ORIGINAL ARTICLE

A prospective cohort study among new Chinese coal miners: the early pattern of lung function change

M-L Wang, Z-E Wu, Q-G Du, E L Petsonk, K-L Peng, Y-D Li, S-K Li, G-H Han, M D Atffield

Occup Environ Med 2005;62:800-805. doi: 10.1136/oem.2005.020271

Aims: To investigate the early pattern of longitudinal change in forced expiratory volume in 1 second (FEV1) among new Chinese coal miners, and the relation between coal mine dust exposure and the decline of lung function.

Methods: The early pattern of lung function changes in 317 newly hired Chinese underground coal miners was compared to 132 referents. This three year prospective cohort study involved a pre-employment and 15 follow up health surveys, including a questionnaire and spirometry tests. Twice a month, total and respirable dust area sampling was done. The authors used a two stage analysis and a linear mixed effects model approach to analyse the longitudinal spirometry data, and to investigate the changes in FEV1 over time, controlling for age, height, pack years of smoking, mean respirable dust concentration, the room temperature during testing, and the group×time interaction terms.

Results: FEV1 change over time in new miners is non-linear. New miners experience initial rapid FEV1 declines, primarily during the first year of mining, little change during the second year, and partial recovery during the third year. Both linear and quadratic time trends in FEV1 change are highly significant. Smoking miners lost more FEV1 than non-smokers. Referents, all age less than 20 years, showed continued lung growth, whereas the miners who were under age 20 exhibited a decline in FEV1. Conclusion: Dust and smoking affect lung function in young, newly hired Chinese coal miners. FEV1 change over the first three years of employment is non-linear. The findings have implications for both methods and interpretation of medical screening in coal mining and other dusty work: during the first several years of employment more frequent testing may be desirable, and caution is required in interpreting early FEV1 declines.

See end of article for authors' affiliations

Correspondence to: Dr M-L Wang, NIOSH, 1095 Willowdale Road, Mail Stop H-G900.2, Morgantown, WV 26505, USA; mlw4@cdc.gov

Accepted 18 May 2005

The association between coal mine dust exposure and pulmonary function has been studied intensively in the United States and the United Kingdom. Cross sectional analyses have provided strong evidence for an exposure-response relation between coal mine dust exposure and decrements in lung function; results from longitudinal analyses have confirmed the association, although the findings tend to be weaker than those provided by cross sectional analyses.¹⁻³

Previous analyses among new US coal miners have suggested that longitudinal spirometry changes may be non-linear—for example, an initial rapid decline may be followed by a plateau or partial recovery.²⁻⁴ Improved understanding of the pattern of lung function change in response to dust exposure among new miners should be useful in providing recommendations concerning medical screening for coal miners.

We sought to elucidate the early pattern of lung function changes in new Chinese coal miners and investigate the relation between coal mine dust exposure and the decline of lung function. The results from this US-China collaborative occupational respiratory disease research project provide an additional scientific basis for evaluating and interpreting longitudinal forced expiratory volume in 1 second (FEV1) changes among coal miners and other workers who participate in medical screening and intervention programmes.

METHODS

Subjects and health surveys

The Bureau of Xuzhou Mine in Jiangsu province, China, recruited about 400 new coal miners in three underground mines for the purpose of this study. Among these newly hired

coal miners, 317 volunteered to participate in the study. One hundred and thirty two students enrolled in a mining technical school were included as unexposed referents. This three year prospective cohort study, completed between October 1995 and January 1999, included an initial (preemployment) and 15 follow up health surveys, performed by Chinese health professions at three mine work sites and the mining technical school.

Initial survey

Between October and December, 1995, the 449 participants completed an initial health survey. The initial questionnaire included demographic parameters, a personal and family medical history, and an occupational and smoking history. Initial spirometry included both a baseline and post-bronchodilator test.

Follow up surveys

Follow up health surveys were done on a monthly basis for the first 3 months, bimonthly for the next six surveys, and every three months for five surveys. The last follow up survey was performed at a six month interval, for an aggregate follow up interval of 36 months. Follow up surveys included a questionnaire and spirometry test. The follow up questionnaire recorded changes in respiratory symptoms, job activities, and smoking status. Follow up spirometry did not include bronchodilator testing.

