A Critical Review of the Scientific Basis for MSHA's Proposal for Lowering the Coal Mine Dust Standard

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EXECUTIVE SUMMARY

Implementation of the coal mine dust ("CMD") interim standard of 3.0 milligrams per cubic meter ("mg/m^3") in 1970, which was reduced to 2.0 mg/m^3 in 1972, produced a steady decline in dust levels and prevalence of coal workers pneumoconiosis ("CWP"). Beginning in the mid-1990s, an apparent increase was reported in what was thought to be severe and rapidly progressive CWP and progressive massive fibrosis ("PMF") despite stability in CMD levels. These "sentinel health" events led to further investigation and, in part, stimulated the October 19, 2010 MSHA proposal to lower the current CMD standard from 2.0 mg/m^3 to 1.0 mg/m^3.

Objectives of this critical review are to evaluate the epidemiological evidence regarding risk factors associated with these "sentinel health" events and the exposure-response relationships of CMD and CWP. This evaluation includes consideration of other risk factors (e.g., quartz, coal rank) plus bias and confounding (e.g., low participation of coal miners in medical surveillance programs and in epidemiology studies, and biased exposure estimates of CMD). The results from our evaluation are then used to assess whether the current CMD standard of 2.0 mg/m^3 protects miners from developing disabling CWP and whether the lowering of the standard is scientifically based.

Rapidly progressing pneumoconiosis to category 2+ and PMF is a "sentinel health" event of low prevalence (less than 0.5%) clustered in the southern Appalachian region ("SAR") of eastern Kentucky, western Virginia and southern West Virginia. It is a factor stimulating a proposal for setting a new CMD standard but is unsuitable owing to a lack of any evidence whatsoever that such sentinel events are primarily being caused by CMD.

Compelling evidence indicates that the rapidly progressive cases of pneumoconiosis recently reported are silicosis which is based on very high quartz exposures and short latency, both factors clearly being consistent with silicosis and unlike CWP. The higher proportion of r-type opacities in the SAR than in the rest of the US is likewise consistent with a silicosis interpretation. Other factors also related to increased quartz exposures include working in small mines, increased hours worked per day, and smaller coal seams.

Exposure-response studies are necessary to determine a safe level of exposure. Studies in the United States ("US") of exposure-response are based on the cohort from the National Study of Coal Workers' Pneumoconiosis ("NSCWP"), which is subject to two primary biases. One is a potential selection bias because of low participation rates in all rounds except the first round.[1] The direction of this potential bias is speculative as it is not known whether unhealthy miners selectively participate or not.

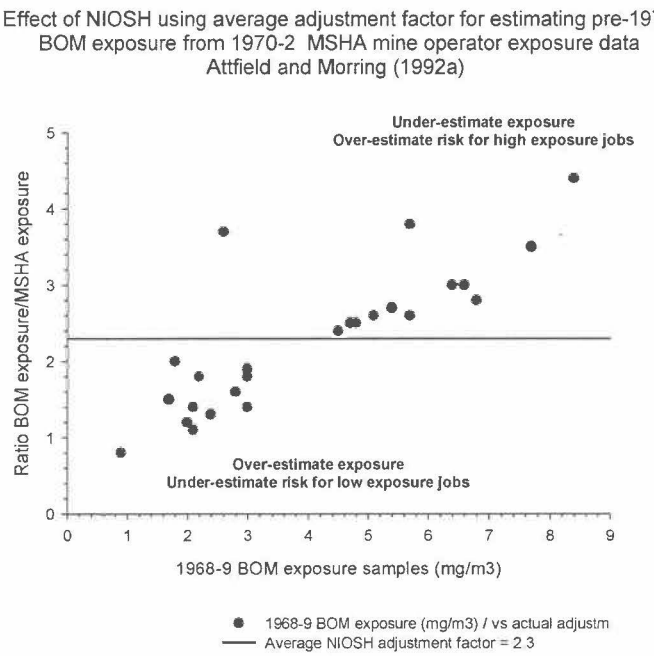
[1] NIOSH refers to periods of medical examinations of coal miners, usually in five-year periods, in its nationwide epidemiology studies and nationwide surveillance program as "rounds". While they are conducted over a period of years they are used to develop cross-sectional prevalence data.

The other potential bias is estimation of pre-1970 exposures which were very high (up to a mean of 8 mg/m^3 in high exposure jobs) as reported in a study of the US Bureau of Mines ("BOM") that began in 1968. The National Institute for Occupational Safety and Health ("NIOSH") used these BOM sample results and post-1970 coal mine operator sample results for indirect back extrapolations to estimate pre-1970 exposures. The procedure was to calculate mean exposures for specific jobs in both pre- and post-1970 data bases. An adjustment factor for estimating pre-1970 exposures was derived from the ratio of mean exposure (expressed in mg/m^3) of BOM job categories divided by the mean exposure for the same job categories from post-1970 compliance data. The mean of all job category adjustment factors was thus calculated (2.3) and used to increase (by multiplication) each BOM mean job exposure. These estimates were then back extrapolated to the pre-1970 work history of the miners.

These extrapolations are biased, however, because they are based on an average ratio of all underground jobs, which appears to over-estimate risks in high-exposure jobs and under-estimate risks in low-exposure jobs.

The following figure shows the bias that this procedure produces.

Figure 1



NIOSH has pointed out that there is a predicted background prevalence of 5% category 1 or greater among non-dust exposed workers. We have used this NIOSH background prevalence rate in interpreting results from exposure-response studies.

Exposure-response analyses of CMD and category 2 CWP show strong associations for high rank coal (coal rank 5 or anthracite and rank 4) with increased prevalence below the current standard.[2] There were no apparent increases in CWP 2 for low rank coals 1-3 at exposures below the current 2.0 mg/m³ standard. When the upward bias in exposure estimation is accounted for, it is probable there are no significant increases in prevalence below the current standard for any rank of coal.

Chronic obstructive pulmonary disease ("COPD"), or reductions in forced expiratory volume in one second ("FEV"), are potentially significant response variables for assessing health effects associated with exposure to CMD. FEV_1 performance is obtained from spirometry collected as part of each round of the NSCWP. Consequently, data for assessment of exposure-response trends are readily available in quantities similar to chest radiographs for assessment of CWP. Major confounding exposure variables include age, sex, height, and cigarette smoking that must be adjusted for in attributing risk of CMD exposure. However, bias from these risk factors is reduced as these data are collected as part of spirometry, thus, adjustment for confounding effects is feasible. The greatest potential for bias occurs in studies of US coal miners due to potential misclassification of exposure that spuriously inflates risk and from low participation rates in NSCWP that produce an unknown effect on results. Reductions in FEV_1 greater than about 300 ml are associated with clinically significant breathlessness and are considered an objective threshold level for determining relatively safe CMD exposure levels for protecting coal miners from COPD.

There are over 20,000 coal miners from four countries (US, UK, South Africa, Sardinia) in nine cross-sectional studies and 13 exposure-response analyses considered relevant for assessing the weight-of-evidence regarding CMD and clinically significant deficits in FEV_1. Associations are weak but consistently show negative trends with increasing CMD exposure. Only two analyses (and one study) show strong associations with deficits of greater than 300 ml (-531 ml and -2750 ml) at exposures below the current standard of 2 mg/m^3 for 45-years. That is, 86% of relevant cross-sectional studies show no apparent clinically adverse deficit in FEV_1 attributable to CMD at exposures less than 90 mg/m^3-years.

There are over 8,000 individual coal miners from five countries (US, UK, Germany, Sardinia, China) in eight longitudinal or prospective studies and 11 exposure-response analyses. Associations are consistently weak or non-existent. Only one study of Sardinian miners shows a deficit greater than 300 ml (-684 ml) at exposures below the current standard. The remaining 10 analyses show no apparent associations of clinically reduced FEV_1 attributable to CMD at exposures below current standards. Average changes in FEV_1 observed at 90 mg/m^3-years ranged from -230 ml to +252 ml with

[2] Coal rank defines the carbon content with higher ranks having more carbon (and lower rank numbers). Coal ranks go from 100 to 900 in the UK and 1 to 5 in the US. Number 1 is the highest ranking coal, anthracite with 93-95% carbon, and number 5 is the lowest ranked high volatile Western coal with <85% carbon.

average FEV_1 values greater than the 95% predicted value. There are basically as many positive exposure-response trends as negative trends.

The epidemiological data from these studies show only two studies with steep negative exposure-response trends, and these are considered outliers because results are at such variance from other studies. The bulk of the evidence (~90%) from 21 exposure-response analyses is consistent in showing negligible and positive trends. The weight-of-evidence indicates negligible occurrences of clinically significant deficits in FEV_1 or any increased occurrence of COPD at exposures equivalent to a working lifetime at the current US standard. The epidemiological evidence displayed herein is contrary to and does not support such summary statements from NIOSH as "Epidemiological studies have clearly demonstrated that miners have an elevated risk of developing…deficits in lung function when they are exposed to respirable coal mine dust over a working lifetime at the current MSHA permissible exposure limit (PEL) of 2 mg/m^3". [3]

Exposure-response of CMD and mortality shows a strong association with nonmalignant respiratory diseases ("NMRD"), but no associations with chronic bronchitis, emphysema, lung cancer or stomach cancer. When stratified by rank, the excess NMRD mortality is confined entirely to miners exposed to anthracite. Exposure-response analysis by rank is needed to confirm whether low rank coal poses a threat for increased NMRD mortality in high exposure jobs.

[3] NIOSH (1995), Criteria for a Recommended Standard – Occupational Exposure to Coal Mine Dust, Public Health Service, CDC, DHHS (NIOSH) Publication No. 95-106.

I. INTRODUCTION

The Mine Safety and Health Administration ("MSHA") published in the Federal Register on October 19, 2010, its proposed rule for "Lowering Miners' Exposure to Respirable Coal Mine Dust, Including Continuous Personal Dust Monitors" (the "NPR"). 75 Fed. Reg. 64,412-64,506. The NPR would lower miners' exposure to respirable coal mine dust by revising the Agency's existing standards. The major provisions of the NPR would: (1) lower the existing exposure limits for respirable coal mine dust from 2.0 milligrams per cubic meter (mg/m^3) to 1.0 mg/m^3 ; (2) provide for the use of a single full-shift sample to determine compliance under the mine operator and MSHA's inspector sampling programs; (3) require the use of a new technology, the Continuous Personal Dust Monitor ("CPDM") for exposure monitoring; and (4) expand requirements for medical surveillance.

The purpose of this report is to critically evaluate pertinent scientific information on the subject of respirable CMD and related diseases, and in particular exposure-response studies, to ascertain if the proposed standard of 1.0 mg/m^3 is supported by the epidemiological evidence. Other factors are also evaluated, such as potential roles of quartz and coal rank with respect to rapidly progressive CWP. We believe the studies evaluated in our critique constitute the seminal studies providing the weight of evidence that either support or do not support the portion of the NPR that would lower the exposure limit for CMD from 2.0 mg/m^3 to 1.0 mg/m^3. These key studies are summarized here and detailed comments on each are presented.

Prior to 1969, detailed research regarding coal miners' health in the United States was meager and dispersed. In 1968, a coal mine explosion in Farmington, WV took the lives of 78 miners and was a major impetus for action by Federal and State governments. At the federal level, the Farmington explosion not only led to a massive revamping of the Nation's coal mine safety laws, but it also resulted in a revolutionary federal program to prevent occupational diseases in US coal miners, especially CWP. This new national, bipartisan consensus led to Congressional passage of the Federal Coal Mine Health and Safety Act of 1969 (the "1969 Mine Act"). Pub. Law 91-173; 83 Stat. 742. Signed into law, by President Richard Nixon on December 31, 1969, the 1969 Mine Act was further strengthened by enactment, in response to other mine disasters, of the Federal Mine Safety and Health Act of 1977 (the "Mine Act"). 30 U.S.C. §§801, *et seq*.

A centerpiece of the coal miner health provisions of the 1969 Mine Act was the establishment of mandatory CMD standards in the Nation's coal mines. Effective in 1970, under the 1969 Mine Act, the average concentration of CMD in underground coal mines was to be maintained at or below 3.0 mg/m^3 through 1972, after which the CMD standard was reduced to 2.0 mg/m^3. The provisions of the 1969 Mine Act remained largely intact under the 1977 Mine Act.

Major responsibilities under the Mine Act rest with MSHA in the Department of Labor and the NIOSH located in the Department of Health and Human Services. A mandate to MSHA was to insure that a safe and healthful work environment was maintained in the

nation's coal mines. For NIOSH, the mandate was for health-related research regarding coal workers' ailments and the prospective monitoring of miners' health, primarily CWP. Prior to the passage of the 1969 Mine Act, research in the United Kingdom ("UK") Institute of Occupational Medicine was well underway with work which came to be known as the Interim Standards Study. Before publication of the results, consultation between US and UK researchers, and evaluation by various US Congressional Committees and others resulted in portions of the Interim Standards Study results being utilized for setting the above noted CMD standard in the US.

The basis for setting the US CMD from the Interim Standards Study was that a miner exposed at 2.0 mg/m^3 over a working lifetime of 35 years would have zero risk of developing Category 2 simple CWP as defined by the International Labor Office ("ILO") Guidelines for the Classification of Radiographs of Pneumoconioses. This was a logical deduction in that it was known that the likelihood of a miner contracting the more disabling and sometimes fatal condition known as progressive massive fibrosis ("PMF") would be dramatically reduced or eliminated if ILO Category CWP 2 was never reached.

Since the passage of the 1969 Mine Act, measured dust exposures in US coal mines have been reduced to a considerable degree, with a large majority of coal mines being in compliance with the 2.0 mg/m^3 dust standard. Likewise, the reported prevalence of CWP in the Nation's coal mines has decreased from around 30 % to about 3%.

The source for determining the prevalence of CWP in US coal miners has been the Coal Workers' X-ray Surveillance Program ("CWXSP") administered by NIOSH where participation (with exception) has been low. Participation rates (by half decades) were 81%, 77%, 38%, 20%, 22%, 29%, and 48% (CDC/NIOSH 2009). Thus, the participants in this program form a select group from which inferences to the entire mining population remain questionable.

In addition, NIOSH carries out epidemiological studies under the NSCWP program established in 1970. Among other things, this work in the US relates to exposure-response estimates based on health data from US miners and environmental measurements taken in US mines. Thirty-one mines were originally selected for study based on criteria including an expected mine-life of 10-years, work force of 100 or more miners, geographical and geological spread, and accessibility. Rounds 1-3 were conducted at nearly the same mines but with steadily declining participation rates of 90%, 75% and 52% respectively. In addition to periodic examinations, Round 4 included follow-up of participants from the previous three rounds and had 70% participation.

In the past decade, there have been reports of a slight increase in the prevalence of CWP. Moreover, the reported increase is coupled with reports of rapidly progressive CWP in younger miners often exposed for a relatively short time period. New exposure-response estimates for predicting the occurrence of CWP at various cumulative exposure levels have provided estimates greater than previously shown. These three points, (1) increased prevalence, (2) rapid progression, and (3) new exposure-response estimates, are mainly the stimuli for the proposal to lower the current CMD standard to 1.0 mg/m^3.

