HHS Public Access

Author manuscript

Occup Environ Med. Author manuscript; available in PMC 2015 August 03.

Published in final edited form as:

Occup Environ Med. 2014 January ; 71(1): 30–39. doi:10.1136/oemed-2013-101597.

Respiratory disease mortality among US coal miners; results after 37 years of follow-up

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Abstract

Objectives—To evaluate respiratory related mortality among underground coal miners after 37 years of follow-up.

Methods—Underlying cause of death for 9033 underground coal miners from 31 US mines enrolled between 1969 and 1971 was evaluated with life table analysis. Cox proportional hazards models were fitted to evaluate the exposure-response relationships between cumulative exposure to coal mine dust and respirable silica and mortality from pneumoconiosis, chronic obstructive pulmonary disease (COPD) and lung cancer.

Results—Excess mortality was observed for pneumoconiosis (SMR=79.70, 95% CI 72.1 to 87.67), COPD (SMR=1.11, 95% CI 0.99 to 1.24) and lung cancer (SMR=1.08; 95% CI 1.00 to 1.18). Coal mine dust exposure increased risk for mortality from pneumoconiosis and COPD. Mortality from COPD was significantly elevated among ever smokers and former smokers (HR=1.84, 95% CI 1.05 to 3.22; HR_K=1.52, 95% CI 0.98 to 2.34, respectively) but not current smokers (HR=0.99, 95% CI 0.76 to 1.28). Respirable silica was positively associated with mortality from pneumoconiosis (HR=1.33, 95% CI 0.94 to 1.33) and COPD (HR=1.04, 95% CI

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Disclaimer The findings and conclusions in this report are those of the authors and do not necessarily represent the views of the National Institute for Occupational Safety and Health (NIOSH).

Competing interests None.

Patient consent Obtained.

Ethics approval The study protocol was approved by Institutional Review Boards at CDC-NIOSH and the University of Illinois at Chicago.

Provenance and peer review Not commissioned; externally peer reviewed.

0.96 to 1.52) in models controlling for coal mine dust. We saw a significant relationship between coal mine dust exposure and lung cancer mortality (HR=1.70; 95% CI 1.02 to 2.83) but not with respirable silica (HR=1.05; 95% CI 0.90 to 1.23). In the most recent follow-up period (2000–2007) both exposures were positively associated with lung cancer mortality, coal mine dust significantly so.

Conclusions—Our findings support previous studies showing that exposure to coal mine dust and respirable silica leads to increased mortality from malignant and non-malignant respiratory diseases even in the absence of smoking.

INTRODUCTION

Mortality from respiratory disease remains an important occupational hazard among coal miners. The prevalence of coal workers' pneumoconiosis (CWP) among US coal miners has increased since the mid-1990s after a steady decline following passage of the 1969 Federal Coal Mine Safety and Health Act which mandated exposure limits for respirable dust.[12] A causal relationship between occupational exposures to coal mine dust and mortality from non-malignant respiratory disease (NMRD), including CWP and chronic obstructive pulmonary disease (COPD), is well established.[3–5] While lung cancer has also been examined extensively in the epidemiological literature, it remains unclear whether coal miners are at increased risk for death from lung cancer.[6–16]

The first research programme that included estimates of cumulative coal mine dust exposure in their studies of coal miners was the British Pneumoconiosis Field Research (PFR) programme. The PFR recruited coal miners from British mines between 1953 and 1958.[17] In the latest mortality follow-up, which included 18 000 miners from 10 mines, evidence of increased risk of mortality from pneumoconiosis and COPD with exposure to coal dust and respirable quartz dust was observed in internal analyses.[6] In the USA, enrolment in a similar study, the National Study of CWP (NSCWP), began in 1969. Mortality data from that study, conducted after an average follow-up of 23 years, found statistically significant relationships between cumulative exposure to coal mine dust (before 1969) and mortality from pneumoconiosis and COPD after controlling for age, smoking and coal rank.[7] A relationship was also observed between increasing coal rank and mortality from pneumoconiosis.

A deficit of lung cancer was first reported among coal miners in 1936.[8] Subsequent cohort studies have found mixed results; however, many did not include smoking histories and may have been negatively biased from smoking bans in the mines and by the healthy worker effect.[9–1618] Neither of the most recent follow-up studies from the PFR or NSCWP observed an overall excess of lung cancer mortality. However, the PFR study reported an excess in the most recent years of follow-up as well as increased risk of lung cancer with increased quartz exposure but not with coal mine dust exposure.[6] An excess of lung cancer was also observed in the extended follow-up of the NSCWP cohort, indicating that reported deficits in lung cancer mortality may not be sustained when the cohorts have longer follow-up.[19]

Our study extended the follow-up of the NSCWP by 13–15 years, for an average total follow-up of 37 years. Cumulative silica exposure was estimated in a new analysis and used to explore its role in respiratory disease mortality. Employment termination date was

obtained for most of the study cohort and used to estimate additional exposures after the initiation of the study in 1969 and to control for time since last exposure (TSLE), as it has been suggested that this may reduce bias from the healthy worker survivor effect.[20]

METHODS

The design of this cohort has been previously described.[2122] In brief, 9078 working underground coal miners were enrolled from 31 US mines between 1969 and 1971. Information on respiratory symptoms, work history, smoking history and demographics were collected at enrolment by questionnaire. Participants received full-format postero-anterior chest radiographs. Geographical region was used as a proxy for coal rank (coal-rank region), a measure of the coal's fixed carbon content. The propensity of coal to cause CWP has been shown to increase with coal rank.[34] As with previous analyses of this cohort, we defined regions in decreasing coal-rank order as follows: eastern Pennsylvania, eastern Appalachia (central Pennsylvania and eastern West Virginia), western Appalachia (western Pennsylvania, western West Virginia, eastern Ohio, western Virginia, eastern Kentucky, Tennessee and Alabama), Midwest (western Kentucky, Illinois and Indiana) and West (Colorado and Utah).[7]