Abbreviations: FEV1, forced expiratory volume in 1 second; PEL, permissible exposure limit

Spirometry testing

Spirometry testing was performed at the worksite immediately before the work shift using a NIOSH dry rolling-seal spirometer (NIOSH, HF6) by Chinese pulmonary function technicians instructed in the 1987 American Thoracic Society spirometry standard.⁵ Data were processed using NIOSH spirometry software. The percent predicted FEV1 (PP FEV1) values were calculated using Hankinson's reference equation for a male Mexican-American population, derived from NHANES III data.⁶

Dust sampling and individual dust exposure estimates

The environmental monitoring included total and respirable dust area sampling, twice a month. Area sampling was performed in the three underground mines at 24 representative work areas by mine inspectors, using a battery operated, two stage area dust sampler (Model AKFC-92A, Changzhou Analytical Instrument Company, Changzhou, Jiangsu Province, China). The first stage of the sampler employs an integral flat impaction plate to capture particles above 10 micron; particles that penetrate the impactor are collected onto an open face 40 mm filter at a flow rate as high as 20 l/min for approximately 15–20 minutes. The sampler determines the total and respirable dust measurements simultaneously. Each individual miner's exposures to total and respirable dust were estimated monthly, based on the sampling results from the miner's work area. At each follow up health survey, estimates of each miner's total and respirable dust exposures were derived using the respective averages of the measurements from the miner's work area during the interval since the previous spirometry. No analysis was performed for silica content.

Data analysis

The statistical analysis was performed using the SAS version 8.0 software package (SAS Institute, Cary, NC, USA). Group comparisons were evaluated using t tests for continuous variables, and χ^2 tests for dichotomous variables. Participants were stratified by group (new miner, referent), age (<20, 20–24, and ≥ 25) and smoking status (current smoker and nonsmoker). The four (1%) former smokers were categorised as non-smokers. Mean total and respirable dust exposures among the miners were dichotomised into "higher" and "lower" at the overall median values.

Preliminary data analysis indicated that miners from the three underground coal mines in Jiangsu Province, China, were similar for initial demographic parameters and spirometry indices; and also that the pattern and the time trend in longitudinal FEV1 changes did not differ significantly among the three mines. Therefore, data from the three mines were combined for analysis.

Longitudinal change of FEV1, often called FEV1 "slope", was computed for each individual across the repeated measures using simple linear regression. The resulting FEV1 "slope" was then used as a variable in the two stage analysis.

The mixed effects model approach was also used to analyse the longitudinal spirometry data. The health outcome variable was the repeated measurement of FEV1. The major interest centred on the patterns of FEV1 changes over time in groups of dust exposed and non-exposed subjects. Mixed model methodology allows detection of the significance of both linear and quadratic time trends in FEV1 changes, and the significance of differences between groups in FEV1 change over the period of study. The group×time interactions included both group×linear time, and group×quadratic time interaction terms.

The selection of the appropriate type of covariance structure was accomplished by considering the biological features of the outcome variable, and also by choosing the smallest Akaike's Information Criterion (AIC) after fitting models with alternative covariance structures. The final models included an unstructured covariance to account for random variation in the intercept and slope parameters between individuals, as well as a spatial power law structure, SP(POW), to count for serial correlation of FEV1 measurements within individuals. The SP(POW) structure for unequally spaced data provides a direct generalisation of the auto regressive order 1 structure, AR(1), for equally spaced data. The AR(1) structure has the property of correlations being larger for proximate times than for distant times.

Covariables included both linear and quadratic terms for baseline age. The time dependent covariables included height, pack years of smoking, mean respirable dust concentration, and the room temperature during testing, with values corresponding to the time of each survey.

RESULTS

Subject characteristics

The study population was relatively young, age averaged 21 years at the initial survey, ranging from 16 to 35. All were male and Asian, with an average 9.2 years of education. At the initial survey, all the referents (students from a mining technical school) were never smokers, and were significantly younger (aged 16–19) and weighed less than the miner group. Among the new miners, 43% were current smokers and 1% former smokers, averaging 0.7 pack years of smoking. The mean initial value of FEV1 and FVC were both significantly higher in the miner group than the referent group. However, the mean percent predicted FEV1 and the mean percent increase in FEV1 after bronchodilator were similar for the two groups. Only 2.5% (11 of 446 subjects) had a $\geq 12\%$ increase in FEV1 post-bronchodilator (table 1).