II. STUDIES ON RAPIDLY PROGRESSIVE CWP

1. Summary of Studies on Rapidly Progressive CWP

In the US, after the implementation of the interim CMD standard of 3.0 mg/m³ in 1970, and the final standard of 2.0 mg/m³ in 1972, the prevalence of CWP and concentrations of CMD began a steady decline. Beginning in the mid-1990s, an apparent increase was observed in what was at first thought to be more severe and rapidly progressive CWP despite the apparent stability in CMD exposure levels. The change in the pattern of CWP occurrence was identified as a "sentinel health" event and commonly occurred in the SAR.

Several potential causal factors have been investigated in an attempt to explain these changes in CWP severity and progression as well as why it is more common in the SAR. According to NIOSH, the greater severity and rapid progression of CWP are more characteristic of silicosis than CWP and are associated with r-type opacities on the chest radiograph. Smaller mines (which often experience higher exposures than larger mines) and thinner seams of coal (with more cutting of sandstone and quartz-containing rock) are almost uniquely a feature of the SAR. Rapidly progressive CWP may also be associated with higher coal rank.

These factors have been investigated in US studies discussed in this section (Antao, Petsonk et al. 2005; CDC 2006; Laney and Attfield 2010; Laney, Petsonk et al. 2010; Pollock, Potts et al. 2010). The evidence is convincing that increased quartz exposure is an important explanatory factor and that these are most likely cases of silicosis and not CWP. There may be additional factors as well, e.g., increased length of shifts or rank of coal.

There are some studies where this pattern of changes in exposure and severity of CWP has been observed outside the US. One involves a Scottish coal mine where there was a period of extensive cutting through quartz that produced increased adverse health effects that did not appear to be due to coal dust (Miller, Hagen, et al. 1998, Buchanan, Miller, et al. 2003). Another relevant study in the UK by Hurley, Copland, et al. 1979, also been reviewed.

In the 1969 Mine Act, as previously noted, strict controls were placed on workplace concentrations of CMD, first at 3.0 mg/m^3 and then 2.0 mg/m^3 where it remains now. Over that time period the reported prevalence of CWP was reduced from about 33% to about 3%. Radiographs taken from 1996-2002 showed the reported prevalence of CWP by state ranged from 0-9.6%.

Two studies, however, have identified rapidly progressive cases of CWP nationwide (Antao, Petsonk et al. 2005) and locally in two counties in Virginia (CDC 2006). The nation-wide analysis showed that despite "excellent progress in reducing dust exposure" severe cases of rapidly progressive CWP and PMF continued to occur "among relatively young US coal miners" (Antao, Petsonk, et al. 2005). The geographic locations of

rapidly progressing CWP were largely in the SAR. Reported prevalence of CWP 1/0+ in 25 counties with rapidly progressive CWP ranged from 0.8% to 17.6%, while the proportion of evaluated miners with rapidly progressive CWP ranged from 41.7% to 80%. Nearly 30,000 miners were evaluated, and the reported prevalence (% of total 29,521) of different categories of CWP was as follows (Antao, Petsonk, et al. 2005):

- All CWP = 866 cases (2.9% CWP $\geq$ 1/0)
  + 783 (2.65%) cases had 2 radiographs so progression could be assessed.
  + 277 (35%) of these 783 case with CWP had rapidly progressive CWP or 0.94 % overall;
  + 41 had rapidly progressive PMF (14.8%) or 0.14% overall;
  + 8 (2.9%) had progression of one subcategory or 0.03% overall;
  + 156 (56.3%) had progression of 2-3 subcategories over 5-years or 0.53% overall;
  + 72 (26%) had a progression of more than 3 subcategories over 5-years or 0.24% overall.

- 73% of rapidly progressive cases (n = 202) had rounded opacities as the primary shape/size profusion, and 13% of these (n=26) of these were r-type;

- 50% of non-rapidly progressive cases (n=392) had rounded opacities, and 4% of these were r-type (n = 16).

- Based on r-type markings (n=42) the reported prevalence of silica-related CWP (42/29,521) appears to be about 0.14%. Based on the rapid progression characteristic of silicosis the reported prevalence of silica-related CWP appears to be about 0.94% (277/ 29,521).

Another study produced results showing r-type opacities (silicosis) are associated with rapidly progressing CWP, which the evidence suggests is due at least in part to quartz (Laney, Petsonk, et al. 2010). These authors reported an overall prevalence of 0.22% primary r-type opacities, 0.21% had secondary r-type opacities, or a total of 0.35% (n = 321) showing r-type opacities. These data are from miners participating in the NIOSH-administered CWXSP. The reported prevalence of coal-related CWP ILO Category 1 has been reduced since 1980 and CWP ILO Category 2+ has remained relatively stable. Silica-related reported prevalence of CWP (based on r-type opacities) has risen steadily for all categories including PMF (Figure 1).

Another feature of CWP needs to be considered for interpreting these data. That is the question of background prevalence of radiological opacities that are read as pneumoconiosis and are found in non-exposed subjects. Unpublished data from 218 blue-collar workers not occupationally exposed to dust with a mean age of 56 years showed a reported prevalence of 1.4% (standard error (SE) =0.8) category 1/0 and greater (Attfield and Seixas 1995), referring to unpublished data from Castellan, et al. (1985). It is unclear why the prevalence is so different than the 0.21% prevalence of rounded opacities reported in the published study. Attfield and Seixas also suggested there was a 5% or greater prevalence of small irregular opacities 0/1 or greater (90% 1/0

or greater) for men 60 years old with zero dust exposure (interpolated from (Collins, Dick, et al. 1988). Attfield and Seixas also reported that the prevalence of small opacities among non-exposed older workers (from Collins, et al.) would naturally rise above the 5% rate The lowest estimate of 1.4% with an upper bound of 2 SE = 3% shown in Figure 1 is greater than the observed prevalence of radiographic CWP (Figure 1).

If r-type opacities are a reliable marker (or radiologic pattern) for silica-related pneumoconiosis (or silicosis) among coal miners, then the data displayed in Figure 1 indicate:

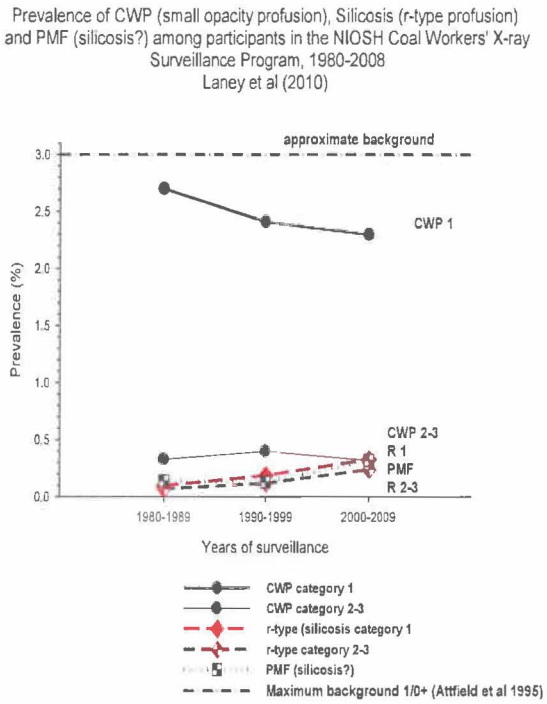
- The overall reported prevalence of coal-attributable CWP since 1980 declines over time with no upturn at any time;
- The reported prevalence of CWP is below the 3% background level for 1/0+, and is well below the predicted background prevalence of 5%;
- The recent increase in reported prevalence of CWP and PMF (Laney and Attfield 2010) appears to be due to silica-related pneumoconiosis. Both categories 1 and 2 doubled in reported prevalence in the 1990s and were three times greater in the 2000s compared to the 1980s. PMF remained stable through the 1990s and then more than doubled in the 2000s (Figure 1). PMF is apparently due to quartz exposure rather than coal dust.

The geological characteristics of coal from the SAR and the character of the mines provide indirect evidence that quartz is a likely contributor to rapidly progressing CWP (Pollock, Potts, et al. 2010). These include small seams that require mining methods that cut large amounts of stone, small mines where small seams and higher exposure are not uncommon and very high proportions of quartz in the dust. These factors are highly correlated in the SAR and provide indirect evidence supporting quartz as an etiological agent in the development of rapidly progressing CWP.

There is an actual example of rapidly progressing CWP in a Scottish colliery (Miller, Hagen et al. 1998; Buchanan, Miller et al. 2003). Figure 6 shows the strong exposure-response association between quartz exposure and Category 2+ CWP and the lack of an association with CMD where the exposure-response is flat. Figure 7 show that rapid progression of 2/1 silicosis can occur over short time periods at relatively low quartz levels in CMD.

In sum, these studies provide strong evidence that the quartz in CMD is producing rapidly progressive silicosis that has been misidentified as CWP. The evidence supports the belief that there has been no increase in the reported prevalence of CWP and that the prevalence of CWP may well be below background levels. The recent increase in CWP prevalence is due to the increasing prevalence of r-type opacities suggestive of silica effects. These exposure-response studies of coal miners exposed to high quartz concentrations do not appear to be showing increases in rapidly progressive CWP caused by CMD. Instead, these increases are due to rapidly progressive silicosis associated with quartz concentration; and, in fact, there is no association with CMD and CWP.

Figure 1



The basis for the conclusion that rapidly progressive CWP is, in fact, rapidly progressive silicosis caused by high quartz levels is from the evidence in the studies summarized in section 2 below.

2. Summary and Comments on Studies of Rapidly Progressing CWP

Antao, V. S., E. Petsonk, et al. (2005). "Rapidly progressive coal workers' pneumoconiosis in the United States: geographic clustering and other factors. Occup Environ Med 62: 670-674.

Summary and Comments

The authors note that about 3.2% of approximately 35,000 current coal miners (1996-2002) show evidence of CWP. This reported prevalence is down from about 33% prevalence found in 1970. According to the authors, despite the progress in decreasing dust levels and the prevalence of CWP, severe cases of CWP (including PMF) continue to occur among younger miners. This report attempts to identify rapidly progressive cases of CWP (including PMF) and investigates some factors that contribute to this disease.

This is a nation-wide study of 29,521 miners in the CWXSP for the years 1996-2002 and includes miners with at least 2 chest radiographs with the most recent showing at least 1/1 pneumoconiosis. Rapid progression is defined as progression of more than 1 ILO subcategory over 5-years after 1985 and/or the development or progression of PMF after 1985.[4]

A crude prevalence of 3% (866 CWP cases) was identified for the years 1996 -2002. Among these 866 cases there were 783 cases with 2 or more radiographs so progression could be evaluated; of these, 277 (35%) were rapidly progressive CWP. This is the study group of interest, and among this group were 41 (14.8%) with rapidly progressing PMF. The extent of progression in less than 5 years included 8 (2.9 %) with progression of 1 subcategory (at variance with the authors definition of rapid progression), 156 (56 %) with progression of 2-3 subcategories, and 72 (26%) with progression of more than three subcategories.

Rapidly progressing cases were compared to non-rapidly progressing cases on several characteristics. The study group is thus finally reduced to 277 workers. It seems that the manner in which the higher percentages are quoted gives rise to a suggestion that the progression is more serious than it really is.

	N	Age	Tenure	Work in smaller mines (<50)	Tenure at face
Rapid progression	277	48(6)yrs	27 (6) yrs	OR = 1.55 (1.2-2.0)	19 (10) yrs
Non-rapid	506	51(6) yrs	26(8) yrs	OR = 1.0	17(10) yrs

The data indicate occurrence of rapid progression to be associated with several factors:

• Geographical clustering in eastern Kentucky and western Virginia. Overall there were 277 cases of rapidly progressive CWP in 14 different states and 137 different counties. There were 295 rapidly progressive cases in 25 counties, and comprised over 40% of all rapidly progressive cases of CWP. [Note: The 277 rapidly progressive cases are from the text and abstract and presumably included all rapidly progressive cases. Table 1 shows 295 rapidly progressive cases and excludes counties with <5 miners evaluated and with <40% of evaluated miners with rapid progression. This discrepancy raises the question of how many actual cases (i.e. >295) are there of rapidly progressive CWP. Cases tended to cluster along the eastern edge of the Appalachian coal field and may in part be explained by rank of coal and other factors such as silica exposure. An earlier study demonstrated rapid progression to have been previously observed more often in West

[4] The ILO has developed a classification system for determining if radiographic lung opacities are consistent with pneumoconioses for use in epidemiology studies. Concentration of small opacities are graded on a 12-point scale of four major categories each with 3 subcategories and progressively increasing profusion:

Major Categories	Subcategories	Characteristics
Category 0	0/-, 0/0, 0/1	No opacities or less than the lowest category 2(<1/0
Category 1	1/0, 1/1, 1/2	Continuation of concentrations between categories 0 and 2
Category 2	2/1, 2/2, 2/3	Profusion concentrations between categories 1 and 3
Category 3	3/2, 3/3, 3+	Profusion concentrations between categories 2 and PMF

PMF (progressive massive fibrosis), subcategories A,B,C indicating increasing larger opacities >10 mm.

Virginia and Pennsylvania than in western states where there was negligible progression (Amandus, Reger, et al. 1973).

• Work in smaller mines (<50 employees) where respirable CMD exposures are higher (Force 1993).

• Longer tenure at face jobs where exposure is typically greatest and face workers have previously been shown to experience more rapid progression of CWP (Seaton, Dodgson, et al. 1981; Seaton, Dick, et al. 1982);

• Younger age "strongly implicating recent mining conditions." The authors characterize cases with rapidly progressive CWP as "sentinel health" events indicating inadequate prevention in those situations where they occur. Such "sentinel health" events should prompt investigation to identify the causal agents that lead to preventive actions.

Additional Comments and Critique of Antao, Petsonk, et al. (2005)

The authors themselves suggest several limitations. These include:

• Inter-reading variability because of independent readings by different readers at different times (separated by 5+ years). Variability is somewhat limited as at least two subcategories are necessary for a diagnosis of rapid progression. Regression can also occur, and it is not too infrequent that some classifications "improve" due to reader variability and film quality. This phenomenon was found in Miner 6 as shown in Figure 2. While minor regression did occur at a point in time, overall progression did occur. On inter-reader variance, the authors indicated there was good reliability of case definition when they selected a subset of 211 films and had them reviewed side by side. The side-by-side readings were compared with the independent assessments and "good" agreement was reached. It was never stated what "good" meant.

• Selection bias may be occurring. The participation rate was about 31%. It is not clear how this is a limitation if the cases with rapid progression are more likely to participate. However, it becomes a limitation if cases do not participate so there are no "sentinel" events to observe. Since the authors did not investigate why miners were more, or less, likely to choose to participate it is pure speculation as to which way this might bias the study. Low participation is a substantial limitation for estimating prevalence, but less so for sentinel events where about 3% is a high enough prevalence to identify a potential health concern and the need for further investigation.