Exposure estimates

Estimates of cumulative coal mine dust exposure for each mine were previously developed as the summation of the products of each job-specific dust concentration and the duration of time worked at that job.[22] For this study, we constructed estimates of respirable quartz dust exposure by using Mine Safety and Health Administration compliance data from 1982 to 2002. Data were obtained from Mine Safety and Health Administration under the Freedom of Information Act and estimates were compiled with technical assistance from the National Institute for Occupational Safety and Health Division of Respiratory Disease Studies. We determined the mean per cent silica within each of the five regions for each Lainhart job grouping.[23] Lainhart groupings include the following job categories: underground face, transportation, maintenance and miscellaneous activities; and, surface transportation, maintenance, tipple, strip mining and miscellaneous activities. We calculated job-specific silica estimates by multiplying the percentage of respirable silica for each region and Lainhart job category by the mean coal mine dust concentration estimate for each job within the region. We then assigned an individual cumulative silica exposure estimate to each study participant by summing the product of the number of years at each job by the corresponding region-specific and job group-specific silica exposure estimate.

Vital status ascertainment

We determined the vital status of this cohort through 31 December 2007. We submitted records of the 5636 participants alive when the previous follow-up concluded (31 December 1993) to the Social Security Administration to determine vital status. We then submitted the 3081 records identified as deceased or unknown to the National Death Index to confirm vital status and obtain cause of death.

Employment termination date

We sought termination date for employment as a coal miner for cohort members from the United Mine Workers of America Health and Retirement Funds (UMWA Funds) and the Department of Labor (DOL), Office of Workers' Compensation Programs. When conflicting dates were provided, we considered the DOL date more reliable. We coded any termination date greater than 1 year after death as missing.

Statistical methods

We conducted modified Life Table Analysis using the National Institute for Occupational Safety and Health Life Table Analysis System (LTAS) mortality programme.[24] The LTAS calculates person-days for follow-up time from the date of enrolment in the study until date of death or end of follow-up. Expected deaths were calculated by applying the age-specific, race-specific and calendar year-specific mortality rates for all US men to the person-years in each corresponding group of the study population. SMRs and 95% CIs were calculated as the ratio of the observed to the expected numbers of deaths for all deaths due to pneumoconiosis, COPD and cancers of the trachea, bronchus and lung (henceforth, 'lung cancer'). Underlying cause of death was assigned by LTAS using the International Classification of Diseases revisions 8 through 10, according to the year of death (for specific codes, see online supplemental table I). We also calculated SMRs for these outcomes stratified by coal-rank region, race, chest X-ray status at enrolment and calendar year.

Cox proportional hazards analysis—We explored the associations between coal mine dust and respirable silica exposure with mortality from pneumoconiosis, COPD and lung cancer using Cox proportional hazards models. The time dimension used was follow-up time. The variables investigated as potential risk factors and/or effect modifiers of mortality associated with the two exposures included (the last level listed was the reference group): coal-rank region (eastern Pennsylvania, eastern Appalachia, western Appalachia, Midwest and West), race (black or white), calendar year of death (1970–1989, 1990–1999 and 2000–2007), and for outcomes other than pneumoconiosis, smoking status (ever, former or never); pack years at enrolment. All models included age at enrolment and birth year. We analysed coal mine dust and silica exposures in separate models (single-exposure models) and same models (dual-exposure models).

To evaluate the best model fit of the exposure-response relationship we explored alternative parameterisations of the continuous variables (eg, log transformed) using the likelihood ratio test and analysed both exposures as categorical variables grouped into approximate quartiles among the deceased. We assessed interaction between the exposure terms and covariates by including a cross-product term and considered interaction present if the p value for that term was significant ($\alpha<0.05$). We included covariates in the model if their addition resulted in a change of greater than 10% in the HR estimate for the exposure(s) or if inclusion of the covariate significantly improved the model fit (using the likelihood ratio test). We tested the validity of the proportional hazards assumption by testing for interaction between follow-up time and each exposure.

Subcohort analyses—We calculated TSLE as the interval between employment termination date and death or end of follow-up. We controlled for TSLE as a continuous variable for all outcomes. We further explored the associations between coal mine dust and lung cancer mortality by stratifying the models by categories of calendar time (grouped as described above) and TSLE. For the categorical TSLE variable the reference category included miners who died of lung cancer within a year of leaving work, we then grouped the remaining by approximate tertiles among the lung cancer deaths (<1 year; 1 year to ≤10 years; 11 years to ≤18 years; and >18 years).

All regression analyses were conducted using SAS V.9.2 (PROC PHREG).

Sensitivity analysis—Exposures after study enrolment were not included in this cohort's original exposure estimates, which could have introduced exposure misclassification. Reports from previous follow-ups of this cohort proposed that any such exposure misclassification may be minimal because participants likely accumulated most of their exposure before enrolment.[7,11] To explore the robustness of these assumptions after 37 years of follow-up we conducted a sensitivity analysis among the miners with a known employment termination date. We calculated extended exposure estimates by assuming that miners remained at the job recorded at time of study enrolment through the end of their coal mining employment. We multiplied the dust concentration associated with this job by the number of years from study enrolment to employment termination. We then added that quantity to the previously cumulative exposure estimate; this became the extended exposure estimate. We assessed the associations between the original exposures calculated through enrolment into the study and extended exposures using Cox proportional hazards models with mortality from each of the three outcomes.

RESULTS

Study participation and inclusion

Of the 9033 participants for whom vital status was determined at the previous follow-up, we included 8829 (97.7%) in the current study. We excluded 137 (1.5%) participants due to missing or invalid data and 67 (0.7%) because they were lost to follow-up.

