, while controlling for important covariates such as smoking and history of TB). The magnitude of the effect estimate was not used as a criterion in selection of final models.

Effects on lung function parameters are presented as per cent predicted, rather than absolute volumes. Development of internal prediction equations for absolute volumes by regressing lung function parameters on age and height would not have been appropriate because of the high correlation between age and exposure in this cohort. To facilitate comparisons to findings in other studies in the literature, per cent of predicted were translated to absolute lung volumes for a standard worker of age (40 years old) and height (1.7 m).

#### Results

#### Demographic data

A total of 896 participants were interviewed, of whom 684 were currently employed on one of the three participating mines. Among the 212 ex-miners, 188 presented for the medical assessments. Height and weight were not available for the 24 miners not reporting for these assessments. Within the total sample there were 222 (24.8%) participants who had never worked underground.

Ex-miners had significantly lower weight and had worked fewer years in coal mining than current workers. The demographics of surface only and ever-underground workers were quite similar (Table 1). The distribution of past history of TB was not significantly different between employment or exposure status strata (current miners = 2.6%; ex-miners = 4.3%; ever underground = 3.1% and surface only = 2.7%).

A total of 237 (26.5%) of workers worked exclusively in mine 1; 201 (22.4%) in mine 2 and 189 (21.1%) in mine 3. The remaining workers [269 (31%)] had worked at two or more of the three mines.

Lung function outcomes and cumulative dust exposure (CDE)

The results of lung function tests of 15 participants were rejected for not meeting American Thoracic Society criteria for either start or end of test and were not used in further analyses.

The mean per cent predicted values of both FEV<sub>1</sub> and FVC were significantly lower in the high exposure category than in the medium exposure category: for FEV<sub>1</sub> (95% CI for the difference: 1.8–8.2% predicted) and for FVC (95% CI: 2.1–7.5% predicted). There were neither statistically significant differences at  $\alpha$ = 0.05 between the high and low exposure categories,

	All		Employ	ment status			Exposi	ire status		
I			Current		Ex-min	er	Ever u	nderground	Surface	only
И	и	Mean (SD)	и	Mean (SD)	и	Mean (SD)	и	Mean (SD)	и	Mean (SD)
Age (years) 8	896	42.45 (8.44)	684	42.46 (7.71)	212	42.42 (10.41)	674	42.03 (8.27)	222	43.59 (8.79)
Height (cm) 8	872	168.90(6.77)	684	168.99(6.91)	188	168.60(6.27)	658	169.29(6.30)	214	168.65 (7.84)
Weight (kg) 8	872	70.12 (12.35)	684	71.52 (12.42)	188	$(5.20^{*}(10.72))$	658	(0.23 (11.30)	214	71.49 (14.61)
Years in coalmining 8	896	15.89(7.96)	684	17.52(7.46)	212	11.05* (7.77)	674	15.73(8.13)	222	16.69(7.69)
Cumulative dust exposure 8	896	58.08 (52.05)	684	67.51 (53.82)	212	27.64 (29.94)	674	72.40 (52.50)	222	14.61* (7.46)
(mg-years/m ) Per cent predicted FEV, 8	857	104.43 (18.34)	699	104.99 (17.69)	188	102.44 (20.39)	649	105.14 (17.98)	208	102.21 (19.29)
Per cent predicted FVC 8	857	103.15(16.05)	699	103.50(15.76)	188	101.93(17.03)	649	104.14(15.61)	208	100.09 (17.02)