It is important to be mindful of this limitation when considering exposure-response studies of radiographic CWP, as it is here that selection bias because of low participation becomes important. *See* (CDC 2003) for more about prevalence rates.

Other comments:

There are no exposure estimates in this paper. Without estimates of CMD, it is impossible to develop safe exposure levels based on science. Since these are "sentinel

events" the lack of exposure estimates are not necessarily important. "Sentinel events" indicate a need for further investigation to determine cause(s). However, sentinel events cannot be used for setting quantitative exposure standards.

Coal rank declines going east to west and CWP risks are greater among high rank coals even at similar dust levels. But rank does not fully explain either the clustering, or other factors such as quartz, mining techniques, mine size, dust control, and enforcement of exposure limits, all of which should be considered.

It would be informative to investigate causes more specifically by conducting a case-control study to explore specific mine characteristics of cases such as CMD exposure, quartz exposure, rank of coal, and lengths of shift. This type of investigation would provide direct evidence regarding the etiology of rapidly progressive pneumoconiosis and PMF.

A case of rapidly progressive CWP was defined as "the development of PMF and/or an increase in small opacity profusion greater than one subcategory over five years." Further on, it is noted that the 1996-2002 time period is the period when the terminal x-ray was taken, and earlier films from the same period (1996-2002) or pre-1996 films are used to assess progression. The terminal film must be at least category 1/1.

If all earlier ILO classifications were zero, the final determination had to be at least category 1/2. This is unclear and was an attempt to minimize false-positive conditions, but terminal films that were classified lower than 1/2 (viz. 1/1) may also have had previous film readings which were normal.

Throughout the article, the term "over 5 years" is used and not "5 years or greater." It looks likely that the authors meant "over" to be synonymous with "greater than."

The case example given is pertinent -- the final determination of category 2/1 small opacities with PMF (large opacity size B) is clearly within the time frame designated, i.e. it occurred in the year 2000 or between 1996 and 2002. The miner's previous x-ray was from 1992 and showed category 1/2. He was young when the last x-ray was taken -- 40 years old. This progression, as did all of the attack rates, indicated it could have been from a multitude of factors; e.g. past exposures (for this particular person) for 18 years at the face, quartz content, residence time of dust in the lungs, mining methods, mine size, area where high grade metallurgical coal is taken, individual susceptibility, and inter-reader variance.

The authors also stated that the younger men were progressing. On average, the ones progressing were 48 years old and those not progressing were 51. That is a three year difference on average, with clearly overlapping distributions. This is hardly a significant age differentiation justifying a conclusion that younger miners were progressing.

In sum, sentinel events cannot be used for setting quantitative acceptable exposure limits in standards setting.

CDC (2006). "Advanced cases of coal workers' pneumoconiosis--two counties, Virginia, 2006." Morbidity and Mortality Weekly Reporter (MMWR) Morb Mortal Wkly Rep 55: 909-913.

Summary and Comments

This report describes some of the characteristics of 11 miners with advanced cases of CWP. In 2006, 31% (328) of the estimated 1,055 underground coal miners in Lee and Wise counties, Virginia were administered questionnaires, spirometry, and chest radiographs. Statistics on the examined miners and the 11 miners with advanced CWP are as follows:

	Mean age yrs	Yrs UG mining	Yrs at face
Examined Miners	47 (21-63)	23 (0-41) yrs	66% worked at face
Advanced CWP	51 (39-62)	31 (17-43) yrs	100% at face=29 yrs (17-33)

The editors make several comments. Nine of the 11 miners had not worked in coal mines prior to 1969. Based on statistical modeling using average dust exposure at the face in these counties and coal rank, the number of expected cases of CWP would be 12 if coal mine dust exposures had been 4.0 mg/m^3.

The editors propose several hypotheses to explain these cases of advanced CWP:

- The current standard of 2.0 mg/m^3 might be too high. This inference is not consistent with the data presented in their Figure (Figure 1a).
    - CMD levels in these two counties were below the standard from 1970 to 2005, and were below the NIOSH Recommended Exposure Limit ("REL") of 1.0 mg/m^3 since 1995.
    - Sampling for silica began in the early-1980s and remained above the standard of 0.1 mg/m^3 until about 1998. About 65% of silica samples collected in 1982-2000 exceeded the NIOSH REL for silica of 0.05 mg/m^3; only since 2001 have mean county levels been below the NIOSH REL for silica (their Figure 1a). [5]

- Actual dust levels might be above the standard. From 1970-2005 about 2.5% of individual samples were greater than 2.0 mg/m^3 but compliance samples may be biased and underestimate exposure levels (Boden and Gold 1984; Weeks 2003).

[5] A NIOSH Recommended Exposure Limit or "REL" is an exposure level for toxic agents that are health-based and are considered safe for various periods of employment, including but not limited to the exposures at which no worker will suffer diminished health, functional capacity, or life expectancy as a result of his or her work experience. NIOSH RELs are recommendations, not mandatory standards, but they can be adopted as such by MSHA, following rulemaking in accordance with Mine Act requirements.

• Silica might be a contributing factor as mean silica levels were above the NIOSH REL of 0.05 mg/m^3 before 2001, and 65% of MSHA samples were above the REL during 1982-2000.

• The rank of coal may be more fibrogenic in the lung, although the rank of coal in these two Virginia counties has not been previously associated with increased fibrogenicity.

Limitations to these data include participation was very low (31%) and the miners worked for only a limited time in these mines (8 of 11 had worked in current mines for less than 5-years).

Additional Comments and Critique of CDC (2006)

The silica and CMD levels may not be relevant for eight of the 11 miners as they were not working in these two counties at the time these samples were collected. If dust levels were known for the mines in which these eight miners were working, these data might support the hypothesis that excessive exposures to silica and/or CMD were etiological agents, and which agent was primarily responsible for the disease endpoint observed.

Progression can occur in a few years if these X-ray readings are reliable. For example, the 'latency' for change was six years from 0/1 to 2/2; five years from 2/1 to 2/3 and 1/2 to 2/2; four years from 0/0 to 1/2, 1/2 to 2/2 and 2/1 to 2/2; and three years from 1/2 to 2/2 (Figure 2).

The data suggest that the rapidity of progression in some cases is caused by a fairly short-term high exposure. For Miner 1 there are 23 years for progression of one sub-category (0/0-->0/1) compared to five years for a full category (0/1-->2/2). Similar changes are seen in Miners 2, 4, 7. In other instances there may be decades for sub-category progression as seen in Miners 2, 4, 7, and 11. In Miner 6 there was a regression from 2/1 to 1/2 (likely reader variability) and then progression to 2/2 in three years.

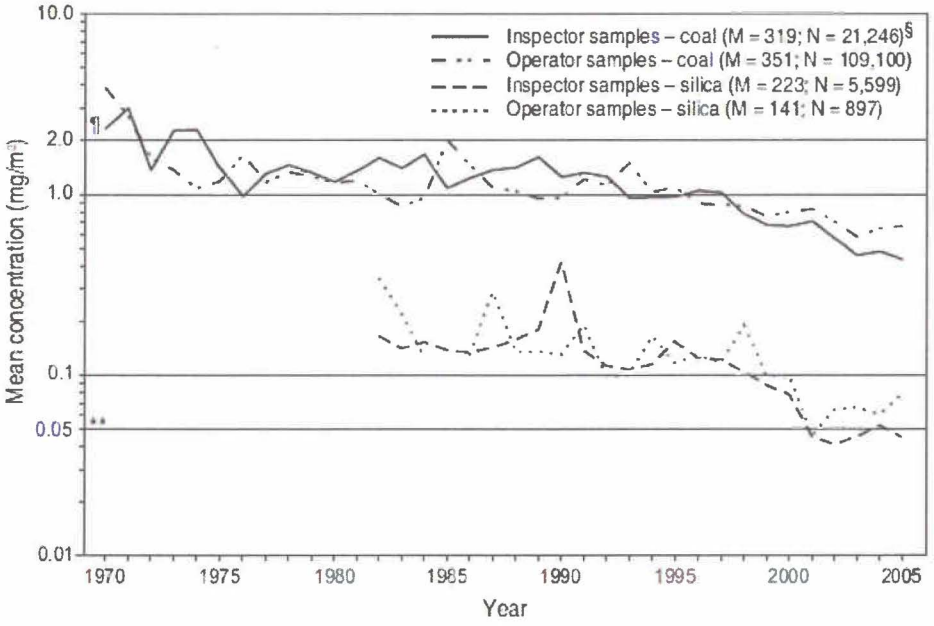
Thus, it appears there are about four miners who show rapid (<6-years) and substantial progression (a whole category or more). Moreover, two of these four miners developed PMF. These miners show the strongest pattern for progression of their condition, which is consistent with silicosis. These patterns require confirmation using additional data, including assessment of r-type opacities on the radiographs.

As the editors note, these are "sentinel health" events and largely confirm Antao, et al. (2005). Their hypotheses remain speculative without individual rather than group analysis. This individual analysis might involve a case-control study assessing individual dust exposure, silica exposure, mine size, rank of coal, height of roof, and mining practices.

High rank coal (anthracite) tends to be in the east, but high grade bituminous coals are located in the SAR. Thus, as the SAR contains high grade bituminous coals, rank probably also contributed to these cases of rapid progression.

Figure 1a

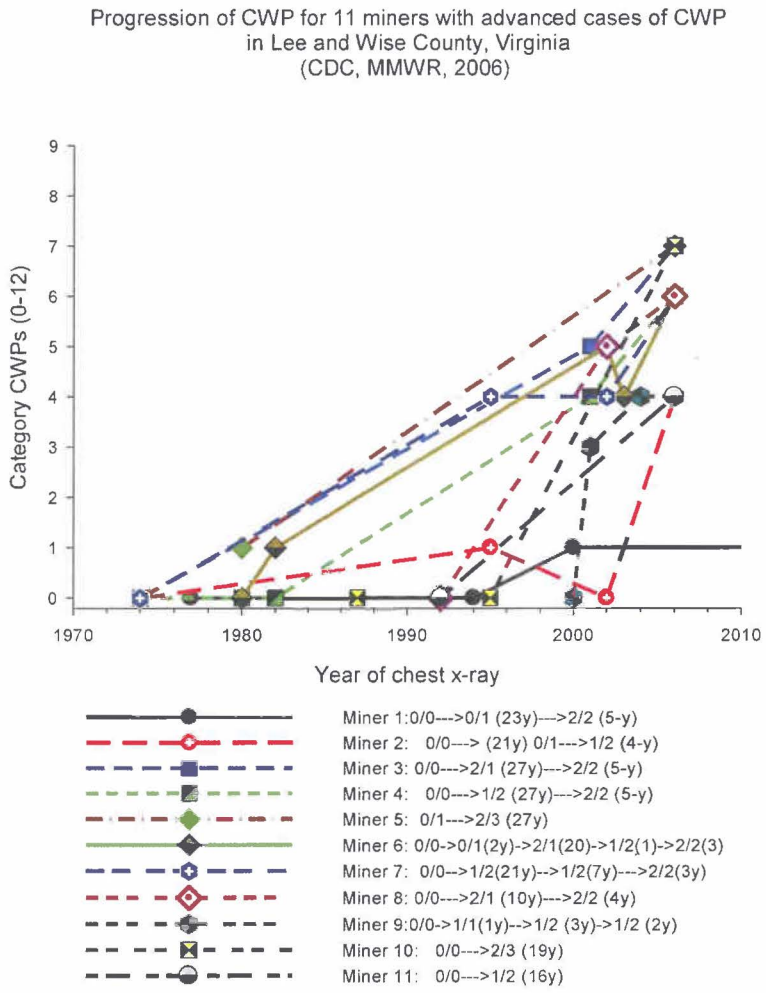
FIGURE. Mean concentrations of respirable coal mine dust and crystalline silica in coal mine dust* for underground workers at the coal face† — Lee and Wise counties, Virginia, 1970–2005



* Data from Mine Safety and Health Administration (MSHA) coal mine inspector and mine operator samples.
† The cutting surface where coal is sheared from the wall and dust levels typically are greatest.
§ M = number of mines sampled; N = number of samples taken.
¶ MSHA permissible exposure limit for coal mine dust with <5% silica content.
** National Institute for Occupational Safety and Health recommended exposure limit for crystalline silica in coal mine dust.

Figure 1a from original article.

Figure 2



The following group of studies provides indirect or circumstantial evidence about some of the hypotheses regarding the etiology of so-called rapidly progressive CWP. Rapidly progressive CWP may be a misnomer as it appears to be rapidly progressive silicosis. The predominant opacities seen on the X-ray are r-type opacities associated with silica; and there are high concentrations of quartz in the coal being mined which produces high exposures to silica, and there is rapid progression of the cases, all of which are characteristic of silicosis but not CWP.

Pollock, D., J. Potts, et al. (2010). "Investigation into dust exposures and mining practices in mines in the Southern Appalachian Region." Mining Engineering 62: 44-49.

Summary and Comments

The objective of this study was to identify mining conditions and exposures that might explain the occurrence of "sentinel health" events showing advanced and rapidly progressing cases of pneumoconioses, which were considered to be CWP, in the SAR (Antao, Petsonk, et al. 2005).

Of immediate concern in this area of the country is the fact that around half of the mines in these MSHA districts are on a reduced dust standard due to the high percentage of quartz in the CMD, per the requirements of the current provisions of 30 C.F.R. §70.101. Thus, silica exposure is a major concern.

The "hot spots" investigated were located in MSHA Districts 4 (southern WV), 5 (Virginia), 6 (eastern Kentucky), and 7 (central Kentucky and states of NC, SC and Tennessee). MSHA compliance data from 2000-2005 were extracted to analyze exposure in all occupations, continuous miner occupation, number of samples > 2.0 mg/m^3 standard and the number exceeding the reduced dust standard after adjustment for high quartz. These data were then used to target specific active mines exceeding these standards more than 5% of the time and mines cited ≥2 times for excessive dust the previous year under MSHA's Respirable Dust Emphasis Program initiative. MSHA reports of these mines were also examined for equipment, mine conditions, etc.

The results are summarized by the topic identified in analysis of these data:

- Small mines < 50 employees and compliance with standards:

Most mines are small and the proportion in compliance varied between 43% and 80% depending on the MSHA district.

Characteristics of small underground mines (<50 workers) in SAR

District	N small (% total)	% not meeting standards >5% of time	% RDEP (2+ times excessive dust	% in Compliance
4	85/148 =57%	43%	57%	43%
5	39/53 = 73.6%	90%	50%	50%
6	88/105 = 84%	83%	50%	75%
7	50/70 = 71%	66%	33%	80%
Total	262/373 = 70%			

RDEP = Respirable Dust Emphasis Program

- Mining conditions in the SAR:

All of these operations mined through substantial rock layers to maintain roof height. Thickness of rock in five mines ranged from 6-12 inches. One mine was cutting through three feet of rock. A large amount (20-30%) of rock was being cut in these mines.