Descriptive statistics

The mean age at enrolment was 45 years (range 17–69). Most participants were either current (54%) or former (26%) smokers (table 1). The average tenure in coal mining was 21 years, with an average of 9 years working at the coal face. The mean cumulative exposure was 64.6 mg/m^3-years (range 0.1–346.9 mg/m^3 years) for coal mine dust and 2.6 mg/m^3-years (range 0.5–14.2 mg/m^3-years) for respirable silica. The correlation between coal mine dust and silica exposures was significant but only moderately strong (Pearson's correlation coefficient=0.29, $p<0.01$).

Modified life table analysis

By the end of follow-up, 5907 (67%) participants had died. There were 399 deaths attributable to CWP pneumoconiosis and 4 to silicosis (analysed as 403 deaths due to

pneumoconiosis); 309 to COPD; and 568 to lung cancer as the underlying cause of death (table 2).

We observed excess mortality from COPD, (SMR=1.11; 95% CI 0.99 to 1.24) and pneumoconiosis-related mortality (SMR=79.70; 95% CI 72.1 to 87.67; table 2). SMRs increased monotonically by calendar year of death for pneumoconiosis and lung cancer and for all outcomes were positive and significant only in the more recent follow-up periods. Concerning regional distribution, for COPD significant excess mortality was seen only in the Midwest (SMR=1.44; 95% CI 1.07 to 1.88). In contrast, SMRs for pneumoconiosis were lowest in the Midwest and dramatically higher in the highest coal-rank region, eastern Pennsylvania, which also had the highest mean cumulative coal mine dust values.

We saw a borderline significant excess mortality due to lung cancer (SMR=1.08; 95% CI 1.00 to 1.18, p=0.06 table 2). Lung cancer SMRs varied by region, with higher risk in western Appalachia and the Midwest and lower risk in the West. These findings may be partially confounded by smoking, the single strongest known population risk factor for lung cancer, as the largest proportion of ever smokers was in the Midwest (86.7%) and a lower proportion was in the West (81.7%). However, the percentage of ever smokers in eastern Appalachia (82.3%), where we saw no excess lung cancer mortality, was equivalent to that in western Appalachia (82.4%), where we did see an excess. We observed a significant excess of lung cancer mortality (SMR=1.13; 95% CI 1.04 to 1.24) among workers who had no evidence of pneumoconiosis on their radiograph at baseline and an apparent decreasing trend in SMRs for lung cancer with increasing severity of pneumoconiosis (from chest X-ray) at the start of follow-up.

Cox proportional hazards analysis

Chronic obstructive pulmonary disease—In models including coal mine dust and silica exposures, the exposure-response relationship between coal mine dust and COPD mortality was modified by smoking status at enrolment (p=0.005 for interaction; table 3). The association was positive among never smokers and former smokers (respectively: HR^{i}=1.84; 95% CI 1.05 to 3.22 and HR^{i}=1.52; 95% CI 0.98 to 2.34), but not among current smokers (HR^{i}=0.99; 95% CI 0.76 to 1.29). The best model fit for cumulative respirable silica exposure was obtained using the log-transformed variable, where silica exposure had a borderline significant association with COPD mortality (HR^{ii}=1.04; 95% CI 0.96 to 1.14).

Pneumoconiosis—We found that in models that included both exposures, the exposure-response relationship between cumulative coal mine dust exposure and mortality from pneumoconiosis was modified by region (p value for interaction=0.03; table 3) such that the strongest associations were seen in eastern Pennsylvania (highest coal rank; HR^{i}=1.86; 95% CI 1.43 to 2.42) and eastern Appalachia (next highest coal rank; HR^{i}=2.58; 95% CI 1.78 to 3.74). We also observed a borderline significant association with silica exposure, best fit as a log-transformed continuous variable, and pneumoconiosis-related mortality (HR^{ii}=1.33; 95% CI 0.94 to 1.90).

[i]HRs for coal-mine dust exposure are presented for the cohort's mean exposure, 64.6 mg/m^3-years.
[ii]HRs for respirable silica exposure are presented for the cohort's mean exposure, 2.6 mg/m^3-years.

TSLE was a strong negative predictor of mortality from COPD and pneumoconiosis (HR^i 0.86, 95% CI 0.85 to 0.88; HR^i 0.81, 95% CI 0.79 to 0.82, respectively; see online supplemental table II). Adding TSLE improved the model fit, generally resulting in a marked increase in the magnitude of the association between exposures and pneumoconiosis-related mortality. The increase in the strength of the association we observed when controlling for TSLE was particularly strong when modelling silica as a continuous variable with pneumoconiosis mortality, and for the association between coal mine dust and COPD mortality within each level of smoking status.

Lung cancer—In all models we obtained the best model fit for the exposure-response association between coal mine dust and lung cancer mortality by log transforming the continuous coal mine dust variable. Coal mine dust exposure was positively and significantly associated with lung cancer mortality in the single-exposure model (HR=1.70; 95% CI 1.02 to 2.83) and the model that included silica (HR=1.71; 95% CI 1.03 to 2.85; table 4). In our model with an untransformed (log linear) continuous coal mine dust exposure, the association between coal mine dust and lung cancer mortality was not significant (coefficient from single-exposure model=0.0010, p=0.4394).