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Table 2 Respira	tory health of South Africa	an coal miners: lung functio	n (mean, per cent predicted)	for categories of cumulati	ive dust exposure stratified t	by employment status
	Employment status					
	Current miner $(n = 670)$			Ex-miner $(n = 197)$		
	CDE categories			CDE categories		
	Low (mean = 11 mg-years/m <sup>3</sup> ) $0.62-20.10$ mg-years/m <sup>3</sup> , $n = 174$ [mean (SD)]	Medium (mean = 38 mg-years/m <sup>3</sup> ) 20.11–72.77 mg-years/m <sup>3</sup> , n = 214 [mean (SD)]	High (mean = $107$ mg-years/m <sup>3</sup> ) 72.78–258.70 mg-years/m <sup>3</sup> , n = 282 [mean (SD)]	Low (mean = 11 mg-years/m <sup>3</sup> ) $0.62-20.10$ mg-years/m <sup>3</sup> , $n = 102$ [mean (SD)]	Medium (mean = 38 mg-years/m <sup>3</sup> ) 20.10–72.77 mg-years/m <sup>3</sup> , $n = 72$ [mean (SD)]	High (mean = $107$ mg-years/m <sup>3</sup> ) 72.77–258.70 mg-years/m <sup>3</sup> , $n = 14$ [mean (SD)]
FEV <sub>1</sub> [L (SD)] FEV <sub>1</sub> percent	3.39 (0.76) 103.97 (18.63)	3.57 (0.65) 109.19 (17.06)	3.25 (0.63) 102.44 (17.03)	3.44 (0.75) 103.19 (19.18)	3.19 (0.86) 102.51 (21.86)	2.89 (0.83) 95.52 (21.96)
FVC [L (SD)] FVC per cent	$\begin{array}{c} 4.13 \ (0.86) \\ 102.29 \ (16.92) \end{array}$	4.36 (0.70) 107.66 (14.88)	4.03 (0.69) 101.10 (15.07)	4.20 (0.79) 102.11 (16.45)	4.03 (0.89) 103.18 (17.03)	3.54 (0.91) 92.82 (20.64)
Ratio (%)	81.71 (7.23)	81.27 (7.25)	79.71 (7.45)	80.97 (8.57)	77.72 (11.76)	79.00 (10.66)

Table 3 Respiratory health of South African coal miners: lung function (mean, per cent predicted) for categories of cumulative dust exposure stratified by exposure status

	Exposure status				
	Ever underground (n	=649)		Surface only $(n=208)$	
	CDE categories			CDE categories	
	Low 0.62–20.10 mg-years/m <sup>3</sup> , n=106 [mean (SD)]	Medium 20.11–72.77 mg-years/m <sup>3</sup> , n = 242 [mean (SD)]	High 72.78–258.70 mg-years/m <sup>3</sup> , $n = 301$ [mean (SD)]	Low $0.62-20.10$ mg-years/m <sup>3</sup> , $n = 151$ [mean (SD)]	Medium 20.10–72.77 mg-years/m <sup>3</sup> , $n = 57$ [mean (SD)]
FEV <sub>1</sub> [L (SD)] FEV <sub>1</sub> per cent predicted [% (SD)]	3.60 (0.73) 105.82 (17.69)	3.55 (0.72) 108.54 (18.48)	3.23 (0.63) 102.16 (17.21)	3.25 (0.75) 101.57 (19.88)	3.25 (0.65) 103.91 (17.69)
FVC [L (SD)] FVC per cent predicted [% (SD)]	4.39 (0.76) 105.00 (15.04)	4.37 (0.75) 107.90 (15.44)	4.00 (0.71) 100.81 (15.26)	3.98 (0.86) 99.67 (17.70)	3.98 (0.75) 101.19 (15.13)
Ratio (%) (SD)	81.59 (7.96)	80.53 (8.78)	79.68 (7.67)	81.14 (7.92)	80.69 (7.10)

nor between the low and medium exposure groupings (data not shown).

Among the currently employed, significant differences were seen between the medium versus high and medium versus low categories for per cent predicted  $FEV_1$  [point differences of 6.7% (95% CI: 2.8–9.3) and 5.2% (95%CI: 1.1-8.6, respectively)] and FVC [point difference of 6.6% (95% CI: 2.5-8.3) and 5.4% (95% CI: 1.7–8.4, respectively)] (Table 2). Although the mean differences between low and high exposure categories were even greater for ex-miners, no significant differences in the lung function outcomes were seen across the exposure categories in the ex-miners, owing to a combination of smaller sample size and greater variability (Table 2). Among ex-miners, (in contrast to current miners),  $FEV_1$  and FVC values for those with medium exposure were not notably higher than those with low exposure.

Within the three cumulative dust exposure categories, there were no statistical differences for prevalence of past history of TB, with the low and medium being identical (2.7%), and the high exposure category being 3.7%.

Statistically significant differences between current and ex-miners were seen with respect to per cent predicted FEV<sub>1</sub> and FVC in the medium exposure category (Student's *t*-test *P* value = 0.03), but not in the low or high exposure categories.