Further dust surveys were conducted at six mines. Results from four of these mines indicated median dust levels were all below 2.0 mg/m^3 for continuous miner operators, shuttle car operators and roof bolters (intake and return air). However, all jobs had area sample levels greater than the standard with maximum levels between 8-10 mg/m^3. Quartz content of the dust in these jobs had median levels between 20-30% and maximum levels between 40-50% quartz. Therefore, quartz percentages ranging from 20-50% in the personal samples and area samples measures ranging from 8-10 mg/m^3 would result in area quartz exposures ranging from 1.6 to 5.0 mg/m^3; whereas the MSHA standard for quartz is 0.1 mg/m^3. Thus, the quartz exposures were a factor of 16 to 50 times the standard.

Cutting through rock drastically reduces life of the cutting bit. As the bits wear, more CMD is generated, often in quantities that prevent sprays and scrubbers from keeping up with the dust generated. In some instances every time the cutter is relocated, bits must be replaced and clogged water sprays and scrubbers have to be cleared.

Often roof bolters were working downwind of the continuous miner and bolter faces were inadequately ventilated. These conditions are demonstrated in similar median and maximum dust and percentage of quartz levels in the intake and return air of roof bolter samples.

Additional Comments and Critique of Pollock, Potts, et al. (2010)

Dust problems in the SAR relate to the fact that around half of the mines in these MSHA districts (4, 5, 6, 7) are on a reduced dust standard per 30 C.F.R. §70.101 because of quartz which is, thus, a major concern. Such high ratios (20 to 30 percent) of rock to roof height are astounding. To cut through this much silica-laden material can surely cause a marked change in the exposure contribution to disease outcomes and produces constant maintenance and ventilation problems that must be of concern just to keep producing coal in addition to health concerns.

This article gives good guidance for a select area of the country's coal fields where most of the recent increases in the reported prevalence of CWP and PMF are occurring. This article gives considerable weight to the importance of equipment maintenance and work practices as well as geological conditions. The circumstantial evidence of Pollock, et al. that characterizes mining conditions in the SAR is consistent with other articles we discuss where rapidly progressive silicosis appears when conditions are similar to those in the SAR that strongly implicate quartz exposure as well as rank and mine size. For example, the quartz exposure experienced in a Scottish colliery (Miller, Hagen, et al.

1998) produced similar cases of silicosis due to geological conditions requiring cutting through quartz-rich faults, which is similar to the descriptions of some mines in the SAR.

Moreover, 70% of the mines in these MSHA districts are small mines that are more likely to have thin seams of coal and therefore more quartz-bearing rock being cut, thereby producing higher exposure to both coal dust and silica. Since small mines are more common in the SAR than elsewhere in the country, it is not necessarily unexpected that a high proportion of rapidly progressive cases of silicosis occur in this area. Also, these small mines are more often out of compliance than large mines, especially when quartz levels are excessive.

This investigation revealed that a majority of underground small coal mines in this "hot spot" area of the SAR are out of compliance, have high CMD and quartz levels, and have difficult mining conditions that can produce rapidly progressive cases (likely silicosis, misdiagnosed as CWP).

It appears there is no more "easy coal" left to mine in this area. All mines have high proportions of rock through which miners must cut. This fact results in increased silica exposure that requires more preventive maintenance, and in the absence of adequate ventilation at the roof bolter and cutting machine faces produces excessively high coal dust and silica exposure levels.

These adverse mining conditions are described over a five-year period at the beginning of the 21st Century, which appears to be long enough for progression to higher ILO sub-categories, and in some instances to PMF. It appears likely that some of these conditions existed before 2000 and therefore could explain a portion of cases showing early signs of CWP in the 1990s or before given the short latency for silicosis progression. *See* CDC (2006).

These results are suggestive that having to mine excessive amounts of rock means that in order to stop increases in CWP, there must be continuous maintenance of dust control systems, replacement of worn bits, continual scrubber maintenance, continual surveillance to insure proper ventilation and reduction of down-wind operations. The large amount of rock through which cutting must be carried out and high quartz levels provide a strong case that silica is more likely than not the major factor producing these sentinel events of rapidly progressive CWP.

What is needed is for NIOSH to do a reanalysis of the data in the Pollock, et al. study to determine if these general characteristics of mines in the SAR, and specifically quartz concentrations, can be correlated with the SAR miners identified in the study as developing rapidly progressive CWP, to confirm whether the disease is actually silicosis.

Laney, A. and M. Attfield (2010). "Coal workers' pneumoconiosis and progressive massive fibrosis are increasingly more prevalent among workers in small underground coal mines in the United States." Occup Environ Med 67: 428-431.

Summary and Comments

The purpose of this study was to assess whether "CWP prevalence and severity are associated with mine size" among participants in the NIOSH-administered CWXSP.

Diagnosis and severity of CWP was determined from the last radiograph with agreement from two readers. All 145,512 miners with X-rays taken 1970-2009 with size and location of the mine were included in the analysis.

The reported prevalence of CWP has consistently dropped in the 1970s, 1980s and the first half of the 1990s, and began to rise in the late 1990s in mines employing less than 50 workers. For example, the reported prevalences through the decades were about 4%, 1.9%, 0.5% and 1% for mines with more than 500 employees. For small mines (less than 50 workers), the reported prevalences were 6%, 3%, 5% and 7.5% respectively. For small mines CWP reported prevalence dropped by 50% in the 1980s compared to the 1970s, but subsequently nearly doubled relative to the lowest small mines' reported prevalence in the 1980s. In general, mines intermediate in size between large and small showed intermediate trends in CWP reported prevalence.

The prevalence of PMF was higher among large mines in the 1970s and 1980s, but changed dramatically in the 1990s and 2000s when PMF became increasingly higher in small mines for the next two decades. Adjusting for age, miners from small mines in the 1990s were three times more likely to have PMF than miners from large mines and five times more likely in the 2000s (Figure 3).

Additional Comments and Critique of Laney and Attfield (2010)

Increases in reported prevalence and severity of PMF since 2000 is well documented (Figure 3), but the reason for these changes is less clear. This study clearly shows that the increasing reported prevalence of PMF beginning around the 1990s is due in large part to PMF in small mines. Reasons for this dramatic shift of prevalence from large to small mines is unknown and cannot be assessed in this study.

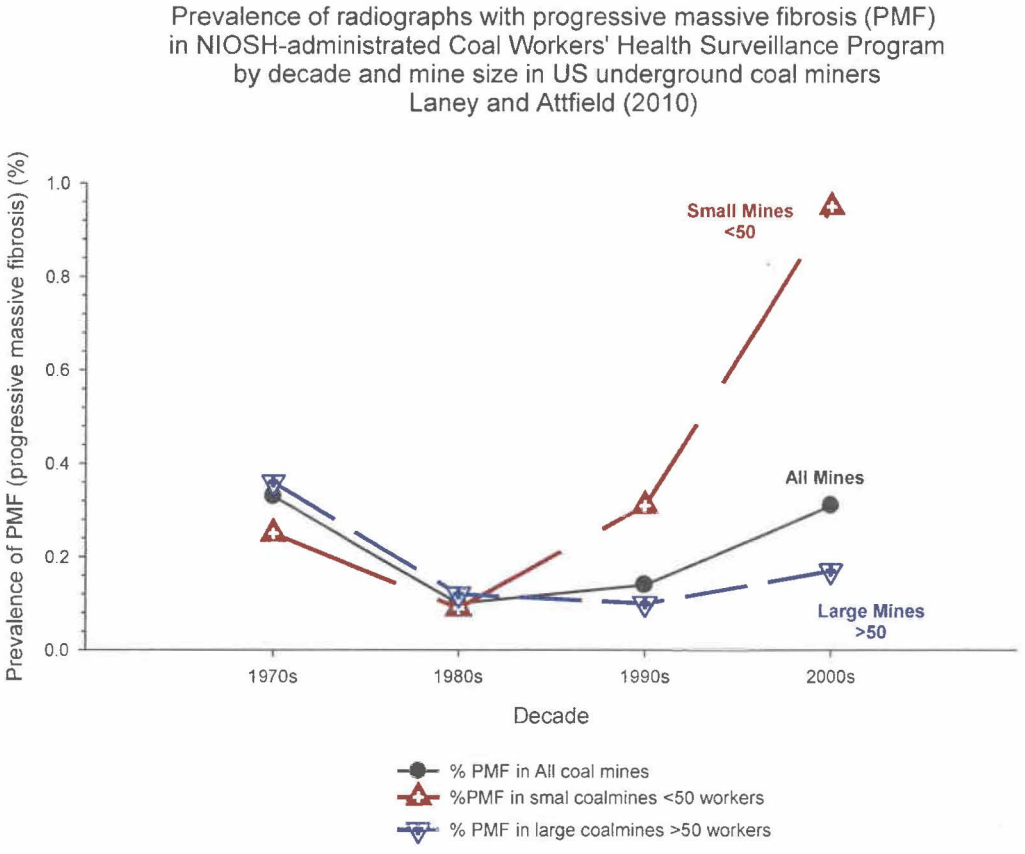
The authors indicate several adverse effects occurring more commonly in small mines. One is that non-fatal disabling injuries and fatalities are more common in small mines (Hunting and Weeks 1993; NIOSH 2006). A reason may be a younger, less experienced workforce (Hunting and Weeks 1993). This is not a plausible reason for size-related PMF effects in this study because differences were modest in absolute terms and because of adjustments for age differences.

Excessive quartz and mixed mine-dust exposures have been suggested as potential causes of severe CWP. Small mines work thinner seams of coal and cut more rock than larger mines. This study does not support this reason as thin-seams are primarily in Kentucky, Virginia and West Virginia while the small mine-effect was observed nationwide. However, the vast majority of thin seam coal being mined is in small mines in the SAR.

Small mines may have higher actual CMD levels than operator-sampled levels indicate. MSHA inspectors made inspections of coal mines to sample CMD levels at the face, and compared them to operator-based samples. At large mines the results were comparable. As the size of the mine decreased, the operator-based sample results tended to become smaller as mine size became smaller. The maximum difference shown was when MSHA samples were about two-fold greater than operator samples (MSHA 1993).

These results suggest CMD and quartz levels in small mines may be (more-or-less) two-fold higher than mine operator samples for equal percentages of quartz in the CMD. This phenomenon produces biased underestimates of exposure, which in turn produces biased overestimates of the potential to produce pulmonary fibrogenicity in the lung.

Figure 3



Laney, A., E. L. Petsonk, et al. (2010). "Pneumoconiosis among underground bituminous coal miners in the United States: Is silicosis becoming more frequent?" Occup Environ Med 67: 652-656.

Summary and Comments

The possible role of silica in the increasing occurrence of reports since 2000 of rapidly progressing CWP led to this investigation. Since 1980, mean CMD levels have been consistently below mandatory standards. This apparent contradiction suggested further explanation was needed. Silica seemed a plausible possibility as dust generated during coal mining now contains a higher proportion of crystalline silica that produces "an increased inflammatory response and potent induction of pneumoconiosis." Lesions typical of silicosis have been observed in some miners (Seaton, Dodgson, et al. 1981; Jacobsen and Maclaren 1982; Castranova and Vallyathan 2000). Also, rapid progression and PMF are more characteristic of silicosis than CWP (Seaton, Dodgson, et al. 1981; Hurley, Burns, et al. 1982; Jacobsen and Maclaren 1982).

To test the quartz hypothesis, chest radiographs collected by NIOSH from 1980-2008 were examined for rounded opacities greater than 3 mm = r-type opacities. Silicosis can also be characterized by "p" and "q" type opacities. Like simple CWP, silicosis is characterized primarily by rounded opacities occurring mostly in the upper lung zones and sometimes with hilar involvement and calcifications. Thus, it is often difficult to distinguish silicosis from ordinary CWP on the chest radiograph.

There were 2868 radiographs (3.2%) showing category ≥ 1. Between 1980 and 2008 the proportion of categories 0 and 1 showed little change. Since 1990, there has been an increase in category 2 and 2.5-fold increases in category 3 and PMF respectively (Figure 4).

There were 321 (0.35%) X-ray readings showing r-type opacities (primary and secondary) overall during 1980-2008. For the SAR, prevalence of both r-type opacities and PMF increased each decade with a 7.6-fold increase in r-type lesions in 2000-2008 compared to the 1980s. For the rest of the US there was no trend for r-type opacities to increase, and slight downward trends for PMF (Figure 5).

Critique of Laney, Petsonk, et al. (2010)

The authors conclude the increasing reported prevalence of r-type opacities, rapid progression and more severe disease (PMF) in the Appalachian coal fields is consistent with an increased exposure to crystalline silica (quartz) and silicosis etiology.

The increase in reported prevalence does not appear to be caused by changes in the readings over this 30-year period as tested in a subset of B readers' employed over this entire time period. R-type opacities are plausible indicators of excessive quartz exposure based on autopsy findings of classical silicotic nodules and high levels of non-combustible ash consistent with silica (Soutar and Collins 1984). CWP commonly does

not progress rapidly, and requires a long latency period. On the other hand, silicosis has these characteristics, particularly at high concentrations well above the quartz standard.

Quartz is not necessarily the only cause of rapidly progressing CWP. Coal production has increased nearly 70% since the 1980s. There has been a trend toward increasing hours worked per shift that leads to higher CMD deposition. Increased reported prevalence could also be due to several other factors, e.g. different miners studied at different times, different x-ray readers interpreting films, and different ILO standards being utilized.

Several factors emphasize quartz as a plausible explanation for the SAR being a "hot-spot" geographic area. Increased mining has reduced available coal in the most easily accessible coal seams. The high demand for coal, its increasing price and increasingly productive equipment for extracting and cleaning coal has led to mining thinner and thinner seams. Silica-containing rock commonly surrounds coal seams. The thinner the seam the greater the proportion of rock and quartz that has to be cut relative to coal. Almost all (96%) of thin coal seams (less than 43 inches) are located in Kentucky, Virginia, and West Virginia.

Under these mining conditions one would expect elevated quartz levels in personal samples taken to enforce the CMD standard. Such an increase has not been noted in compliance samples, but this has been explained as not happening because quartz measurement is indirect and complicated.

This study is one of several implicating quartz rather than CMD and suggesting that the increased reported prevalence of CWP and rapidly progressive pneumoconiosis observed over the last 20-years may actually be rapidly progressive silicosis.

While not known for sure, this study (like others) strongly points towards a serious quartz effect. As the study authors note, further evaluation of quartz exposures and control strategies is necessary in all underground coal mines, but the SAR should be a primary target. While there are many limitations regarding the use of the NIOSH surveillance records, this is nonetheless worthy information.