Log-transformed cumulative silica exposure was associated with a significant increase in lung cancer (HR= 1.76; 95% CI 1.45 to 2.14) in the single-exposure morel but not when controlling for coal mine dust (HR=1.33; 95% CI 0.94 to 1.90). Untransformed respirable silica was not a significant predictor of lung cancer mortality in either the single-exposure (HR=1.05; 95% CI 0.90 to 1.23) or the dual-exposure (HR=0.99; 95% CI 0.84 to 1.18) model. Smoking at enrolment strongly predicted lung cancer mortality in all models (table 4). The risk of lung cancer declined across increasing levels of body mass index (BMI) (HR for overweight vs normal=0.84; 95% CI 0.70 to 1.00; HR for obese vs normal=0.59; 95% CI 0.42 to 0.82), consistent with most other studies that assessed BMI and lung cancer mortality.[25–29]

Stratifying the models by follow-up time, within the most recent follow-up period (2000–2007) in models which included both exposures we saw a positive and significant exposure-response association for coal mine dust exposure (HR=1.55; 95% CI 1.16 to 2.08) and a positive association for silica (HR=1.07; 95% CI 0.72 to 1.59; table 5), consistent with the long latency of this cancer and the mitigation of the healthy worker effect over time.

In the analysis stratifying by TSLE, we observed that the exposure-response relationships between coal mine dust and silica exposure with lung cancer mortality declined monotonically with increasing time after exposure ceased (see online supplemental table III). Including a continuous term for TSLE increased the estimate of the HR for lung cancer in all models. In the model which included log-transformed coal mine dust exposure, the HR increased 20% with the addition of TSLE (HR without TSLE 1.20; 95% CI 1.04 to 1.39, and HR with TSLE 1.44; 95% CI 1.24 to 1.91). In the model which included the continuous untransformed coal mine dust exposure the HR increased 10% and became significant with the addition of TSLE (HR without TSLE 1.13; 95% CI 0.95 to 1.92, and HR with TSLE 1.26; 95% CI 1.05 to 1.51). In the model which included continuous respirable silica

exposure the HR increased 13% with the addition of TSLE (HR without TSLE 1.11; 95% CI 0.94 to 1.32, and HR with TSLE 1.34; 95% CI 1.09 to 1.66).

Sensitivity analysis—The DOL identified employment termination dates for 5749 (65.1%) miners and UMWA Funds identified such dates for 6458 (73.1%) miners. The termination dates we obtained from the two organisations were highly correlated (Pearson's correlation coefficient=0.77, $p<0.01$). Jointly the DOL and UMWA Funds identified termination of employment dates for 7397 (83.8%) cohort members, who we then included in the sensitivity analyses. We excluded the remaining records due to missing (1419) or invalid (13) termination dates. The mean extended cumulative coal mine dust and respirable silica exposure estimates were 83.0 mg/m^3-years (SD=41.3) and 4.1 mg/m^3-years (SD=1.8), respectively. The coefficients for the exposure-response relationships with each of the outcomes were statistically similar for the extended compared with the original estimates (table 6).

DISCUSSION

This mortality follow-up, extended to almost four decades, confirms the excess mortality from NMRD in US coal miners observed in prior studies, and provides some evidence of an increased risk of from lung cancer. Exposure to respirable silica has been included in analyses of this cohort for the first time, making a significant contribution to our understanding of respiratory related mortality in US coal miners.

Nonmalignant respiratory disease (NMRD)

We observed positive exposure-response relationships between cumulative coal mine dust exposure and COPD among never and former smokers but not among current smokers, which is consistent with the latest findings from the PFR and a previous study of pulmonary function in the NSCWP.[630] Our finding of a relationship between coal mine dust and COPD mortality among former and never smokers may be due in part to selection bias, that is, smokers with more severe lung deficits may have stopped smoking or may have left coal mining earlier in their work life than non-smoking workers of the same age, and hence introduce negative bias. We observed a clear healthy worker effect in the SMR analysis for all outcomes. For COPD and lung cancer related mortality we saw a deficit in overall mortality in the first two decades of follow-up, which disappeared in subsequent decades. It has been proposed that there may be a negative interaction between coal mine dust exposure and COPD among smokers attributable to a number of theories including that tobacco smoke induced mucous hypersecretion protecting the distal lung from dust deposition.[31] However there is little supporting evidence for this theory.

The strong positive exposure-response relationship between coal mine dust and pneumoconiosis-related mortality that we observed is consistent with previous studies from this and other coal miner cohort studies.[6711] The strength of that relationship varied by region, generally declining with coal rank, that is, from east to west in the US coal-rank region has previously been observed as a strong risk factor for pneumoconiosis-related mortality in this cohort.[7]

Our finding that silica exposure is significantly associated with mortality from COPD in single exposure models dust (HR 1.08; 95% CI 1.00 to 1.17) is consistent with those from the latest mortality follow-up from the PFR study.[6] These findings are generally supportive of the accumulating evidence of the importance of silica exposure in the excess of obstructive lung disease among coal miners, and in the increasing prevalence and severity of pneumoconiosis in US miners.[3233] Chronic exposure to silica dust has been shown to cause chronic bronchitis and emphysema even in the absence of radiological silicosis.[34] However autopsy studies of US and Australian coal miners found quantity of coal mine dust, but not silica, significantly predicted emphysema severity after accounting for cigarette smoking and age.[3135] In our study the effect of silica exposure on COPD was weakened when we controlled for coal mine (HR 1.04; 95% CI 0.94 to 1.94).

Our silica estimates were based on data from 1982 to 2002, and more removed in time from exposure than the data used to develop our coal mine dust estimates. There is therefore more uncertainly and potential for non-differential misclassification bias in the estimates of disease occurrence associated with the silica exposure data compared with those associated with the coal mine dust exposure. Hence the impact of silica exposure may be underestimated in our study.

The negative coefficients for TSLE, which we observed in all models, reflect an increased mortality rate in the years immediately after leaving employment. The tendency for mortality rates to rise in the time period following leaving work has been described by Steenland *et al*,[36] who proposed that such a trend likely reflects aspects of selection due to the healthy worker survivor effect. Controlling for TSLE significantly improved the model fit and increased the estimate of the exposure-response associations for nearly all models. While controlling for TSLE likely reduced some bias from the healthy worker survivor effect,[2036] traditional epidemiological methods, as used here, may not fully control for the healthy worker survivor effect.[37]

Lung cancer

Many earlier studies have reported a deficit in lung cancer mortality among coal miners.[9–111416] In sharp contrast to other studies, we observed an overall excess of lung cancer mortality (SMR=1.08; 95% CI 1.00 to 1.18) and a significant association with cumulative coal mine dust exposure and lung cancer. This association with coal mine dust was present in models with and without silica exposure.