When comparing lung function in ever underground and surface only workers, statistically significant differences (P < 0.05) were seen in the per cent predicted FEV<sub>1</sub> and FVC between the two groups in all exposure categories, with the lower values seen in the surface workers (Table 3).

Correlation coefficients were calculated for CDE (as a continuous variable) with each of the lung function outcomes. Per cent predicted  $FEV_1$  for current and exminer were not statistically significantly correlated with CDE, but were in the expected direction (increasing dust exposure results in declines in outcomes). None of the

coefficients for per cent predicted of FVC were statistically significant.

Linear regression models of lung function outcomes

In all multivariable linear regression models, CDE, job status and history of TB were statistically significantly associated with lung function outcomes at  $\alpha = 0.05$ . The three smoking-related terms (current smoker, ex-smoker and pack-years) were statistically significant in a number of models (not shown in tables). An interaction term between job status and cumulative dust exposure was not significant when introduced into the model.

Table 4	Respirato	ry health	of South	African c	oal m	iners.	Linear
regressio	on models	for lung	function	outcomes	. The	table	shows
coefficie	nt estimate	e, standar	d error ar	nd P value			

	Per cent predicted FEV <sub>1</sub>	Per cent predicted FVC
Model $R^2$	0.062	0.048
Intercept	104.87	101.21
CDE $(mg-year/m^3)$	-0.036	-0.028
	0.012	0.011
	0.004	0.009
Current smoker	2.12	5.016
(yes = 1; no = 0)	1.700	1.499
	0.213	0.001
Ex-smoker (yes = 1; $no = 0$ )	-3.016	-0.78
<b>.</b> . ,	1.828	1.612
	0.099	0.629
Employment status	3.91	3.67
(current miner $= 1$ ;	1.582	1.395
ex-miner = 0)	0.014	0.009
Doctor-diagnosed TB	-20.81	-13.56
(yes = 1; no = 0)	3.487	3.075
• • •	< 0.001	< 0.001
Pack-years	-0.26	-0.20
•	0.106	0.094
	0.015	0.033

Linear regression model selection and diagnostics

Model selection procedures were used to suggest appropriate models (adjusted  $R^2$  ( $R_a^2$ ), Mallow's  $C_p$  and *PRESS*<sub>P</sub>). Those models that were statistically appropriate and biologically plausible were subjected to regression diagnostics. Most models were reasonably similar in statistical terms. Based on the research objectives, it was decided that cumulative dust exposure and smoking variables should be retained in the final models. The models shown in Table 4 met these criteria and were subjected to diagnostic assessment. Model diagnostics indicated a good fit for these models.

These models are notable for the statistical significance of CDE, the marked impact of previous history of TB, the protective effect of being a current miner suggestive of the "healthy worker" effect, the negative association with pack-years and the variable positive association with current smoker status and negative association with ex-smoker status, suggesting a current healthy smoker effect.

Independent estimates of effect on lung function of current miners and ex-miners

To better characterise the effects of employment status on lung function, separate regression models were run for those who were still currently employed and subsequently on those who were ex-miners. Models were run for per cent predicted  $FEV_1$  and FVC (Table 5).

The model for current miners looks similar to the unstratified model (Table 4). There is only a marginal decrement in the value of the coefficients for cumulative

**Table 5** Respiratory health of South African coal miners. Independent linear regression models for per cent predicted  $FEV_1$  and FVC outcomes for current and ex-miners. The table shows coefficient estimate, standard error and *P* value

	Per cent j FEV <sub>1</sub>	predicted	Per cent FVC	predicted
	Current miners	Ex-miners	Current miners	Ex-miners
Model $R^2$	0.038	0.124	0.029	0.105
Intercept	108.18	110.08	104.55	104.51
CDE ( $mg$ -year/ $m^3$ )	-0.033	-0.065	-0.027	-0.055
	0.013	0.047	0.011	0.039
	0.009	0.172	0.019	0.166
Current smoker	1.681	-1.045	4.449	3.458
(yes = 1; no = 0)	1.916	4.096	1.714	3.459
	0.3804	0.799	0.009	0.319
Ex-smoker	-2.575	-9.452	-0.601	-4.849
(yes = 1; no = 0)	1.930	5.403	1.727	4.563
	0.183	0.082	0.728	0.289
Doctor-diagnosed	-17.540	-29.379	-9.991	-21.876
TB (yes $=$ 1; no $=$ 0)	4.167	6.747	3.729	5.697
	< 0.001	< 0.001	0.008	< 0.001
Pack-years	-0.153	-0.442	-0.128	-0.306
	0.125	0.208	0.011	0.176
	0.223	0.035	0.253	0.084

dust exposure and doctor diagnosed TB for the current miners.