Figure 4

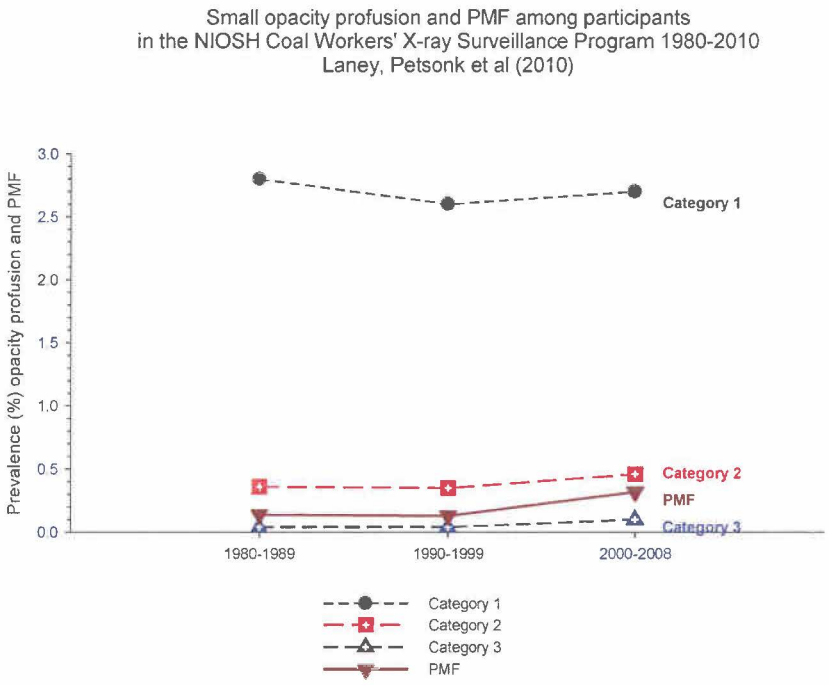
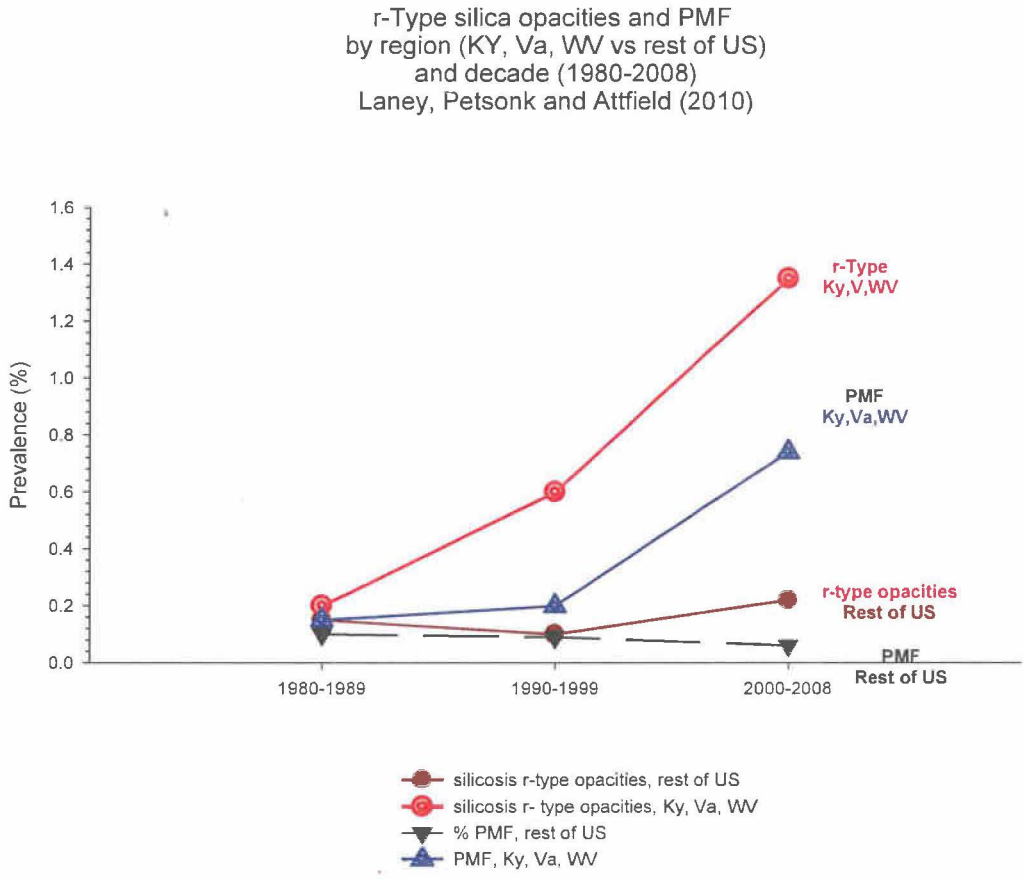

Small opacity profusion and PMF among participants
in the NIOSH Coal Workers' X-ray Surveillance Program 1980-2010
Laney, Petsonk et al (2010)
Prevalence (%) opacity profusion and PMF
3.0
2.5
2.0
1.5
1.0
0.5
0.0
1980-1989
1990-1999
2000-2008
Category 1
Category 2
PMF
Category 3
Category 1
Category 2
Category 3
PMF

Figure 5



Miller, B., S. Hagen, et al. (1998). "Risks of silicosis in coalworkers exposed to unusual concentrations of respirable quartz." Occup Environ Med 55: 52-58.

Summary and Comments

The purpose of this study was to describe radiographic changes and their relationships to dust exposure among Scottish coal miners exposed to unusual concentrations of respirable quartz.

Chest radiographs were available on 547 coal miners who had worked at one Scottish colliery during the 1970s. The colliery participated in six medical surveys of the British Pneumoconiosis Field Research ("PFR") conducted from 1954 to 1978. At the sixth survey there were 21/623 (3.4%) coal miners who showed unusually rapid progression of pneumoconiosis compared to radiographs taken four years earlier. A small case-control study of the 21 cases (Seaton, Dodgson, et al. 1981; Seaton, Dick, et al. 1982) showed

clear exposure-response relations with respirable coal dust, and an even stronger relationship with the respirable quartz exposures in the 1970s. The radiographic changes resembled silicosis. Normally there is <10% quartz in CMD. In this colliery there were two seams of coal being mined in the 1970s. In seam A mean exposures were less than 1.0 mg/m^3 and the proportion of quartz never exceeded 15%. In seam B more than 10% of samples were >1.0 mg/m^3, two work groups had means (>10 samples) that were > 10 mg/m^3, and in some instances there were proportions of quartz up to 60%. In all the surveys the mean percentage of quartz in environmental samples was 4.8%, 7.7%, 8.6%, 9.1% and 7.3 %; maximum % quartz in these samples was 7.6%, 17.5%, 29.4%, 26.6%, and 16.1% respectively. During the 1970s both quartz and coal dust exposures were high.

These data show a clear and strong exposure-response relationship between CWP ≥ ILO Category 2 small opacities (CWP 2+) and respirable quartz from mining in this particular colliery. This clear trend is seen in a categorical analysis (Figure 6). The best logistic regression models were with quartz exposures from surveys 3-6 either with or without non-quartz dust in the model. Non-quartz CMD showed no association with CWP 2+ at any concentration and a slightly negative association in the model with respirable quartz (Figure 6). The authors summarize this association as: "with quartz exposure in the model, non-quartz dust gave no significant improvement, whereas the inclusion of quartz after dust was highly significant. This is strong support for the conclusion that the abnormalities found are the result of the exposure to respirable quartz, rather than to the non-quartz content of the dust."

Additional Comments and Critique of Miller, Hagen, et al. (1998)

These data do not support an association of CWP 2+ with CMD up to cumulative exposure around 10 gh/m^3 (5.7 mg/m^3) (Figure 6).

A reason for suspecting quartz exposure is because much higher risks than expected were produced for low CMD levels with the typical composition according to the authors. The rapid progression occurred after the high quartz exposures were diminished, which is atypical for CWP but typical of silicosis.

The best predictor of risk for category 2/1+ was quartz exposure particularly during 1964-78 when concentrations were high. During this inter-survey period of about 15-years, the model predicted that an average quartz exposure of 0.1 mg/m^3 or cumulative exposure of 1.5 mg/m^3-years produced a risk of about 5%. About 20% of the miners had exposures greater than 3.25 mg/m^3-yrs and risks of about 10% of category 2/1+. These data suggest that coal miners with quartz exposures at these levels may be showing increased risk of silicosis incorrectly interpreted as CWP. To avoid this misclassification, exposure estimates should include both quartz and CMD, radiographs should be carefully examined for the appearance of silicosis and the relationship between progression of disease with and without quartz should be analyzed.

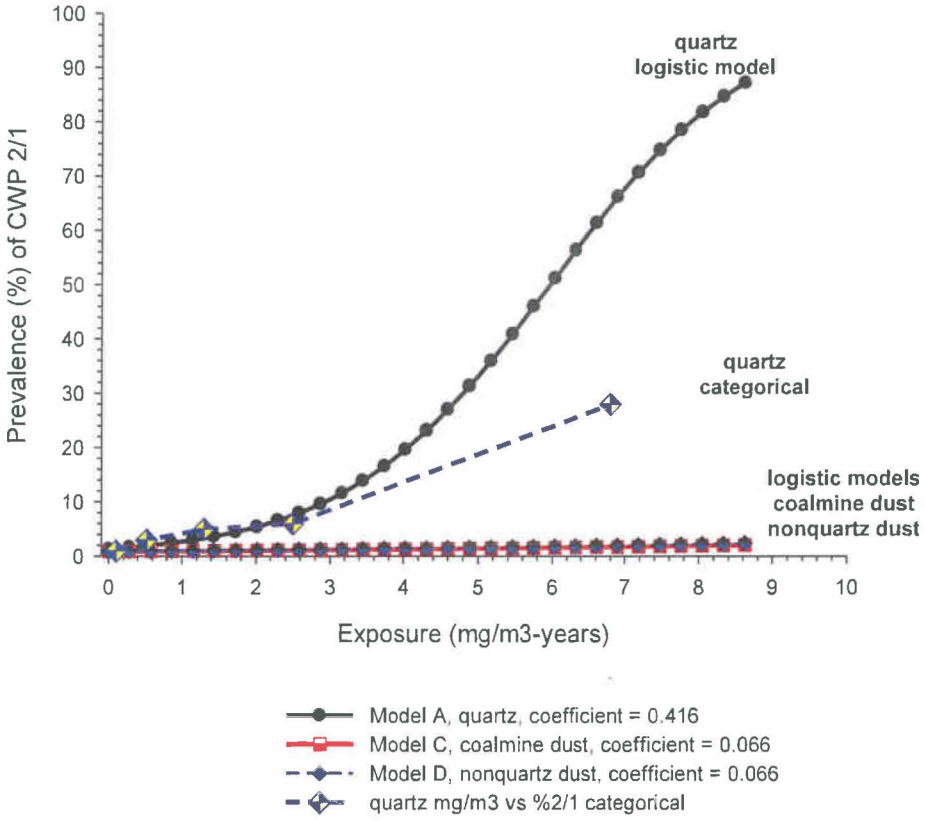
The logistic regression results indicated no risk from non-quartz CMD at any exposure level in this mine (Figure 6).

A limitation of this study is that it is not clear how exposure to quartz and non-quartz CMD were determined for the miners as "data are differentiated by seam" and miners worked in different seams at different times. The use of gh/m^3 units is confusing as it was not clear when the units were for average and when for cumulative exposure. There is a clear difference between the strong association quartz with 2/1+ and no association with CMD or non-quartz dust. The estimated risk at average or cumulative exposure to quartz is unclear because the distinction between average and cumulative exposure is not made by the authors.

This is a well-done but small study. It clearly demonstrates the importance of quartz content in CMD exposures. Rapid progression of pneumoconiosis was very likely silicosis, and the predicted risk of 2/1+ at follow-up provides good evidence for exposure-response to respirable quartz.

Figure 6

Exposure-Response of CWP 2/1 and quartz, coal mine dust,
and non-quartz coal mine dust by logistic regression
in British coalmine with unusual concentrations of respirable quartz
(Miller et al, 1998)



Buchanan, D., B. Miller, et al. (2003). "Quantitative relations between exposure to respirable quartz and risk of silicosis." Occup Environ Med 60: 159-164.

Summary and Comments

This study is a re-analysis of the exposure-response data from the Scottish colliery (Miller, Hagen, et al. 1998) and considered alternative quartz indices taking into account variable intensities and time elapsed since those exposures.

Risks of CWP 2+ were evaluated by cumulative exposures to CMD and quartz for all periods and for pre- and post-1964. For CMD there was no association with CWP, with an odds ratio ("OR") = 1.03 (1.02-1.04) for all time periods. For quartz, there were clear associations with pneumoconiosis with ORs of 1.70 (1.46-1.99) for all time periods and 1.81 (1.54-2.14) for the post-1964 time period. There were no increased risks of CWP associated with age, smoking or CMD.

The risk of category 2/1 silicosis with long exposure to low concentrations of quartz combined with high short-term exposures (2.0 mg/m^3 in this example) shows a dramatic increase in silicosis risk with relatively short periods of high quartz exposure (Figure 7).

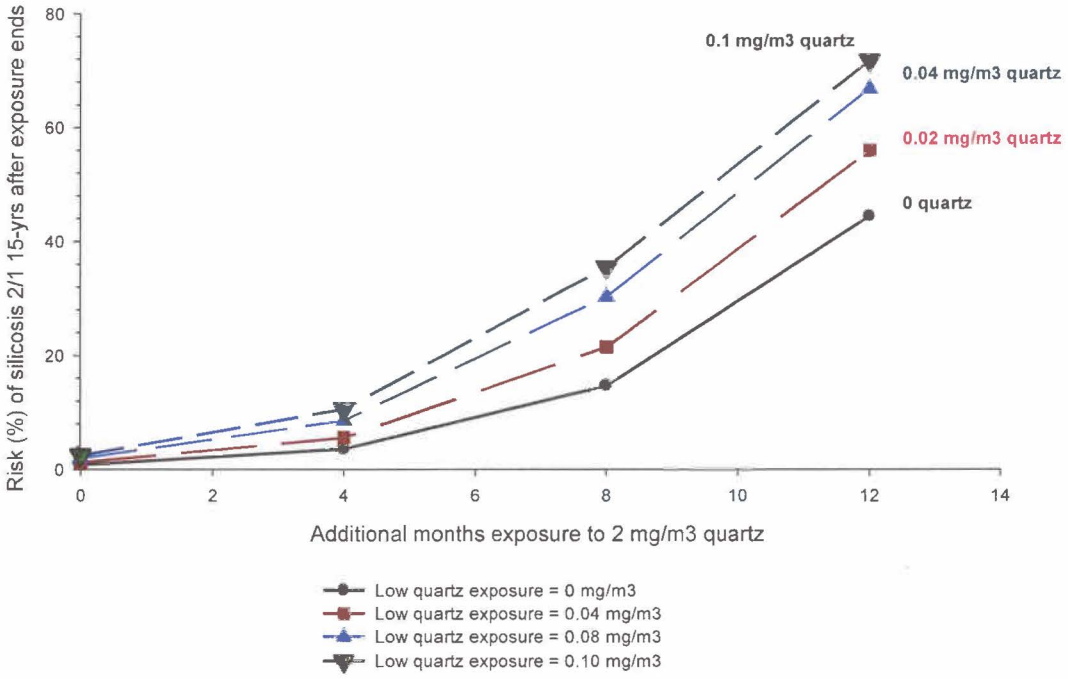
Additional Comments and Critique of Buchanan, Miller, et al. (2003)

This paper shows a dramatic effect of short but high exposures to quartz in CMD that is not associated with CWP. Using data from the Scottish colliery cohort (Miller, Hagen, et al. 1998) the regression models predict the occurrence of silicosis after 15 years CMD exposure with variable (0-0.10 mg/m^3) quartz exposure, and added months of high quartz exposure (2.0 mg/m^3) (Figure 7). The effect of cumulative CMD exposure is negligible, while cumulative quartz exposure produces a substantial increase in silicosis prevalence. The model then predicts the effect of high quartz exposures of 2.0 mg/m^3 occurring over a year. The 2.0 mg/m^3 concentration is representative as maximum concentrations were 3.0 mg/m^3. Four months exposure to 0.04 mg/m^3 quartz increases 4.4 fold the occurrence of CWP 2+ from background prevalence (zero months quartz exposures) (Figure 7). The NIOSH REL for quartz is 0.05 mg/ m^3 and the American Conference of Governmental Industrial Hygienists Threshold Limit Value is now 0.25 mg/m^3. For 1-year high quartz exposure the risk of CWP 2+ increases 56-fold. Coal mined from Seam B greatly increased quartz exposure and is the period when quartz effects are greatest. The high quartz exposures essentially drown out other exposure effects from low quartz and CMD.