We did not see an overall significant association between silica exposure and lung cancer mortality, which was surprising as inhaled crystalline silica is classified as a Group 1 lung carcinogen by The International Agency for Research on Cancer.[38] In the most recent follow-up of the British cohort, an overall significant exposure-response relationship was observed for lung cancer mortality with silica but not coal mine dust exposure.[6] The PFR had more robust exposure estimates and a longer follow-up time than our study (1959–2005 and 1969–2007, respectively). In the most recent follow-up period, 2000–2007, we saw a positive and significant association between lung cancer mortality and coal mine dust exposure and a positive association with silica exposure. This may be attributable to the long latency of lung cancer and/or the mitigation of the healthy worker effect over time.

We observed an inverse trend with lung cancer mortality and radiographic CWP status at study enrolment. Similar trends have been reported by some other studies.[939] While CWP may be considered a surrogate marker for coal mine dust exposure, in the current study the findings for CWP are likely attributable to selection biases. Selection bias may have occurred in this cohort because it initially included actively employed miners, many of whom were well into their work experience at the start of this study (average 21 years). Negative bias may have occurred if miners who had higher dust exposures and were at increased risk of lung cancer were more likely to leave work before other men their age, and thus would not be eligible for enrolment in the study. Another possible explanation is that the latency period for lung cancer is longer than that for CWP, so miners may die with pneumoconiosis before lung cancer could be diagnosed.

The analysis of TSLE and lung cancer mortality provided some insights into how mortality rates vary by work status. The risk of death from lung cancer associated with coal mine dust declined with time after leaving work. The same pattern was seen for the association between coal mine dust and gastrointestinal cancer mortality (data not shown). Hence, the observations may reflect the tendency for mortality rates to rise in the time period following leaving work.

Early studies have previously observed a deficit of lung cancer mortality among coal miners.[9–1114] These observations led to a theory that clay particles may partially detoxify silica by coating it, potentially rendering it less carcinogenic. Our findings, and those of the British coal miners' cohort, suggest that the deficit might be simply explained by a strong healthy worker effect that has diminished with extended follow-up. It also might be attributable to the prohibition of smoking in underground mines which may also diminish with time as miners leave work,[6] although there is no empirical evidence for or against this hypothesis.

Smoking is the strongest risk factor for lung cancer in the general population. US male smokers are about 23 times more likely to develop lung cancer than non-smokers.[40] In our models all measures of smoking at enrolment were strong predictors of lung cancer mortality. Compared with the general US male population in 1970, the miners in our study were more likely to be current smokers, but on average smoked fewer cigarettes per day (see online supplemental table IV), consistent with the prohibition on smoking in the mines. Whatever other factors may contribute to lung cancer incidence and mortality in this population, interventions to reduce smoking and smoking initiation among miners and their communities should be investigated.

Limitations

There were a number of limitations to our study. Perhaps of greatest concern was the lack of job histories on which to base exposure estimates after study enrolment. For previous studies of this cohort, it was assumed that most exposure was accumulated before enrolment.[7] Our sensitivity analysis found no meaningful differences between the exposure-response relationships for death from NMRD using the original and extended estimates for either coal mine dust or silica exposure, lending empirical support to our assumptions. A limitation of the sensitivity analysis was the assumption that miners continued to work in the same job

and the same level of exposure after study enrolment until termination of employment. We have no empirical way to test this assumption. However, our estimates were likely exaggerated as dust levels in US mines declined dramatically after the passage of the 1969 Mine Health and Safety Act. Thus it is unlikely that the lack of work histories in this study had a large impact on our findings.

The electronic data archive from this cohort did not include the start and end dates for each job. As with previous mortality studies from of this cohort, this prevented the evaluation of exposure lags and construction of internal time-varying variables (through enrolment) in the Cox analyses.

Cause of death misclassification is a source of potential bias in occupational studies.[41] Of particular concern for our study, using underlying cause of death from death certificates may preferentially underestimate COPD.[4243] Among coal miners is it likely that NMRD may be preferentially classified as CWP, hence COPD would be under-reported. In the general US population the accuracy of reporting lung cancer on death certificates is high (94%).[44] However, it is possible that lung cancer mortality in coal miners may be underdiagnosed in the presence of other radiographic findings.[4546]

In addition to silica, coal miners may be exposed to other substances that are recognised to cause respiratory cancer in humans including diesel exhaust[4748] and radon gas.[49] Diesel exposure is unlikely to have contributed significant to lung cancer related mortality in this cohort as many of the miners worked much of their mining tenure in coal mines with little or no diesel use. Subsequently some of these miners were used as non-exposure controls for a study of diesel exhaust exposure and respiratory health outcomes among coal miners.[50] There is no information regarding radon exposure in the study mines and it is unclear to what extent, if any, radon exposure may vary with coal or silica exposure.