In the models for ex-miners alone, there is a considerable increase in the overall fit of the model (increased adjusted  $R^2$ ) compared with the models including all miners. The regression coefficients for FEV<sub>1</sub> and FVC for cumulative dust exposure are roughly double those for current miners, as from the previous unstratified models. However, coefficient estimates are no longer statistically significant. Among the models run for the ex-miners, doctor-diagnosed TB showed a statistically marked effect, pack-years is significant and ex-smoker, while not significant at  $\alpha = 0.05$ , shows a large effect.

A similar pattern was observed for FVC predicted outcomes (Table 5). Among current miners, there is little difference in the cumulative dust exposure variable from the unstratified model (Table 4), with a reduction in the estimate for doctor-diagnosed TB.

In the ex-miner regression models, the cumulative dust effect and ex-smoker effect is increased compared with the unstratified models (95% CI: -0.13-0.02 mg-year/m<sup>3</sup>), however, with the exception of doctor-diagnosed TB showing a marked effect, none of the variables reach statistical significance, although packyears is marginally significant.

Clinically important decrements in lung function

In this study, 2.7% (n=24) [1.8% (n=12) of current workers and 5.7% (n=12) of ex-miners] of workers had a FEV<sub>1</sub> of less than 65% predicted. Logistic regression models were developed to determine predictors of reduced lung function outcomes at different levels of clinical significance (less than 65% predicted and 80% predicted, respectively) (Table 6).

A reported history of TB and ex-smoking status was consistently a statistically significant predictor of clinically poor outcomes of  $FEV_1$ . Notable was the statistically significant odds ratio for those in the high exposure

 Table 6 Respiratory health of South African coal miners: odds ratios from logistic regression models for clinically important lung function outcomes

	Odds ratios from models (95% confid	logistic regression lence intervals)
	FEV <sub>1</sub> < 65% ( <i>n</i> = 24)	$FEV_1 < 80\%$ (n = 196)
Medium CDE category High CDE category Current smoker Ex-smoker History of TB Current miner Current miner × high CDE Current miner × medium CDE	$\begin{array}{c} 1.36 \ (0.48-3.83) \\ 2.15 \ (0.40-11.48) \\ 1.39 \ (0.68-2.85) \\ 2.65 \ (1.21-5.81) \\ 8.091 \ (3.34-19.61) \\ 0.65 \ (0.23-1.81) \\ 0.51 \ (0.076-3.39) \\ 0.47 \ (0.11-2.01) \end{array}$	1.43 (0.69–2.93) 4.21 (1.31–13.51) 1.00 (0.68–1.47) 1.68 (1.07–2.65) 5.29 (2.37–11.78) 1.35 (0.73–2.52) 0.21 (0.06–0.74) 0.41 (0.16–0.98)

category of 4.2 compared with those in the low exposure category for  $FEV_1 < 80\%$  of predicted. Among miners with either high or medium cumulative dust exposure, being currently employed had an apparently "protective" effect against abnormal  $FEV_1$ .

# **Discussion and conclusions**

The key findings of this study are the respirable dust related lung function outcomes, for which statistically significant dose response relationships were identified. There still remains some degree of controversy in the international literature for these outcomes. The key findings of this study with respect to these outcomes are contained in the final best linear regression models presented in Table 5.