Dust exposure estimates

Overall, during the three years of the study, both total and respirable dust levels were very high. Of the total 36 monthly estimates of mean respirable dust concentration, 24 exceeded four times the 2 mg/m³ permissible exposure limits (PEL). Only for five months, in 1997, was the monthly average respirable dust concentration under the PEL (see fig 1). During this period in 1997, mean dust levels decreased markedly due to a flood and interruption of mining at one of the three mines. Table 2 shows that the overall means were 23.8 mg/m³ and 8.9 mg/m³ for total and respirable dust, respectively; the median levels were also high, 8.7 mg/m³ for total and 2.7 mg/m³ for respirable dust, and even the 25th percentile value of respirable dust was above 2.0 mg/m³.

Table 1 Group comparison of demographic parameters, pre-employment spirometry, and bronchodilator tests

Grouping	Miners (n = 317)	Referents (n = 132)	p Value
Age	22.3 (2.6)	17.5 (0.8)	0.0001
Height (cm)	170 (4.7)	170 (5.5)	0.5124
Weight (kg)	63 (5.6)	58 (7.5)	0.0001
Smoking (pack years)	0.7 (1.7)	0.0 (0.0)	0.0001
FEV1 (I)	4.47 (0.50)	4.28 (0.48)	0.0002
FVC (I)	5.29 (0.58)	4.82 (0.60)	0.0001
FEV1/FVC (%)	84.8 (7.0)	89.0 (5.9)	0.0001
PP FEV1 (%)	103.5 (10.1)	105.4 (9.8)	0.0668
∆ FEV1-BD (%)†	3.1 (5.5)	2.8 (3.7)	0.5131

Value represents mean (standard deviation).
†Percent change in post-, and prebronchodilator FEV1; one miner missed branchodilator test

802 Wang, Wu, Du, et al

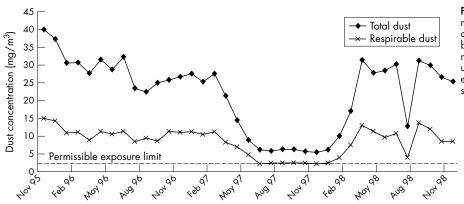


Figure 1 Monthly estimated overall mean total dust and respirable dust concentrations (in mg/m³), based on bimonthly area dust sampling at 24 representative workplaces in three underground mines. Permissible exposure limit (PEL) for US mines is shown for comparison.

Table 2 Estimation of individual miner's exposure to total and respirable dust: distribution of three year mean dust concentration

Dust fraction	Maximal	75th percentile	Median	25th percentile	Minimum	Mean
Respirable (mg/m³) Total (mg/m³)	78.7	3.7	2.7	2.4	0.6	8.9
Total (mg/m³)	186.0	10.7	8.7	7.2	1.8	23.8

Thus, it was not possible to identify miners exposed to a truly low level of dust. The measurements of respirable and total dust were highly correlated (r = 0.987).

Spirometry data overview

In this study, the 449 participants performed over 28 000 forced expiratory manoeuvers, comprising over 5000 spirometry tests, averaging about five tracings per test. We excluded 64 tests due to quality issues. Table 3 shows the number of individuals who completed each survey. The referent group (students) was absent when school was not in session, at the 4th, 13th, and 15th follow up surveys.

Over 90% of the study subjects had five or more valid spirometry results and about 75% completed 10 or more tests; however, only 31 subjects performed all 16 spirometry measurements, excluding post-bronchodilator tests.

Group comparisons of FEV1 slope

Individual FEV1 slopes were calculated for each study participant who had at least three valid FEV1 measurements during the three year study (285 miners, 132 students) by simple linear regression, using all the data points available. The resulting FEV1 slopes were then used as an outcome variable for subsequent analysis. Among the new miners, the individual FEV1 slope averaged -39 ml/year, while an increase of about 160 ml/year was noted among the students; the difference was highly significant. However, age and smoking status were not entirely comparable between the

two groups (see table 1)—the mining technical school students were all less than 20 years old (mean 17.5, range 16–20 years) and never smokers. To facilitate comparisons with the referent group, the miners were stratified by age and smoking status. Among the new miners, there were 30 who were less than 20 years old (mean 19.1, range 16–20 years) and had never smoked and were thus comparable to the referent group. Figure 2 shows that among these non-smoking miners <20 years of age, the yearly decline in FEV1 averaged 22 ml; which was also significantly different than the referent group. Smoking miners lost more FEV1 than non-smokers. The greatest smoking effect was seen among the youngest miners (fig 3).