This analysis suggests that coal miners without radiographic indications of CWP and exposed for even a short time (months), may show unexpectedly large increases in radiographic indications of silicosis. These progressive changes appear to be silicosis, not CWP, and are consistent with the recent and unexpected increase in rapidly progressive silicosis (Scarisbrick and Quinlan 2002; Antao, Petsonk, et al. 2006; Antao August 25, 2006) observed in the SAR.

Figure 7

Predictions of risk (%) of category 2/1 silicosis after 15-years exposure
to low centrations of quartz plus additional months exposure to
high (2 mg/m3) silica exposure
Buchanan et al (2003)



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III. COAL RANK AND EXPOSURE-RESPONSE RELATIONSHIPS WITH CWP

1. Summary of Exposure-Response Studies of CWP by Coal Rank

Rank of coal is a classification based on fixed carbon, volatile matter, and heating value of the coal. Coal rank indicates the progressive geological alteration (coalification) from lignite to anthracite. The term 'rank' refers to the quality of the coal. High rank coal has higher carbon content and is relatively smokeless. It includes anthracite, steam coal and high-grade coking coal. Low-rank coal has lower carbon content such as smoke-producing house coal. The British National Coal Board ("NCB") uses nine major ranks of coal:

Rank	Description	Approximate Carbon Content
100	Anthracite	95-93%
200	Low volatile steam coal	93-91.5%
300	Prime coking coal	90.5-89
400	"	89-87
500	Coking /gas coal	87-85
600	"	85-84.5
700	General purpose coal	84.5-83.5
800	High Volatile steam	83.5-81.5
900	and house coal	81.5-80

Coal rank has historically been understood to be related to the incidence and prevalence of CWP. A 1942 study in 16 collieries in South Wales found the highest prevalence of radiological abnormalities in anthracite mines and the lowest in bituminous mines with steam-coal mines intermediate. Using three broad rank categories (100-400; 500-600; and 700-900) a study in the UK found it took eight years to produce a 20% prevalence of CWP when exposed to highest rank, 16 years for the intermediate ranks, and 36 years for the lowest ranks (Bennett, Dick et al. 1979). In 1949 the first British coal dust standard for anthracite was 650 particles/cm^3 compared to 850 for lower ranked coals.

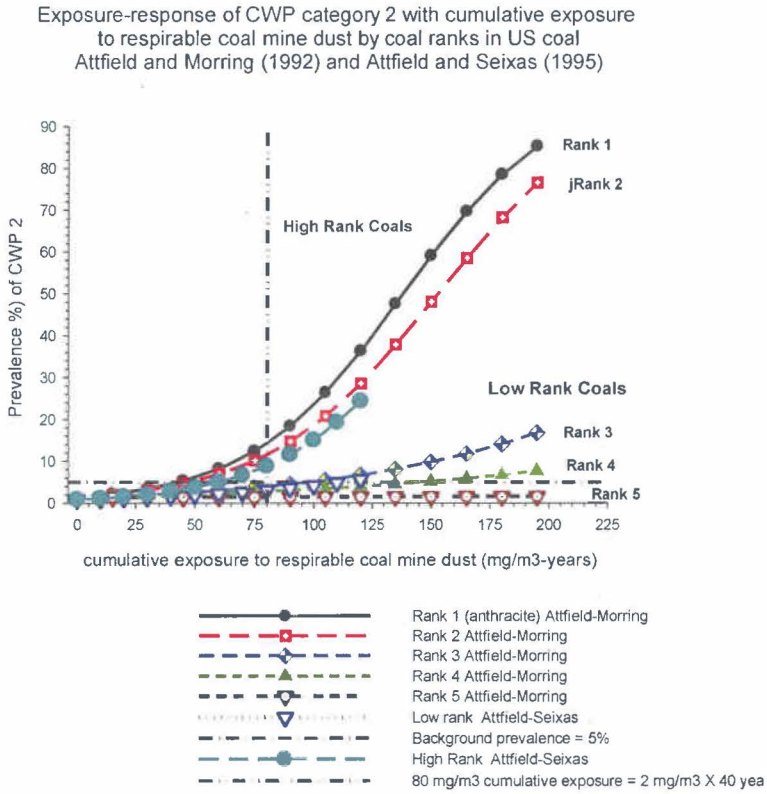
We reviewed more recent studies to confirm the important role of rank in development of CWP and whether there is a substantial difference in pulmonary fibrogenicity that might warrant a different standard for high vs. low rank coals.

These studies consistently show that exposure-response associations are in part defined by coal rank. The higher the rank of coal, the greater the prevalence of all categories of CWP for equivalent CMD exposures. These associations were observed in all the studies from both the UK and the US without exception.

All studies show higher prevalence of CWP at higher ranks compared to lower ranks without regard to dust concentration. Assuming a background prevalence of 5% among

non-dust exposed workers, the evidence suggests that below 2.0 mg/m^3 there is no excess CWP 2+ for coal ranks 3-5 (low-medium ranks) in the US (Figure 1).

Figure 1



2. Comments on Studies of Exposure-Response Studies of CWP by Coal Rank

Page, S. and J. Organiscat (2000). "Suggestion of a cause-and-effect relationship among coal rank, airborne dust, and incidence of workers' pneumoconiosis." AIHAJ 61: 785-787.

Summary and Comments

This paper is a summary of results from other studies that have investigated characteristics of CMD that could produce different exposure-response associations. These include:

- Degree of surface coating of coal in part determines the biological availability of silica, with the greater the occlusion the less the biological availability (Bauer 1982);
- Fresh-fractured coal and rock on the surface of high rank coal is more reactive *in vivo* than aged silica;

- Higher ranked coal produces a higher electromagnetic charge on breaking;
- Coal fractions are positively correlated with moisture and negatively correlated with electrostatic field. The largest amount of respirable particles are produced from lower rank coals;
- The higher the electrostatic charge the greater the lung deposition (Melandri, G, et al. 1983);
- Freshly broken coal and quartz contain highly reactive free radicals (electric charges) and potentially greater cytotoxic effects.

The "charging" characteristics of coal suggest a significant cause-and-effect relationship between the coal rank-related charging characteristics, enhanced respiratory deposition and toxicity of airborne respirable particles, and the increased incidence of CWP in high rank coal regions.

Additional Comments and Critique of Page and Organiscat (2000)

This article provides support and possible reasons for increased prevalence of CWP in higher ranked coals. The evidence is reasonable but indirect in that it is largely lab-generated and not measured in the field. It is clearly reasonable that the amount of occlusion determines (i.e. at least partially) the amount of biologically available silica in an inverse relationship. A second factor relates to free radicals found on freshly fractured rock and coal from high rank coal areas. There is a consistent positive correlation with the amount of respirable sized particles related to increased coal rank. The authors' discussion relates to both quartz and coal rank. Nonetheless, they reason that the amount of airborne respirable dust produced from different coals can be predicted based on coal rank parameters. Moreover, the authors call for more effective dust generation and abatement (for higher rank coals) through engineering control technology.

Bennett, J., J. Dick, et al. (1979). "The relationship between coal rank and the prevalence of pneumoconiosis." Brit J Ind Med 36: 206-210.

Summary and Comments

This paper studies the relationship between rank of coal mined and the prevalence of CWP among all face-workers in the UK during the 3rd survey of the NCB's periodic x-ray surveillance program. There were 250 collieries and the rank of coal in each colliery was determined.

Rank refers to the quality of the coal with the higher the ranking (lower numbers) the higher the carbon content. The authors note that the quartz content of airborne dust is higher when low-rank coal is mined than when high-rank coal is mined. From the paper, it is not clear whether this quartz is quartz admixed in the coal or from rock surrounding the coal seam. High rank coals have a low number and include anthracite, low volatile steam coal and high-grade coking coal (starting at rank 100). Low rank (high number) coal is bituminous and smoke-producing house coal (ranks coming down from 900).

Coal rank of each colliery in this study was based on one of the following criteria:(a) all coal of one rank; (b) if two ranks are mined the one with highest tonnage was selected; (c) if three ranks are being mined the ranking is based on the rank with tonnage greater than the other two, or the central rank if output is similar; (d) when coal is limited to three or four adjacent ranks the extreme rank is selected if represented by at least ¾ of output.

There were 62,362 face-workers with at least five years tenure, the earlier job being at the face. Prevalence rates were the percentage of radiographs showing category 1/0 and greater collected at each colliery 1969-73.

Mean colliery exposure was gravimetric (mg/m^3) measurements collected at the face from 1970-1976, so prevalence of CWP is based on exposures experienced around the time the relevant X-rays were taken, but exposures causing the CWP were during an earlier period before gravimetric sampling was introduced.
The authors conclude that for ranks 200-900 there is a progressive fall in CWP prevalence with decreasing coal rank that cannot be ascribed to a rising gradient of mean age nor to dust concentrations with lower exposures occurring at the higher ranks of coal.

Additional Comments and Critique of Bennett, Dick, et al. (1979)

Figure 2 displays the exposure-response trend between CWP 1/0+ prevalence and mean exposure by coal rank. These data suggest two significant results are related to coal rank. Miners working in higher ranked coals (100-400, with rank 200 being an exception) tend to have a higher prevalence of CWP (13-21%) but lower dust exposures (3.1-5.0 mg/m^3). Miners working in lower ranked coals (500-900) tend to have a lower prevalence of CWP (3.9-11%) but higher CMD exposures (5.1-5.5 mg/m^3). The higher prevalence of CWP in some bituminous coal mines might be related to the higher quartz content in airborne dust in lower-rank coals than higher ranked coals. Whether this is because there is more quartz admixed in the low-ranked coal deposits, or whether it is necessary to cut into more of the strata above and below the low rank coal seam encountering more quartz in waste rock, is unclear.

These data grouped by colliery suggest no apparent exposure-response trend for either low or high category of coal. For low-rank (bituminous) or high-rank (anthracite, high-grade coking and steam) coals there are no trends for prevalence of CWP to increase with increasing exposures.

Note that the average exposures among face-workers in this study are well above the US standard of 2.0 mg/m^3; most exposures were above 5.0 mg/m^3. These mean gravimetric exposure estimates in mg/m^3 are quite high. Unfortunately, earlier non-gravimetric sample results prior to 1970 are not evaluated. The absence of these data is a limitation that over-estimates the toxicity of CMD if concentrations at the face were higher before 1970.

The exposure-response trends are further limited as the pre-1970 period is when CWP would be developing in these miners. The exposure estimates are based on the average of

all mines, so exposure is an ecological (group-based) estimate rather than a preferred estimate based on individual exposures over an entire work-life in coal mining.

There is an apparent downward trend in CWP prevalence with increasing mean exposure except for the outliers of low-ranked coals 300 and 200 where prevalences are highest and exposures are at the low end of the high-ranked coals.

The overall data without regard for rank suggest a negative exposure-response trend of decreasing prevalence of CWP with increasing exposure. If rank is considered there are no apparent exposure-response trends among low- and high-rank coals.

"Exposure" in this study is a group rather than individual estimates. An individual exposure estimate considers years of exposure and variations in intensity of exposure over time, thereby providing reasonable measures of cumulative exposure. This study provides an estimate of intensity (mg/m^3) only at the time the response (CWP) is being measured, without consideration for the entire work history and earlier exposures to coal mine dust. As a result data from this study should not be considered reliable for determining exposure-response trends between CWP and exposure to CMD.

These data are consistent with other findings suggesting that high rank coal (i.e., low numbers, anthracite) appear to produce CWP at lower exposure levels than low rank soft bituminous coal.

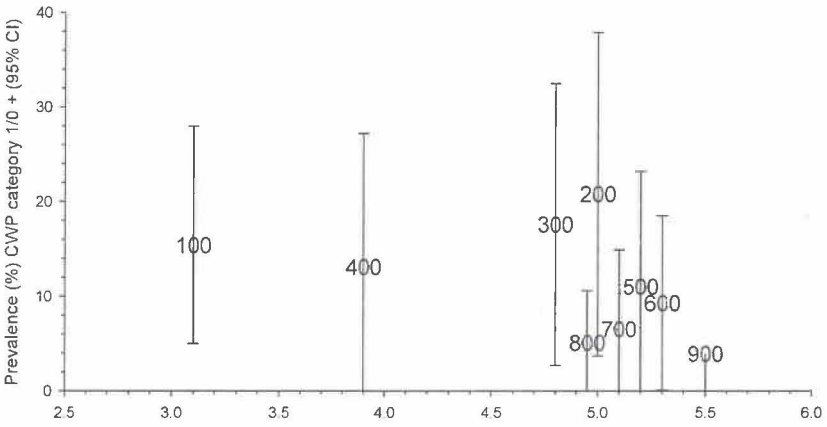
The authors indicated they were attempting to achieve an unbiased estimate of progression of CWP. What is shown is that the prevalence of CWP for high rank coal is much greater than for low rank coal.

The authors' Table 4 is interesting and one wonders why exposure data are not shown for different areas with equal rank coal. While rank appears to be important, there are other factors involved affecting the prevalence of CWP that were not included such as silica content and past exposures.

In sum, these study results are not useful for determining a standard.

Figure 2

Relationships between coal rank, pneumoconiosis equal to or greater than category 1/0 and mean colliery respirable dust concentration 1970-76 among 247 colleries in UK National Coal Board's Periodic X-ray Scheme
Bennet et al, 1979



100 Rank 100, anthracite, 93-95% carbon
200 Rank 200, low volatile steam coal, 93-90.5% C
300 Rank 300, prime coking coal, 90.5--89% Carbon
400 Rank 400, Coking/gas coal, 87--89% carbon
500 Rank 500, Coking/gas coal, 87-85% carbon
600 Rank 600, Coking/gas coal, 85--84.5% carbon
700 Rank 700, general purpose coal, 84.5--83.5% C
800 Rank 800, High volatile steam, 83.5--81.5% C
900 Rank 900, house coal

Attfield, M. and K. Morring (1992a). "The derivation of estimated dust exposures for U.S. coal miners working before 1970." AIHAJ 53(4): 248-255.