The study showed important differences in the lung function deficits among current and ex-miners, respectively. For a representative 40-year-old, 1.7-m tall man (Louw predicted values of  $FEV_1 = 3.3 L$ and FVC = 4.1 L), our estimate of coal-dust related effect on FEV<sub>1</sub> in current miners is 1.1 ml/mg-years/m<sup>3</sup> (equivalent to 2.3 g h/m<sup>3</sup>) compared with 2.2 ml/mg-year/m<sup>3</sup> in ex-miners. Among current miners the dust-related effect on FVC is 1.1 ml/mg-years/m<sup>3</sup> (2.2 g h/m<sup>3</sup>) and 2.3 ml/ mg-year/m<sup>3</sup> among ex-miners. For a coal miner with average current exposure at the face  $(1.9 \text{ mg/m}^3)$ , this translates into loss of 2.54 ml/year in FEV<sub>1</sub> and 2.4 ml in FVC for each year of exposure—while controlling for smoking habits and previous TB. This finding suggests that unmeasured factors represented by "employment status" may be leading to an underestimate of the actual dust-related effect on lung function. This supposition is supported to some extent by the findings that, in models run separately for current and ex-miners, the point estimates of effect were greater amongst the ex-miners. These findings of lower lung function in ex-miners than in current miners are consistent with both a "healthy worker" selection (into initial employment) and "healthy worker" survivor effect (i.e. those who are healthier are more likely to be selected for and to remain on underground work compared with surface work and retiring early). Similar differential employment status effects in lung function have not been reported in previous studies among coal miners. Soutar and Hurley (1986) found no statistically significant dust-related difference in  $FEV_1$  between current and ex-miners (a 0.21 ml lower  $FEV_1$  in ex-miners under age of 65, P > 0.05).

Several reasons could explain the differences between this South African coal mining cohort and other studies, including selection of ex-miners into the study, high retrenchment levels in a shrinking industry, allowing for removal of less productive, ill workers or for voluntary exit by sick workers. In South Africa, workers diagnosed with compensable occupational diseases are removed from working underground, and are possibly at greater risk for loss of jobs during retrenchment programmes.

The true extent of the "healthy worker" survivor effect is somewhat uncertain because of the methods of sampling of ex-miners. It is not known to what degree the participating ex-miners are representative of the entire ex-miner population. In South African settings, this general methodology of identifying ex-miners has proved necessary and has been used previously (Trapido et al. 1996; Steen et al. 1997). Ex-miners were drawn from surrounding communities, where migration is much less than it is on the South African gold mines (as reported in the previously quoted studies); thus, the sampling is probably from a substantial fraction of the population. The fact that participation rates of those successfully contacted were quite high, offers some reassurance of limited selection bias among those residing in local communities. The, perhaps surprisingly, low average age for a group of ex-miners (mean age of 42.4 compared with a mean 42.5 years in the current miners) is of uncertain interpretation: this could indicate older workers are likely to relocate elsewhere, or that this is a population of miners developing clinically significant disease relatively early, or simply that those more recently unemployed are more easy to track and find in the community.

Previous studies of coal miners have reported findings consistent with "healthy worker" survivor effects (Lewis et al. 1996; Petsonk et al. 1995). Henneberger and Att-field (1996) found that recently hired current miners showed substantially greater dust related effects on FEV<sub>1</sub> than longer term current workers (-5.9 ml in new compared to -1.2 ml/mg-year/m<sup>3</sup>).

The findings among current workers in our study are quite comparable to those cross-sectional studies reported in the international literature looking at current miners with similar levels of seniority: ranges from 1.3 to 1.6 ml/mg-years/m<sup>3</sup> (Soutar and Hurley 1986; Henneberger and Attfield 1996; Rogan et al. 1973; Attfield and Hodous 1992).

A critical element in our analysis is the reliability of exposure estimation. The absence of historical dust data prior to 1991 meant that certain assumptions had to be made in extrapolating exposures. The regression models used in developing the exposure matrices for each of the different zones in each of the mines was intended to address these shortcomings in the available historical measurements. However, to ensure that our modelling was robust, sensitivity analyses of the exposure estimation and dose responses in lung function were conducted. Each cell in the exposure matrix that described the dust levels across all the years (historical and current) at the face, backbye and surface for each of the three mines, respectively, was multiplied by factors of 3.5, 2.5 and 1.5 for the face, backbye and surface, respectively, for the years prior to 1985. The latter date was used as a cutoff based on the information supplied by key officials at the mining operations, that since this calendar year, greater investment in dust suppression techniques and ventilation has been made. These new exposure levels were then used to re-calculate a revised cumulative dust exposure (CDE) variable. This new variable was then introduced into the previous regression models. This process was repeated with new factors of 3.5, 1.5 and 1, respectively. This sensitivity analysis showed only small changes in the effect of dust on lung function decline—varying from 0.9 to 1.30 ml in FEV<sub>1</sub> per mg-year/m<sup>3</sup>, dependent on the model used. This non-substantial difference in effect suggests that the dose response estimates derived are quite stable. Furthermore, if the "default" assumption that the mean pre-1991 levels were similar to measured levels in the early 1990s is largely correct, this would imply that the apparent toxicity of South African coal dust is within the range found in international mining operations. It should be noted that this assumption regarding the pre-1991 levels was supported in part by the lack of a temporal trend in post-1991 levels (Naidoo 2002).