We stratified miners into higher and lower dust exposure groups for both smokers and non-smokers, using the median values of 8.7 mg/m³ for total dust and 2.7 mg/m³ for respirable dust as cut points. Dust effects were more apparent in non-smokers. A greater dust effect was observed for respirable dust in comparison to total dust, although this was not statistically significant (fig 4).

The pattern and the time trend of longitudinal change in FEV1

To investigate the pattern and the time trend of longitudinal change in FEV1, we used a mixed effects model approach. As the room temperature during testing varied considerably over the course of the study, we included room temperature as a covariate in the mixed effects model analysis to adjust for any

Table 3 Initial (I) and 15 follow up (F) spirometry tests: the time interval from the initial survey and the number of participants for each survey

	Survey															
	I	F1	F2	F3	F4	F5	F6	F7	F8	F9	F10	F11	F12	F13	F14	F15
Interval* Miners (n)	0 317	1 228	2 225	3 229	5 210	7 214	9 241	11 220	13 225	15 225	18 193	21 154	24 167	27 190	30 164	36 190
Referents (n)	132	73	96	121	0	131	130	110	121	125	122	110	114	0	119	0

*Months from initial survey.

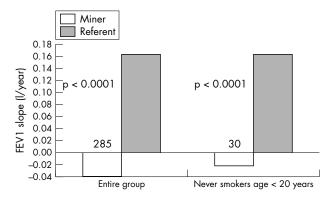


Figure 2 Comparisons of group mean three year FEV1 slopes (I/year) for 132 referents versus 285 new miners and also for 132 referents versus the subgroup of 30 non-smoking new miners less than 20 years of age. For both comparisons, p values were highly significant.

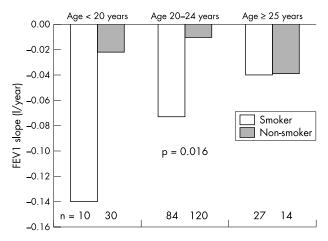


Figure 3 Comparisons of group mean three year FEV1 slopes (I/year) in 285 new coal miners by smoking status: current and former smokers versus non-smokers in three age categories. A significant smoking effect was observed in the 20–24 year age group.

temperature effects. Table 4 lists the parameter estimates and p values obtained, after adjusting in the model analysis for baseline age, and the time dependent variables of height, pack years of smoking, room temperature during testing, and mean respirable dust concentration. Linear and quadratic time trends for FEV1, and the group × time interaction terms, were all highly significant.

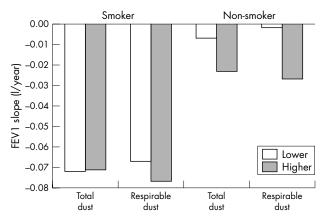


Figure 4 Comparisons of group mean three year FEV₁ slopes (I/year) in 285 new coal miners by dust level in both smokers and non-smokers—higher dust level versus lower dust level, using the median values of 8.7 mg/m³ for total dust and 2.7 mg/m³ for respirable dust as cut points.

The mixed effects model analysis was also performed after stratifying the new coal miners by age: age <20, or age ≥20. The results were very similar to those listed in table 4. To illustrate the patterns of FEV1 change over time among miners and referents, we plotted FEV1 changes over time using the estimated partial regression coefficients for "time" and the "group × time" interactions from the age stratified model (fig 5). Miners in both age groups showed relatively sharp FEV1 declines during the first year, a plateau during the second year, and a partial recovery during the third year. In contrast, the referents showed a fairly linear increase throughout the study period.

DISCUSSION

The study miners showed a relatively sharp decline in FEV1 during their first year of coal mining, followed by a plateau during the second year, and a partial recovery during their third year. A dust effect was apparent when comparing miners and referents, particularly using respirable dust measures, but a dose response relation among new miners was not clearly observed, possibly related to the absence of a "low" dust exposure level. By testing frequently during the first three years of employment in a large number of new coal miners, by including a comparison group, and by applying a mixed effects statistical model, we were able to identify highly significant linear and quadratic time trends in FEV1 in relation to the duration of coal mine exposures.