Summary and Comments:
This study derived estimates of cumulative CMD exposures applicable to the exposures prior to the first round of the NSCWP. These estimates were subsequently used in two morbidity studies (Attfield and Morring 1992b; Attfield and Seixas 1995) and a mortality study (Attfield and Kuempel 2008).

Estimates of pre-1970 job exposures were derived from back-extrapolation of MSHA compliance sample data collected 1970-72 to pre-1970 (1968-69) BOM data collected in 17 mines (Doyle 1970). Ratios of BOM data by job ÷ MSHA job exposure provided the relative difference between pre- and post-1970 job exposures. The average of these ratios was calculated to be 2.3, which means that on average the pre-1970 mean exposures were 2.3 times greater than post-1970 job exposures. This ratio was used for adjustment in the back-extrapolation. Cumulative exposure for individual miners was calculated from work histories obtained by interview in the first round of the NSCWP. The summation of years spent in each job x mean exposure for each job gives cumulative exposure in

mg/m^3-years. Mean job exposure in mg/m^3 was derived from the back-extrapolation of MSHA data.

The authors' noted that "the resulting estimated exposures have been shown to correlate well with various measures of respiratory morbidity."

Additional Comments and Critique of Attfield and Morring (1992a)

A concern with the NIOSH data is the recall ability of miners on the work history. No validation of recall ability has been made, and neither the direction nor magnitude of the bias is known.

Development of CMD exposures before the first round of the NSCWP (or pre-1970) was the primary objective of this paper. The procedure followed attempted to convert the 1970-2 MSHA data to the 1968-9 BOM data for use in estimating pre-1970 cumulative exposures in the exposure-response studies. Unfortunately, these converted estimates appear to be biased relative to the BOM data. Assuming the pre-1970 data provide the best exposure estimates for this time period, the effects of this bias are to elevate the slope of exposure-response curve and reduce thresholds of effect, thereby spuriously over-estimating risk. The logic and arithmetic of this premise are discussed following.

The BOM data collected in 1968-69 were the first gravimetric sampling done in US mines and 17 of the mines were part of the NSCWP. The differences in CMD levels between BOM and MSHA data were calculated for each job, and can be calculated from the authors' Table 1. The BOM data are also discussed in Doyle (1970). An overall mean ratio of 2.3 was calculated, indicating that BOM job exposures levels were on average about 2.3 times greater than MSHA levels for the same jobs. This conversion factor of 2.3 was used to back-extrapolate from the MSHA post-1970 compliance data to be used as the measure of pre-1970 exposures in place of the BOM exposure data. Or stated in a slightly different manner, the 1970-72 MSHA job-specific mean dust levels were multiplied by a factor of 2.3 and back-extrapolating these values to the pre-1970 experience.

For example, CMD exposure of a continuous miner operator using the NIOSH method versus direct use of the BOM data leads to different answers.

- The BOM data for a continuous miner operator indicated a mean concentration of 6.8 mg/m^3.
- The MSHA data for the 1970-72 period indicated a mean concentration of 2.4 mg/m^3.
- The calculated conversion factor for a continuous miner operator would be $6.8 \div 2.4 = 2.8$.
- Using this conversion factor, the estimated exposure concentration would be $2.8 \times 2.4 = 6.7$ mg/m^3.

- Rather than using job specific conversion factors or the actual BOM sample results, NIOSH calculated a universal factor of 2.3 from the mean of all 25 job-specific conversion factors that can be calculated from the authors' Table 1.
- Using the NIOSH universal conversion factor, the estimated exposure concentration for a continuous miner operator calculated and used in NIOSH studies would be 2.3 X 2.4 = 5.5 mg/m^3.
- Thus, for the continuous miner operator job category, the NIOSH approach would underestimate the exposure by 22%.

These back-extrapolations are biased because they are based on an average ratio rather than job-specific ratios. The biases are displayed in Figures 3 and 4, which also show that exposures are generally under-estimated in high exposure jobs and under-estimated in low exposure jobs.

Figure 3 shows the universal conversion factor of 2.3 and the BOM job-specific data points above and below this line. Points below the line are lower exposure jobs based on the BOM data. When their MSHA exposure is multiplied by 2.3 to estimate pre-1970 exposure, the MSHA exposure is larger than the BOM estimate. That is, exposure is greater than expected so risk is over-estimated or biased upward.

BOM data points above the 2.3 conversion factor are higher exposure jobs. When the MSHA job mean is multiplied by 2.3 to estimated pre-1970 exposures, the calculated NIOSH estimate is less than the BOM mean. That is, the NIOSH estimated exposure under-estimates exposure, which produces a biased increased risk.

Cumulative CMD exposure is estimated by the summation of tenure x job exposure. Since job exposure is biased, cumulative exposure will be biased in the same directions. There is a rough breaking point for higher and lower exposure jobs at about 4 mg/m^3. This point is a metaphorically a kind of fulcrum. To the left the exposure-response curve is biased downward and to the right the curve is biased upward; the effect is a spuriously steeper slope and spuriously increased risk at higher exposures. If the biases were adjusted or removed, the exposure-response slope becomes flatter and the association weaker.

This bias is applicable to the first morbidity study of CWP (Attfield and Morring 1992b) and the last mortality study (Attfield and Kuempel 2008) where only pre-1970 data are used. The other morbidity study used both pre- and post-1970 exposure (Attfield and Seixas 1995). The latter authors noted the potential for the under-estimation bias in exposure via "probable systematic underestimation of higher dust levels brought about by certain mine operator sampling practices over the years" and special sampling exercises that showed "operator sampled dust levels were indeed systematically lower than those collected by inspectors" (Attfield and Seixas 1995). This operator bias increases the effect of the NIOSH calculation bias,

Because of these biases, estimated risks from these studies will be spuriously high and actual effects of CMD exposure somewhat less than those derived from the exposure-response data as presented.

The bias effect could be calculated by NIOSH. Using the actual BOM pre-1970 sample data appears to be a more direct way than back extrapolation based on ratios of two incomparable data sets. The data sets are incomparable with regard to time (1968-9 vs. 1970-2) and sample source (BOM-collected samples vs. operator-collected samples).

Another method might relate to the non-use of the 2.3 factor that was calculated as an average for all jobs. Actual job-specific means were available for both BOM and MSHA data. Their use could possibly have been applied directly and the bias issue would have been ameliorated.

Figure 3

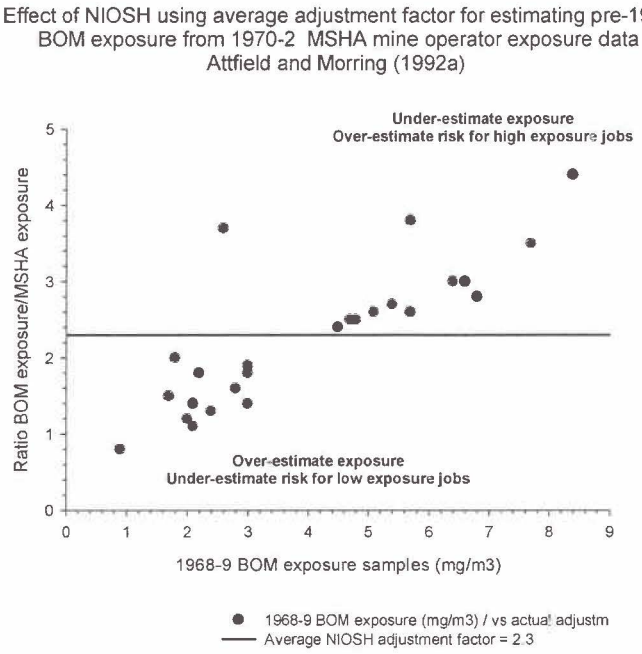
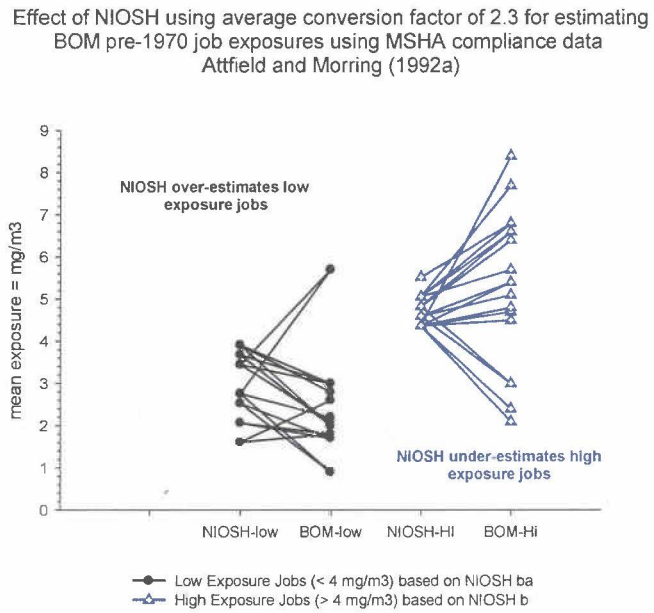


Figure 4



Attfield, M. and K. Morring (1992b). "An investigation into the relationship between coal workers' pneumoconiosis and dust exposure in U.S. coal miners." AIHAJ 53(8): 486-492.

Summary and Comments

This is the first exposure-response study of US coal miners using quantitative estimates of exposure (gh/m^3) instead of tenure or job. The present exposure limit of 2.0 mg/ m^3 is largely based on results from studies of British miners. The prime objective of this study was to develop exposure-response relationships between CWP and CMD in US coal mines.

The cohort consisted of miners from 31 underground US mines examined in 1969-1971 as part of the first round of the NSCWP. The relevant parts of the examination for this study included chest radiograph, spirometry, work and smoking histories.

Three data sets were utilized to estimate cumulative CMD exposures that occurred prior to the miners' examinations; viz. the work histories from the miners in the NSCWP 1969-1971, MSHA compliance data 1970-1972, and BOM data 1968-1969. The BOM data were collected at 17 of the mines included in this study and are the only body of gravimetric data prior to 1970 that were available for this study. Exposure estimates used in exposure-response analyses were based on 1970-72 compliance samples and back extrapolated to pre-1970 miner work experience by using an average factor derived from

the ratio of job specific BOM/MSHA data and then applying this factor to the MSHA compliance data in 1970-1972. These estimates are described in the derivation of pre-1970 exposure estimates study.

Each coal mine was classified into one of five rank categories with Rank 1 = anthracite, Rank 2 = medium/low volatile bituminous (89-90% carbon) coal in central Pa, and southeastern West Virginia; Rank 3 = High volatile "A" bituminous coal (80-87% carbon) in western Pennsylvania, West Virginia, eastern Ohio, eastern Kentucky, western Virginia and Alabama; Rank 4 = High volatile Midwestern coal in western Kentucky and Illinois; Rank 5 = High volatile West in Utah and Colorado.

There are clear, strong associations of CWP 2+ and exposure to high rank coals 1 and 2 with excess prevalence occurring at exposures below the current standard. Associations with coal ranks 3 and 4 are weaker with excess prevalences at exposures above the current exposure standard. There is no apparent association with coal rank 5 as the exposure-response curve is flat with some separation from rank 3 beginning around 70 mg/m^3-years The exposure-response slopes for ranks 3-5 from the logistic regression models are similar but with slopes becoming less steep with each increase in rank for category CWP 2+ (Figures 5, 6, and 7).

Additional Comments and Critique of Attfield and Morring (1992b)

The authors' note a limitation of this study in that there was only one reader of chest films, although the similarity with readings from the UK provided some comfort that it should not lead to major errors in prevalence or exposure-response relationships.

CWP 2+ is more reliable than CWP 1+ and should be the response-variable used to establish exposure-response trends. We say that because profusion of small opacities can be from other causes (e.g. smoking and lung conditions other than CWP). Classification of CWP 2+ is a relatively clear and reliable indicator of CWP when coupled with CMD exposures.

The background level of CWP is estimated to be about 5% (Attfield and Seixas 1995). At this background level there is no excess PMF for low ranking coal 3-5 and no excess CWP 2+ for low ranking coal below 110 mg/m^3-years, (Figures 5, 6, and 7).

Figure 8 shows the effect of coal rank on prevalence of different categories of CWP. This graph is based on statistical models predicting prevalence based on the effects of a 40-year work life at 2 mg/m^3. There appears to be no excess prevalence of categories CWP 1 and CWP 2 for ranks 3-5 when background levels of abnormal radiographs are taken into account. The predictions are also based on exposures prior to 1970, a time when concentrations could be as high as 8 mg/m^3.

A major limitation of this (and other US studies) is that exposure is based on sample results taken about the time the 3.0 mg/m^3 standard was being initiated. The period

before about 1970 was a period of high exposures with 21 of 25 jobs above the current standard and ranging as high as 8.4 mg/m^3 (Attfield and Morring 1992a)

The last sentence in the abstract admits possible weaknesses in the exposure estimates, but indicated the results are in general agreement with data from the UK, except for somewhat higher predictions of CWP prevalence. The US predictions are quite high and well above background prevalence and general findings from other studies. The authors contend that between 2% and 12% of workers exposed to 2.0 mg/m^3 are predicted to have category 2 or greater CWP after a 40-year working life. Smaller prevalence is noted for PMF, but it too is very high. This is an unexpected result when compared with the original British Interim Standards which the US adopted to stop miners from progressing to category 2 or greater. It is noted in the body of the paper that exposure-response estimates would permit more precise assessment of health risks. Very true, but this assumes that both the environmental exposure and the biological response are measured accurately or nearly so.

This study was done to derive exposure-response estimates based on US data because there was concern regarding extrapolation of UK information to the US experience. The miners of choice were from the 1st round of the NSCWP and the x-ray readings were from one reader and only rounded opacities were considered. This is reasonable as only rounded opacities were used in the earlier UK studies. The use of one x-ray reader in the US could be of great concern, but the similarity of the one reader with median British readers was reassuring to the authors. It is appropriate that the readings from the other two readers were discarded, although concern regarding the use of a single reader lingers.

The authors' Figure 2 shows exposure-response by coal rank and clearly shows prevalence is associated with both dust exposure and rank. Alternate statistical models produced no improvement. They are similar to UK models where the exposure is a continuous variable and begins at zero exposure. There are no threshold estimates in this study and the authors do comment that perhaps their models may be inadequate at very low exposure levels. Exposure-response trends are clear and consistent, but prevalence estimates of CWP in the US are dramatically higher than for the UK. Reasons for the gross disparity are not resolved. Thus, the authors advise caution in using the information in this report. (*See* (Attfield and Seixas 1995) for comparison.)

The data in this report provide strong evidence that rank of coal is an important factor to be considered and seems implicated in the etiology of CWP.