Although approximately 3% of miners (1.7% of current and 5.7% of ex-miners) suffer from respiratory impairment which is likely to have an important bearing on their daily lives (FEV<sub>1</sub> less than 65% of predicted), it is probable that the countervailing tendencies of the "healthy worker" effect and the dust related effects are reflected in this percentage. The mean loss in  $FEV_1$  for a worker at the coalface with the study average of 1.9 mg/ m<sup>3</sup> dust exposure, over an approximate 30 years underground, would be approximately 90 ml. This is equivalent to approximately a 5-year loss due to age alone in a non-exposed man. Some individuals are likely to be more susceptible to dust-related effects and have substantially greater losses than this predicted mean loss. Workers with already compromised lung function might be driven toward the 65% of predicted level by dust exposure, resulting in disability.

Our pulmonary function data are cross sectional, whereas coal-related decrements measured longitudinally in the same individuals would be the parameter of greatest interest. Several longitudinal studies of declines in lung function among coal miners exposed to respirable dust have been described in the literature. The dose-response relationships found in these studies were somewhat smaller than those found in cross-sectional studies, ranging from 0.05 to 0.07 ml/mg-year/m<sup>3</sup> (Henneberger and Attfield 1996; Attfield 1985; Love and Miller 1982). Ware et al. (1990) have shown that the relationship between cross-sectional and longitudinal data is likely to be complex, with variable findings across different study designs and across age differentials. Therefore, pending a prospective study with repeated measures of pulmonary function on the same individual, our cross-sectional results represent the best available estimates for dust-related decrements in lung function among South African coal miners.

The association of the history of TB variable with lung function outcomes deserves further comment. For pulmonary function outcomes, a history of previous doctor-diagnosed TB, though relatively uncommon (3.0%), was associated with a highly significant and strong relationship to outcomes (an estimated loss of

699 ml FEV1 and 536 ml FVC, in a 40-year-old man, 1.7-m tall). This striking finding may be related to the likelihood that, especially among the Black miners constituting this cohort, TB may be inadequately treated, resulting in more extensive irreversible lung damage than would occur otherwise. These results are similar to those of Hnidzo et al. (2000), who found increasing declines in lung function associated with increasing numbers of episodes of TB and associated with an increasing period from diagnosis to subsequent lung function test among South African gold miners. This latter study, which did not control for dust exposure or smoking history, found a range of loss of  $FEV_1$  from 180 ml (for a single episode of TB) through to 964 ml (for four or more episodes of TB). These results support the idea that TB is a significant contributor to important lung function changes among South African miners.

Smoking is a well recognised independent contributor to declines in lung function. In the multivariable modelling, pack-years was statistically significantly associated with declines in lung function-with, on average, a marginally bigger effect than that of coal dust: each pack-year of smoking contributed to a 8.6-ml decline in the predicted FEV<sub>1</sub> (for a 40-year-old man, 1.7 m tall, equivalent to a lifetime loss of 63.1 ml, given a mean 7.3 pack-years, compared with lifetime dust-related loss of 39.3 ml). Interaction of pack-years with cumulative dust exposure did not show any statistical significance in any of the linear regression models in this study, suggesting that effects of smoking and dust exposure on pulmonary function were independent and additive in this population. The present findings are in keeping with other studies that have found dose related smoking declines in FEV<sub>1</sub> controlling for dust exposure (Soutar and Hurley 1986; Ware et al. 1990).

The generalisability of the findings of this study to the rest of the South African coal mining industry is uncertain owing to the selection of mining operations being essentially a "convenience sample"—based on the co-operation of the mining company and the operations they owned. On the other hand, there is no particular reason to believe that this sample was not representative. The fact that the dose-response estimates are within the range reported in the international literature increases the probability that the findings are representative.