CONCLUSION

Our findings add to the strong existing evidence that occupational exposure to coal mine dust, and possibly silica dust, leads to death from pneumoconiosis and also from COPD. The cumulative exposures to silica were low in our study and yet were associated with increased risk of death from COPD. This study underlines the need to continue efforts to further control and reduce exposure to coal and respirable silica dust in coal mines. Also, we found excess lung cancer mortality increased with cumulative coal mine dust exposure. Our findings and those from the British coal miners' cohort suggest the need for continued investigation of lung cancer mortality and incidence among coal miners, especially in the modern-day mining industry, where the prevalence of dust-related respiratory disease has been increasing.[2]

Evidence of bias from the healthy worker effect was observed, including a strong healthy worker survivor effect, which would have exerted a negative bias on the exposure-response relationships we observed.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgments

The authors would like to acknowledge the contribution of the many people who helped with data access and linkage, including: Janet Hale, National Institute for Occupational Safety and Health (NIOSH), Centers for Disease Control and Prevention (CDC); Robert Bilgrad and Michelle Goodier, National Center for Health Statistics, CDC; Brenda South, Social Security Administration; George Niewiadomski, Mine Safety and Health Administration, Department of Labor (DOL); and Lorraine Lewis, United Mine Workers of America Health and Retirement Funds.

Funding The research was supported in part by the US National Institute of Occupational Safety and Health training T42/OH008672 grant.

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What this paper adds

The issues

- Occupational exposure to coal mine dust causes coal workers' pneumoconiosis (CWP) and chronic obstructive pulmonary disease (COPD). The prevalence of CWP among US coal miners has increased since the mid-1990s after a steady decline following passage of the Coal Mine Health and Safety Act of 1969. The causes of the resurgence of CWP remain largely unknown.
- The possible role of coal mine dust exposure in the risk for the development of lung cancer has also been examined extensively in the epidemiological literature with mixed findings.
- The current study extended follow-up of a US coal miner's cohort for 37 years and added estimates of cumulative silica exposure as well as a sensitivity analysis assessing whether exposure estimates at the time of enrolment are a useful surrogate for lifetime exposure.

What we found

- Significant and positive exposure-response associations were observed for mortality from pneumoconiosis and COPD with coal mine dust exposure. The latter was modified by smoking status such that the effect was strongest among never smokers. Positive associations were also observed for COPD and pneumoconiosis with coal mine dust silica exposure; these associations were not significant when coal dust was added to the model.
- Excess mortality due to lung cancer was seen in the last decade of follow-up (2000–2007). Positive exposure-response associations were observed with coal mine dust and silica in the last decade of follow-up (2000–2007).

Public health importance

- Our findings build upon previous studies showing that coal mine dust exposure leads to increased mortality from non-malignant respiratory disease.
- Our findings also suggest that coal miners may be at an increased risk of lung cancer from cumulative exposures to coal mine dust, silica and/or other unmeasured mining-related exposures.
- This study underlines the need to continue efforts to further control and reduce exposure to coal mine dust and respirable silica in coal mines.

Table 1

Demographic characteristics at enrolment of the 8829 coal miners included in the study

Baseline categorical characteristic	**N (%)**
Smoking status at enrolment	
Current smoker	4770 (54.0)
Former smoker	2257 (25.6)
Never smoked	1802 (20.4)
Region	
Eastern Pennsylvania	513 (5.8)
Eastern Appalachia	1335 (15.1)
Western Appalachia	4838 (54.8)
Midwest	1198 (13.6)
West	945 (10.7)
Race	
White	8403 (95.2)
Black	426 (4.8)
Baseline continuous characteristic	Mean (SD)
Age (years) at start of follow-up	44.6 (11.9)
Years coal mining	20.8 (13.2)
Years underground	17.6 (13.7)
Years at the coal face	8.7 (11.2)
Cumulative coal mine dust exposure (mg/m^3-years)	64.6 (46.4)
Cumulative respirable silica exposure (mg/m^3-years)	2.6 (1.0)

Table 2

Overall and stratified SMRs for selected underlying causes of death and percentage of ever smokers, mean cumulative coal mine dust and respirable silica exposure category by coal-rank region, radiographic status at enrolment, race and calendar year of death

	Pneumoconiosis*		COPD		Lung cancer		Ever smoked at enrolment	Mean cumulative exposure*	
Category	**Obs.**	**SMR**	**Obs.**	**SMR**	**Obs.**	**SMR**	**Per cent**	**Coal mine dust mg/m^3-years**	**Respirable silica**
Total	403	79.70	309	1.11	568	1.08	79.6	81.0	3.2
Region									
Eastern Pennsylvania	181	365.29	11	0.61	26	0.79	77.0	97.7	2.6
Eastern Appalachia	65	86.91	48	1.26	77	1.01	82.4	77.4	2.8
Western Appalachia	101	38.21	157	1.05	334	1.17†	82.3	82.3	3.8
Midwest	14	17.38	53	1.44†	101	1.47†	86.7	72.8	2.7
West	42	53.74	40	1.10	30	0.49†	81.7	77.5	2.5
Race									
White	389	67.44	293	1.09	542	1.09†	82.5	80.4	3.3
Black	14	129.84	16	1.60	26	0.88	78.1	90.4	3.8
Baseline radiograph									
Category 0	237	48.50	250	1.06	510	1.13†	83.0	76.4	3.2
Category 1	56	92.67	29	1.15	39	0.89	78.9	99.3	3.6
Category 2	65	192.82	24	1.85†	14	0.62	75.7	113.0	3.6
Category 3	45	409.78	6	1.39	5	0.61	82.5	122.0	3.6
Calendar year of death									
1970–1989	170	63.25	85	0.86	233	0.95	83.60	n/a	
1990–1999	143	106.20	118	1.19	208	1.31†	81.90		
2000–2007	90	127.59	106	1.26†	127	1.23†	80.90		

*SMRs from pneumoconiosis are artificially high as there is no valid comparison group in the general population. We included them to show comparisons within levels of covariates and for consistency with previously published studies of this cohort. We do not include statistical testing given the lack of a valid comparison group.

†Statistically significant at p≤0.05.

COPD, chronic obstructive pulmonary disease.