Table 4 Parameter estimates obtained from mixed effects model analysis of repeated measures of FEV1 p Value **Effect** Estimate (litres) Standard error Grouping 0.2560 0.08374 0.0023 Baseline age (year) Age² (year²) -0.00580.001792 0.0012 Height (cm) 0.0288 0.003188 < 0.0001 -0.01000.01163 0.3904 Pack years Mean respirable dust (mg/m³) -0.00020.000210 0.3033 Temperature (℃) 0.0100 0.000276 < 0.0001 Group Referents 3.4005 1.0868 0.0019 -3.3475 1.1417 0.0035 Group Miners 0.0084 0.001527 Referents < 0.0001 Time × group 0.000997 < 0.0001 Time×group Miners -0.0128Referents -0.0001 0.000046 0.0080 Time×time×aroup Time×time×group 0.0003 0.000026 < 0.0001 Miners

804 Wang, Wu, Du, et al

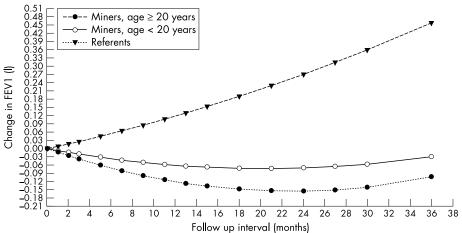


Figure 5 Pattern of FEV1 change (litres) over three years of follow up using coefficients from mixed effects model analysis, for referents, new miners age <20, and new miners age ≥20 groups.

The time course of lung function change observed among coal miners in the current study is consistent with the findings from two previous reports. Seixas and colleagues reported longitudinal and cross sectional analyses of pulmonary function in 977 new miners.2 The report by Seixas' et al documented exposure related loss of lung function among the study miners early in their mining tenure, but the losses over time were not linearly related to cumulative exposure. During the first few years of mining (less than five), the miners seemed to experience a rapid loss of lung function associated with their exposure to respirable coal mine dust, followed by a subsequent slowing of the decline, or recovery. Lung function changes during the initial years of coal mining have also been reported by Hodous and Hankinson.4 In their study, pulmonary function tests were completed by a group of 65 new miners every six months for two years, and once more five years later. The 65 miners showed an accelerated loss of function during the first two years of mining, with the rate of decline in FEV1 levelling off in subsequent years.

An additional important observation from the current study relates to the relative youth of most of the study participants. The unexposed comparison group (mean age 17.5 years at initial survey) showed continuing lung growth during the three year study, while the comparable group of young, non-smoking miners (mean age 19.1 years at initial survey) experienced a decline in FEV1 over the period. The effect of smoking on FEV1 was also greatest among those under 20 years of age. Although there have been few studies of the functional effects of dust exposures among young adults, the exposure related differences we observed in the time course of lung function changes among individuals less than age 20 are consistent with previous observations.⁸⁻¹⁰

Multiple mechanisms appear to be responsible for the lung function loss observed among coal miners. Complicated pneumoconiosis, emphysema, and mineral dust airway disease have all been associated with important lung function deficits among coal miners,11 but all three conditions have latencies measured in years, and are thus unlikely to explain the loss in lung function observed during the first few years of coal mine employment. Bronchospasm may result from the inhalation of coal mine dust, particularly among individuals with airway hyperresponsiveness, and could potentially result in early loss of lung function among miners.12 13 However, airway hyperresponsiveness occurs only in a minority of individuals, and increased responsiveness may be particularly uncommon among individuals who work in dusty jobs, making it less likely that bronchospasm explains the early FEV1 declines seen among many new miners.14 In contrast, symptoms of bronchitis are frequently

reported by miners, and several studies have associated the presence of these symptoms with a significant deficit of lung function. ¹⁵ We speculate that the early sharp decline in lung function observed in this and other studies of dust exposed workers may be related to the development of inflammation in the larger conducting airways. The associated bronchial gland enlargement and increased mucous production may result in a reduction in the caliber of the large conducting airways, as observed in association with bronchitic symptoms by Hankinson and colleagues. ¹⁶ Lung function loss may also result from inflammatory processes in small airways among dust exposed individuals, and small airways disease in coal miners has been previously reported. ¹⁷