In conclusion, this study has confirmed the effect of coal dust exposure on spirometric lung function. The findings in this study add to the existing body of literature that has found respirable coal-dust-related declines in lung function amongst coal miners, while controlling for various respiratory risk factors, such as smoking and history of past TB. While the dose response found in this study, the first among South African coal miners, suggests that the inherent toxicity of respirable dust in South African coal mines is in a range similar to that found in other parts of the world, it is likely that the true magnitude of effect has been attenuated by the "healthy worker effect". No other study to date has previously Some of the limitations in the interpretation of this study could be addressed by a more comprehensive longitudinal cohort study, focusing on newly hired coal miners. Alternatively longitudinal follow up of the participants in the current study would allow more robust estimates of dose related effects and better evaluation of a "healthy worker survivor effect".

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#### References

- American Thoracic Society (1995) Stardardisation of spirometry—1994 update. Am J Respir Crit Care Med 152:1107–1136
- Attfield MD (1985) Longitudinal decline in FEV1 in United States coal miners. Thorax 40:132–137
- Attfield MD, Hodous TK (1992) Pulmonary function of US coal miners related to dust exposure estimates. Am Rev Respir Dis 145:605–609
- Department of Health and Human Sciences (1994) NIOSH method for particulates not otherwise regulated, respirable, method 0600. NIOSH manual of analytic methods (NMAM), 4th edn. DHHS (NIOSH) Publication, Washington, pp 94–113
- Ehrlich R, White N, Myers J et al (2000) Development of lung function reference tables suitable for use in the South African mining industry. Final Report. Pretoria: Department of Minerals and Energy, SIMRAC Report No.610A

- Eisen EA, Robins JM, Greaves IA et al (1984) Selection effects of repeatability criteria applied to lung spirometry. Am J Epidemiol 120:734–742
- Henneberger PK, Attfield MD (1996) Coal mine dust exposure and spirometry in experienced miners. Am J Respir Crit Care Med 153:1560–1566
- Hnidzo E, Singh T, Churchyard G (2000) Chronic pulmonary function impairment caused by initial and recurrent pulmonary tuberculosis following treatment. Thorax 55:32–38
- Hurley JF, Soutar CA (1986) Can exposure to coalmine dust cause a severe impairment of lung function. Br J Ind Med 43:150–157
- Lewis S, Bennet J, Richards K et al (1996) A cross-sectional study of the independent effect of occupation on lung function in British coal miners. Occup Environ Med 53:125–128
- Louw SJ, Goldin JG, Joubert G (1996) Spirometry of healthy adult South African men. Part I. Normative values. S Afr Med J 86:814–819
- Love RG, Miller BG (1982) Longitudinal study of lung function in coal-miners. Thorax 37:193–197
- Naidoo N (2002) Respiratory health of South African coal miners. Dissertation. University of Michigan, Ann Arbor
- Petsonk EL, Daniloff EM, Mannino DM et al (1995) Airway responsiveness and job selection: a study in coal miners and non-mining controls. Occup Environ Med 52:745–749
- Rogan JM, Attfield MD, Jacobsen M et al (1973) Role of dust in the working environment in the development of chronic bronchitis in British coal miners. Br J Ind Med 30:217–226
- Seixas NS, Robins TG, Attfield MD et al (1992) Exposure-response relationships for coal mine dust and obstructive disease following enactment of the Federal Coal Mine Health and Safety Act of 1969. Am J Ind Med 21:715–734
- Soutar CA, Hurley JF (1986) Relation between dust exposure and lung function in miners and ex-miners. Br J Ind Med 43:150– 157
- Steen TW, Gyi KM, White NW et al (1997) Prevalence of occupational lung disease among Botswana men formerly employed in the South African mining industry. Occup Environ Med 54:19–26
- Trapido ASM, Mqoqi NP, Macheke CM et al (1996) Occupational lung disease in ex-mineworkers—sound a further alarm (letter). S Afr Med J 86:559
- Ware J, Dockery D, Louis T et al (1990) Longitudinal and crosssectional estimates of pulmonary function decline in neversmoking adults. Am J Epidemiol 132:685–700