Table 3

HRs for mortality due to COPD and pneumoconiosis as the underlying cause of death estimated in single-exposure and dual-exposure Cox proportional hazards models

	Single-exposure models				Dual-exposure model	
	Coal mine dust		Respirable silica		Coal and silica in same model	
Variables	**B coeff.**	**HR* (95% CI)**	**B coeff.**	**HR* (95% CI)**	**B coeff.**	**HR (95% CI)**
Outcome=COPD (309 deaths)†						
Cumulative exposures (mg/m^3-years)						
Coal mine dust modified by smoking at enrolment‡						
Never	0.0102	1.93 (1.12 to 3.34)			0.0095	1.84 (1.05 to 3.22)
Former	0.0074	1.61 (1.06 to 2.44)			0.0065	1.52 (0.98 to 2.34)
Current	0.0007	1.04 (0.81 to 1.34)			−0.0009	0.99 (0.76 to 1.29)
Respirable silica						
Continuous (log)			0.0798	1.08 (1.00 to 1.17)	0.0438	1.04 (0.96 to 1.14)
Categorical						
<2.22			Ref.		Ref.	
2.22 to <3.30			0.2839	1.33 (0.95 to 1.85)	0.2541	1.29 (0.92 to 1.81)
3.30 to <4.13			0.4258	1.53 (1.10 to 2.13)	0.3684	1.45 (1.02 to 2.06)
≥4.13			0.4317	1.54 (1.09 to 2.19)	0.3463	1.41 (0.95 to 2.10)
Outcome=Pneumoconiosis (403 deaths)§						
Cumulative exposure (mg/m^3-years)¶						
Coal mine dust modified by coal-rank region*,§						
Eastern Pennsylvania	0.0103	1.95 (1.50 to 2.52)			0.0096	1.86 (1.43 to 2.42)
Eastern Appalachia	0.0156	2.74 (1.92 to 3.92)			0.0147	2.58 (1.78 to 3.74)
Western Appalachia	0.0080	1.67 (1.22 to 2.29)			0.0061	1.52 (1.09 to 2.13)
Midwest	0.0097	1.88 (0.90 to 3.90)			0.0085	1.72 (0.82 to 3.62)
West	0.0034	1.25 (0.80 to 1.92)			0.0024	1.17 (0.75 to 1.82)
Respirable silica†						
Continuous (log)			0.5931	1.76 (1.45 to 2.14)	0.2953	1.33 (0.94 to 1.90)
Categorical						

	Single-exposure models				Dual-exposure model	
	Coal mine dust		Respirable silica		Coal and silica in same model	
Variables	**B coeff.**	**HR* (95% CI)**	**B coeff.**	**HR* (95% CI)**	**B coeff.**	**HR (95% CI)**
<2.22			Ref.			
2.22 to <3.30			0.2769	1.32 (1. 01 to 1.57)		
3.30 to <4.13			0.2568	1.29 (1.08 to 1.56)		
≥4.13			0.5644	1.76 (1.45 to 2.1)		

*HRs for continuous exposure were calculated for the change in the HR for mean cumulative exposure (coal mine dust=64.6 mg/m^3-years; silica=2.6 mg/m^3-years).

†Controlling for coal-rank (region), race, age at study entry and year of birth.

‡The interaction terms for COPD-related mortality and cumulative coal mine dust exposure with smoking status had a p-value of 0.0046 for COPD.

§Controlling for race, age at study entry, and year of birth.

¶The interaction term for pneumoconiosis-related mortality and cumulative coal mine dust exposure with coal-rank region.

COPD, chronic obstructive pulmonary disease; HR, hazard ratio.

Table 4

HRs for mortality due to lung cancer mortality (568 deaths) estimated in Cox proportional hazards models controlling for age at study entry, race and year of birth, and other covariates as listed

	Single-exposure models				Dual-exposure model	
Variables	**B coeff.**	**HR (95% CI)**	**B coeff.**	**HR* (95% CI)**	**B coeff.**	**HR (95% CI)**
Cumulative exposures (mg/m^3-years)						
Coal mine dust (log)*,†	0.1271	1.70 (1.02 to 2.83)			0.1290	1.71 (1.03 to 2.85)
Respirable silica†			0.0191	1.05 (0.90 to 1.23)	−0.0028	0.99 (0.84 to 1.18)
Categorical						
Coal mine dust						
<52.4	Ref.				Ref.	
52.4–80.7	0.1354	1.15 (0.90 to 1.47)			0.1062	1.11 (0.87 to 1.43)
80.8–97.7	0.0356	1.04 (0.80 to 1.36)			−0.0214	0.98 (0.73 to 1.31)
≥99.7	0.1831	1.20 (0.89 to 1.62)			0.0959	1.10 (0.79 to 1.53)
Respirable silica						
<2.22			Ref.		Ref.	
2.22–3.30			0.0769	1.08 (0.85 to 1.37)	0.0711	1.07 (0.84 to 1.37)
3.31–4.12			0.1845	1.20 (0.95 to 1.52)	0.1735	1.19 (0.93 to 1.52)
≥4.13			0.1590	1.17 (0.92 to 1.50)	0.1463	1.16 (0.88 to 1.52)
Covariates‡						
Smoking status at enrolment						
Never	Ref.				Ref.	
Former	0.9872	2.68 (1.50 to 4.79)	0.9948	2.70 (1.51 to 4.83)	0.9874	2.68 (1.50 to 4.79)
Current	2.2190	9.20 (5.30 to 15.98)	2.2268	9.27 (5.33 to 16.11)	2.2195	9.20 (5.30 to 16.00)
Pack-years at enrolment§	0.0213	1.24 (1.18 to 1.30)	0.0212	1.23 (1.17 to 1.30)	0.0213	1.24 (1.18 to 1.30)
Region						
Eastern Pennsylvania	0.5029	1.65 (0.96 to 2.86)	0.5407	1.72 (0.99 to 3.00)	0.5018	1.65 (0.95 to 2.86)
Eastern Appalachia	0.7547	2.13 (1.36 to 3.33)	0.7907	2.20 (1.41 to 3.45)	0.7538	2.13 (1.40 to 3.32)
Western Appalachia	0.8224	2.28 (1.55 to 3.35)	0.8212	2.32 (1.57 to 3.42)	0.8242	2.28 (1.54 to 3.36)
Midwest	0.9753	2.65 (1.76 to 4.00)	0.9845	2.67 (1.77 to 4.03)	0.9750	2.65 (1.76 to 3.99)