Two separate methodologies were used to analyse the lung function results from the current study: a two stage analysis and a linear mixed effects model approach. In the two stage analysis, the "slope" represents a lung function outcome that is conceptually easy to interpret, but which cannot precisely describe non-linear effects over time. Mixed model methodology offers new capabilities in analysing longitudinal data. Historically, missing data have caused serious problems in the statistical analysis of repeated measures, but such problems do not generally arise with the mixed model approach, as long as the missing data are random.7 In this study, a proportion of the survey results were missing. However, aside from the school breaks, we did not detect any patterns or specific reasons for missing results. Most absences were not due to health problems and it appeared that failure to attend a health survey was a random event. In addition, the high number of tests requested for each participant in this study (total 16 measurements in three years) may partially compensate for the influence of missing data. Mixed model methods also permit modeling the covariance structure of the data, which is especially important for analysis of repeated measures. SAS PROC MIXED provides a rich assortment of covariance structures, including those applicable to unequally spaced data.18 In the present study, the final models included an unstructured covariance to account for random variation in the intercept and slope parameters between individuals, as well as a spatial power law structure, SP(POW), to account for serial correlation of FEV1 measurements within individuals. The results emphasise the utility of mixed effects models in evaluating non-linear patterns of FEV1 change over time.

The current study has several limitations. Firstly, the miners and the referents were not entirely comparable, especially for age and smoking status. To help mitigate the effect of these differences in the analysis, study participants were stratified by age and smoking. A second drawback of the study is the

excessive temperature variation that occurred during spirometry tests. Room temperatures less than 17°C are not recommended by the American Thoracic Society, but could not entirely be avoided in the Chinese mining facilities.5 To account for the temperature effects, room temperature was included in the statistical models.19 Mining conditions also varied considerably during the study, including a temporary closure of one of the mines (due to flooding), and this reduced the mean exposures for miners at that location. Finally, the airborne dust exposures documented during the study were quite high, compared with current coal mining conditions in Europe and North America. None of the miners experienced a truly "low" dust exposure, and this diminished the ability of the study to detect exposure-response relations.

CONCLUSION

This prospective study of lung function among new Chinese coal miners demonstrated that a rapid decline in FEV1 occurs during the first year of mining, while the second year shows little change. A partial recovery may be seen during the third year. Both linear and quadratic time trends in FEV1 are highly significant. The finding of an early steep decline in lung function has implications for workplace health monitoring in underground coal miners and probably among other dusty trades. During the first several years of dusty work, an important FEV1 decline may occur, and periodic testing is desirable to document these early changes. However, due to the non-linear pattern of change, caution is required in interpreting the early declines in lung function, and linear projections based on the first years of exposure are likely to be inaccurate. The long term implication of these findings requires further study, particularly to determine if dust exposures in young adulthood preclude the attainment of full ventilatory capacity, and to further evaluate the relation of early rapid FEV1 declines to the development of chronic obstructive pulmonary disease in later life.

Main messages

- A three year prospective study of the early pattern of lung function and dust exposure was done among newly hired Chinese underground coal miners and non-mining referents.
- FEV1 change over the first three years of mining employment is non-linear.
- New miners experience an initial rapid FEV1 decline, primarily during the first year of mining, little change during the second year, and partial recovery during the third year.
- Referents, all <20 years of age, showed continued lung growth, whereas miners of the same age exhibited a decline in FEV1

Policy implications

- During the first several years of dusty work, an important FEV1 decline may occur, and periodic testing is desirable to document early changes.
- Caution is required in interpreting the early declines in lung function in dusty trades, and linear projections based on the first two years of exposure are likely to be inaccurate.

ACKNOWLEDGEMENTS

We want to thank Dr John Hankinson for his support and thoughtful suggestions in evaluating the study lung function data and the manuscript, Dr James Wassell for his comments in data analysis, Raymond Petsko for superb technical support for the spirometry systems, and Diana Freeland for instructing our Chinese colleagues on the spirometry systems. Many other NIOSH staff made valuable contributions to the project, including Barbara Bonnett, Al Dieffenbach, Kathy Fedan, and Betsy Viola. We also greatly appreciate the efforts by our Chinese colleagues Chenghong Wei and Junyao Li from Tongji Medical University; and the staff of the Mine Hospital, the mine bureau leadership, the coal mine inspectors who performed the sampling, and the mining technical school students and the coal miners who completed the many surveys essential to the success of this projects. This research was supported by the Centers for Disease Control and Prevention, National Institute for Occupational Safety and Health.

Authors' affiliations

M-L Wang, E L Petsonk, M D Atffield, National Institute for Occupational Safety and Health, Division of Respiratory Disease Studies, Morgantown, WV, USA

Z-E Wu, K-L Peng, Tongji Medical College of Huazhong University of Science and Technology, Wuhan, People's Republic of China Q-G Du, Y-D Li, S-K Li, G-H Han, Xuzhou Mining Group Company Ltd., Xuzhou, Jiangsu, People's Republic of China

Supported by NIOSH.

REFERENCES

- 1 Attfield MD, Hodous TK. Pulmonary function of U.S. coal miners related to dust exposure estimates. Am Rev Respir Dis 1992;145:605–9.

 2 Seixas NS, Robins TG, Attfield MD, et al. Longitudinal and cross sectional
- analyses of exposure to coal mine dust and pulmonary function in new miners. Br J Ind Med 1993;**50**:929–37.
- 3 Henneberger PK, Attfield MD. Coal mine dust exposure and spirometry in experienced miners. Am J Respir Crit Care Med 1996;153:1560-6.
- 4 Hodous TK, Hankinson JL. Prospective spirometric study of new coal miners. In: Proceedings of the international symposium on pneumoconiosis. Shenyang, PR China, May 30-June 2, 1988:206-10.
- 5 American Thoracic Society. Standardization of spirometry: 1987 update. ATS statement. Am Rev Respir Dis 1987;136:1285–98.
- 6 Hankinson JL, Odencrantz JR, Fedan KB. Spirometric reference values from a sample of the general U.S. population. Am J Respir Crit Care Med 1999;159:179–87.
- Littell RC, Milliken GA, Stroup WW, et al. SAS System for Mixed Models. Cary, NC: SAS Institute Inc, 1996:87-134.
- 8 Bakke PS. Factors affecting growth of FEV1. Monaldi Arch Chest Dis 2003:59:103-7.
- 9 Apostol GG, Jacobs DR Jr, Tsai AW, et al. Early life factors contribute to the decrease in lung function between ages 18 and 40: the Coronary Artery Risk Development in Young Adults study. *Am J Respir Crit Care Med* 2002; **166**:166-72.
- Carta P, Aru G, Barbieri MT, et al. Dust exposure, respiratory symptoms, and longitudinal decline of lung function in young coal miners. Occup Environ Med 1996;**53**:312–19.
- Petsonk EL, Attfield MD. Respiratory Diseases of Coal Miners. In: Rosenstock L, Cullen M, Brodkin CA, Redlich CA, eds. Textbook of clinical occupational and environmental medicine, 2nd edn. Philadelphia: WB Saunders Company,
- 12 Dubois AB, Dautrebande L. Acute effects of breathing inert dust particles and of carbachol aerosol on the mechanical characteristics of the lungs in man: Changes in response after inhaling sympathomimetic aerosols. J Clin Investigation 1958;37:1746-55.
- Investigation 1958;37:1740-55.
 Lapp NL, Hankinson JL, Burgess DB, et al. Changes in ventilatory function in coal miners after a work shift. Arch Environ Health 1972;24:204-8.
 Petsonk EL, Daniloff E, Mannino DM, et al. Airway responsiveness and job
- selection: a study in coal miners and nonmining controls. Occup Environ Med
- 15 Rogan JM, Attfield MD, Jacobsen M, et al. Role of dust in the working environment in development of chronic bronchitis in British coal miners. Br J Ind Med 1973:30:217-26.
- 16 Hankinson JL, Reger RB, Morgan WK. Maximal expiratory flows in coal miners. Am Rev Respir Dis 1977;116:175–80.
- Hall DR, Lapp NL, Reger R, et al. Small airways disease in coal miners. A longitudinal study. Bull Physiopathol Respir (Nancy) 1975;11:863-77.

 Cnaan A, Laird NM, Slasor P. Using the general linear mixed model to
- analyse unbalanced repeated measures and longitudinal data. Stat Med 1997;**16**:2349–80.
- 19 Hankinson JL, Viola JO. Dynamic BTPS correction factors for spirometric data. J Appl Physiol 1983;55:1354-60.