	Single-exposure models				Dual-exposure model	
Variables	**B coeff.**	**HR (95% CI)**	**B coeff.**	**HR* (95% CI)**	**B coeff.**	**HR (95% CI)**
West	Ref.				Ref.	
Body mass index						
Normal	Ref.				Ref.	
Overweight	−0.1771	0.84 (0.70 to 1.00)	−0.1678	0.85 (0.71 to 1.01)	−0.1776	0.84 (0.70 to 1.00)
Obese	−0.5265	0.59 (0.42 to 0.82)	−0.5185	0.60 (0.43 to 0.83)	−0.5265	0.59 (0.42 to 0.82)

*Continuous coal mine dust exposure was log transformed (natural log).

†HRs for continuous exposure were calculated for the change in the HR for mean cumulative exposure (coal mine dust=64.6 mg/m^3-years; silica=2.6 mg/m^3-years).

‡Results presented are from the models with the continuous exposures.

§HRs for pack-years of smoking were calculated for 10-unit change.

HR, hazard ratio.

Occup Environ Med. Author manuscript; available in PMC 2015 August 03.

Table 5

HRs for mortality due to lung cancer as the underlying cause of death, stratifying on calendar time (follow-up time), estimated in a dual-exposure Cox proportional hazards model controlling for age at study entry, race, coal-rank region, year of birth, smoking status, pack years and body mass index

	Single-exposure models		Dual-exposure models	
Variables	**B coeff.**	**HR* (95% CI)**	**B coeff.**	**HR* (95% CI)**
Cumulative exposure (mg/m^3-years) stratified by follow-up time				
Coal mine dust (log)†				
1970–1989 (233 deaths)	0.0357	1.04 (0.82 to 1.22)	0.0430	1.20 (0.49 to 2.90)
1990–1999 (208 deaths)	−0.0070	0.99 (0.85 to 1.18)	0.0055	1.02 (0.48 to 2.17)
2000–2007 (127 deaths)	0.3445	1.55 (1.19 to 1.67)	0.3415	1.55 (1.16 to 2.08)
Respirable silica				
1970–1989 (233 deaths)	0.0010	1.00 (0.77 to 1.31)	−0.0094	0.97 (0.69 to 1.36)
1990–1999 (208 deaths)	−0.0214	0.94 (0.72 to 1.24)	−0.0203	0.94 (0.66 to 1.34)
2000–2007 (127 deaths)	0.0731	1.21 (0.89 to 1.66)	0.0216	1.07 (0.72 to 1.59)

HRs for pack-years of smoking were calculated for 10-unit change.

*Results presented are from the models with the continuous exposures.

†Coal mine dust exposure was log transformed (natural log).

HR, hazard ratio.

Table 6

Results of sensitivity analysis among cohort members with known termination of employment date (n=7397) comparing estimated HRs for mortality due to pneumoconiosis as the underlying cause of death, using original and extended cumulative dust exposure estimates

	Original estimates		Extended estimates	
Cumulative exposure (mg/m^3-years)	**B coeff.**	**HR (95% CI)**	**B coeff**	**HR (95% CI)**
COPD (282 deaths)				
Coal mine dust exposure modified by smoking status[*,†]				
Never	0.0076	1.64 (0.92 to 2.94)	0.0052	1.42 (0.77 to 2.53)
Former	0.0068	1.55 (0.98 to 2.47)	0.0060	1.47 (0.92 to 2.34)
Current	−0.0002	0.99 (0.74 to 1.30)	−0.0016	0.90 (0.68 to 1.18)
Respirable silica[†,‡]				
Continuous	0.0421	1.04 (0.94 to 1.14)	0.0054	1.01 (0.93 to 1.09)
Pneumoconiosis (320 deaths)				
Coal mine dust exposure modified by coal-rank region[*,†]				
Eastern Pennsylvania	0.0097	1.87 (1.34 to 2.60)	0.0092	1.81 (1.28 to 2.53)
Eastern Appalachia	0.0160	2.80 (1.92 to 4.10)	0.0132	2.35 (1.57 to 3.52)
Western Appalachia	0.0075	1.62 (1.14 to 2.31)	0.0060	1.47 (1.04 to 2.09)
Midwest	0.0113	2.08 (0.94 to 4.60)	0.0113	2.07 (0.86 to 4.98)
West	0.0025	1.17 (0.74 to 1.86)	0.0015	1.09 (0.69 to 1.76)
Respirable silica[†]				
Continuous (log)	0.3124	1.36 (0.90 to 2.06)	0.0834	1.08 (1.00 to 1.14)
Lung cancer (490 deaths)				
Cumulative exposure				
Coal mine dust[†] (log)	0.1600	1.95 (1.17 to 3.24)	0.1803	2.12 (1.16 to 3.89)
Respirable silica	0.0165	1.04 (0.87 to 1.26)	−0.0115	0.97 (0.83 to 1.13)

[*] Controlling for coal-rank region, and age at enrolment, race and birth year; continuous silica exposure was log transformed.

[†] HRs were calculated for continuous exposure for the change in the HR for mean cumulative exposure (CMD=64.6 mg/m^3-years; silica=3.2 mg/m^3-years).

[‡] Controlling for smoking status, pack years, age at enrolment, race and birth year.

COPD, chronic obstructive pulmonary disease; HR, hazard ratio.