Figures 5 & 6 from Attfield & Morring (1992)

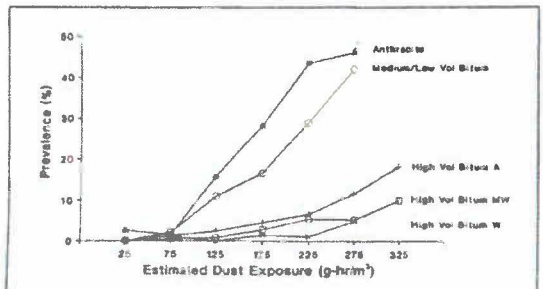


FIGURE 3. Exposure-response by coal rank group using prevalence of CWP Category 2 or greater and estimated dust exposure

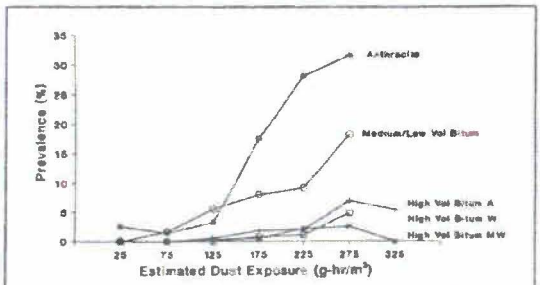


FIGURE 4. Exposure-response by coal rank group using prevalence of PMF and estimated dust exposure

Figure 7

Exposure-Response by coal rank of CMD exposure and CWP 2+
in logistic regression adjusted for age, predicted prevalence for 40-year tenure
at age 58, Attfield and Morring (1992b)

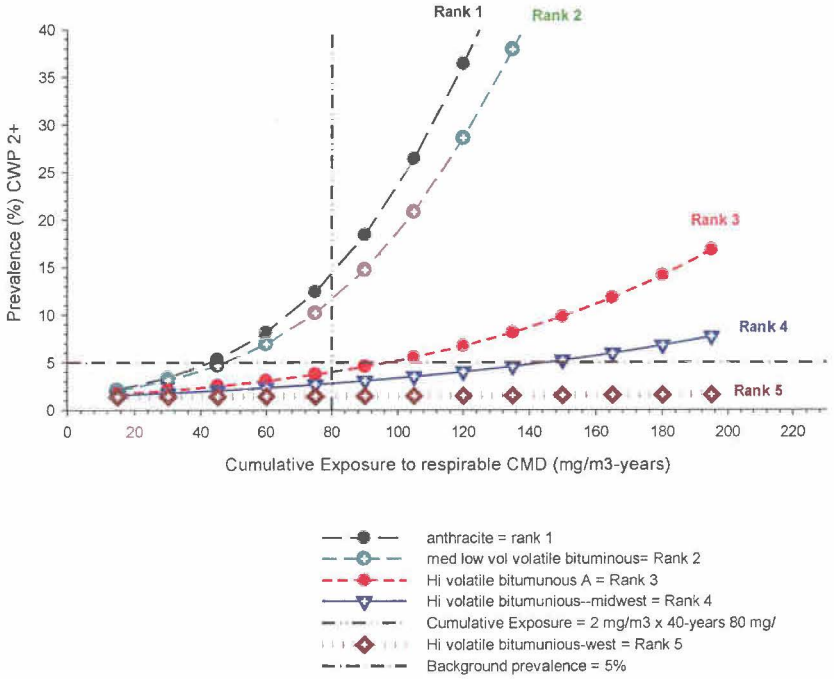
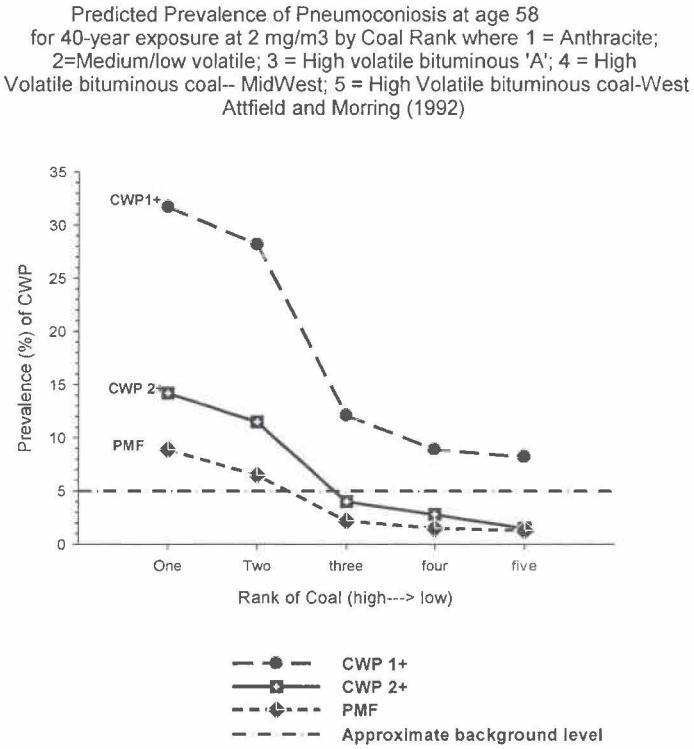


Figure 8 (Data plotted from Table III from Attfield & Morring ,1992b)



Attfield, M. and N. Seixas (1995). "Prevalence of pneumoconiosis and its relationship to dust exposure in a cohort of U.S. bituminous coal miners and ex-miners." Am J Ind Med 27: 137-151.

Summary and Comments

This is a cohort study of US underground miners and ex-miners. There were three broad categories of coal rank. The high coal rank category of miners were from Pennsylvania and southwestern West Virginia (about 2000); the low rank group was from Kentucky, Illinois, Colorado and Utah (about 2200); the medium rank comprised all the other states including Ohio (350), Tennessee (100), and Virginia (600).

The entire cohort comprised 7,281 miners who participated in Rounds 1 and 2 of the NSCWP begun in 1970. There were 3,194 (44%) participants selected for study who were <59 years old in 1985 and were examined in Round 4. Miners excluded from the study were from areas where it was not feasible to conduct further surveys.

Cumulative exposure ranged from 0 to 211 mg/m^3-years with a mean of 34 mg/m^3-years. Most (75%) of the cohort had low exposures between 13-41 mg/m^3-years.

The overall prevalence of CWP 1+ (all major categories) was 4% (n = 131); 0.7% (n=23) for CWP 2+ (categories 2, 3) and 0.8% (n= 28) for PMF. Exposure-response trends for prevalence of CWP 1+ were similar for all three ranks but became steeper at about 70 mg/m^3-years for high rank > low rank > medium rank coal.

Age, cumulative dust exposure and effects of exposure to high rank coal dust were significant factors affecting prevalence of CWP 1+, CWP 2+ and PMF. There were clear exposure-response trends of increasing CWP with increasing cumulative coal dust exposure. The exposure-response slope became even steeper from the added effect of exposure to high rank coal dust (Figure 9).

Predicted prevalence of CWP at high- and low-ranked coal from this study, from the first round of the US coal mine survey (Attfield and Morring 1992b) and from British coal miners (Hurley and Maclaren 1987) show a clear exposure-response trend for CWP prevalence to be higher in hard coal than in soft coal. These data are calculated from statistical models for miners after 40 years exposure at 2.0 mg/m^3 (Figure 10).

Additional Comments and Critique of Attfield and Seixas (1995)

These data show clear exposure-response trends for CWP to increase with increasing cumulative exposure. The trends of CWP 1+ and CWP 2+ are essentially the same. When the effects of high ranked coal are added, the slopes are increased substantially showing high rank coal produces more CWP than low rank at the same mass exposures (Figure 9 derived from the authors' Table IV).

There are several issues relating to evaluating associations of CWP and CMD exposure relating to exposure-response and the proposed CMD standard. One of these is the issue of coal rank, which is the subject of this section. Misclassification of exposure and resulting biases was discussed above (Attfield and Morring 1992a). Another issue is background prevalence of radiographic findings that mimic CWP in non-exposed workers and potential biases from low participation. These issues will be discussed in Section IV where reliable exposure-response trends are necessary for deriving safe exposure levels greater than background prevalence levels and without selection and exposure biases. These biases are likely to not be correlated with coal rank, in which case they are not confounding the association between CWP and rank of coal mine dust. We are assuming potential bias from participation rates and pre-1970 exposure estimates are similar by region and coal rank. If so, results regarding effects of coal rank should not be biased.

The authors' Table VI is enlightening. The authors say there is reasonable consistency of findings from three different studies. The graphic display of these data in Figure 10 does not completely support this interpretation nor does the authors' data in their Table VI where the prevalence of CWP in the UK are consistently lower than in the US for both ranks of coal.

In sum, these data indicate the prevalence of CWP is clearly elevated above background at levels for high rank coal but not low rank coal at exposure levels that appear to be below the current standard.

Figure 9

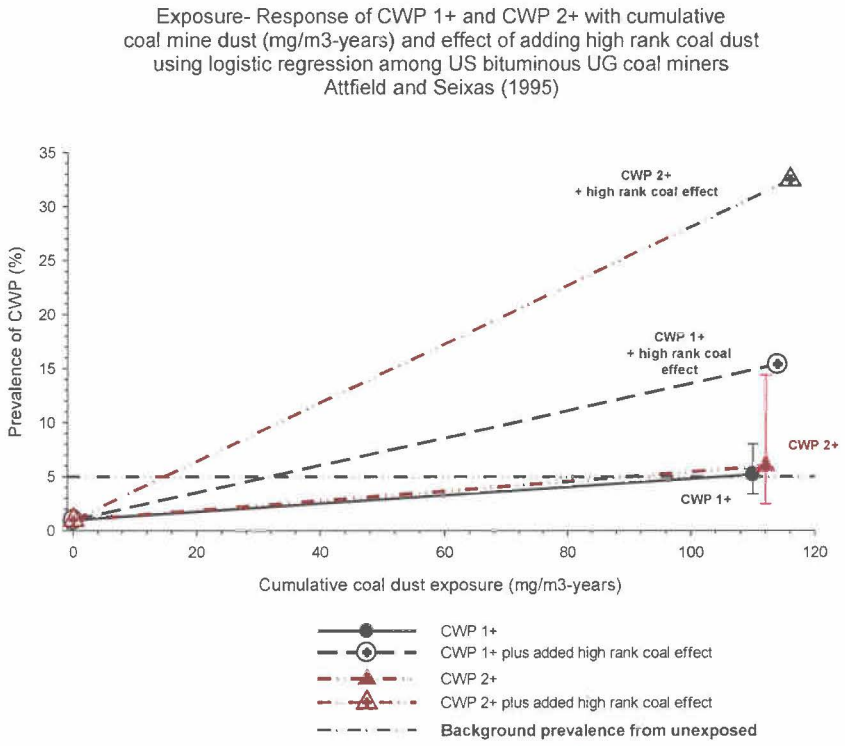
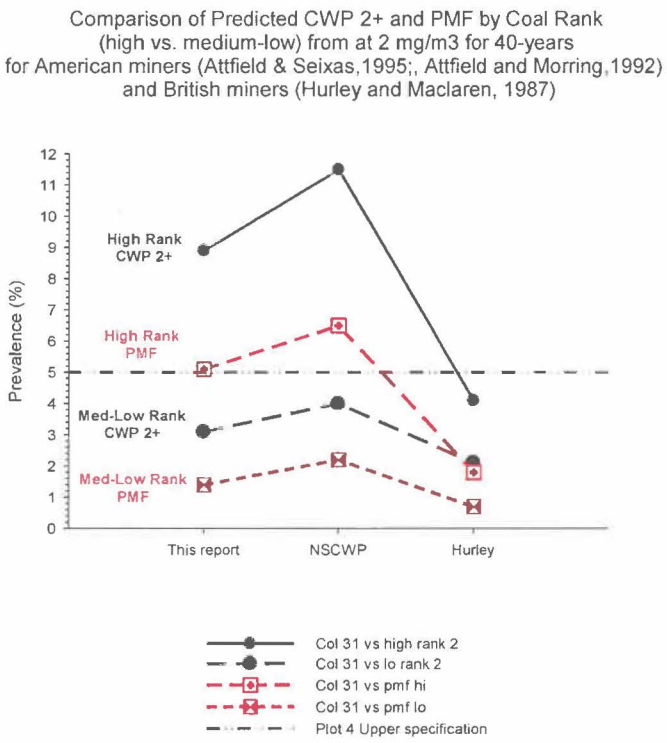


Figure 10



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IV. EXPOSURE-RESPONSE STUDIES OF RADIOGRAPHIC CWP

1. Summary of Studies of Exposure-Response Studies of Radiographic CWP

CWP was first identified in a 1928 study of the Coal Trimmers Union in Cardiff, South Wales where there were excesses of bronchitis and pneumonia, but no excesses from TB.[6] Case studies showed a radiological pattern similar to silicosis. This led to an understanding of a CWP entity distinct from silicosis and the modern era of studies into CWP (Merchant, Taylor, et al. 1986).

The US Public Health Service completed an important study of anthracite coal miners in Pennsylvania in 1936. Radiographs identified "anthracosilicosis" in 23% of the miners and a clear exposure-response relationship that led to a recommended standard of 50 mppcf. Most of the recommendations were not implemented and several studies in the 1940s suggested fairly low prevalences of CWP among bituminous miners in Appalachia and Utah.

The next important study was in Raleigh County, WV which established that CMD exposure was producing a high occurrence of CWP (46%) and PMF (7%) that was related to tenure (Hyatt, Kistin, et al. 1963). This study led to a flurry of studies to document the prevalence of CWP in the US, UK and Germany.

In the 1960s, the Pennsylvania Board of Health found an increasing gradient of CWP from 11% in Western Pennsylvania to 35% in Central/Eastern Pennsylvania (Lieben, Pendergrass, et al. (1961), McBride, Pendergrass, et al. (1963), and McBride, Pendergrass, et al. (1966). In Appalachian counties nearly 10% of working miners (9% with PMF) and 18% of nonworking miners had CWP. The 1969-71 first round of the NIOSH NSCWP of 31 mines and over 9000 miners found a very high prevalence of CWP: 60% in anthracite coal, 30% in Appalachia, 25% in the Midwest, and 10.5% prevalence in Western coal.

These high prevalences were thought to be in part attributable to the use of a new classification system and standard radiographic films for classifying chest x-rays for the pneumoconioses developed by the Union for International Cancer Control and the University of Cincinnati Radiology Department referred to as the UICC/Cincinnati 1968 classification. The prevalences were markedly reduced in the second round using the 1971 ILO/UC (University of Cincinnati) classification system and different B readers for the pneumoconiosis, but this change was not considered to have contributed to lower prevalences (Merchant, Taylor, et al. 1986).

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[6] Coal trimmers were workers who shoveled coal in the holds of ships to evenly spread the coal from side to side. Originally pulmonary disease in coal miners was thought to be a result of silica exposure in the CMD. Since the coal being loaded on ships had been cleaned and the silica admixed in the coal had been largely removed this was the first recognition that CMD without silica was related to a pneumoconiotic disease.

Prevalence of CWP by year worked was the same between rounds so reduction in dust did not seem to influence CWP prevalence. Prevalence was reduced to below 5% in the 1970s due to dust controls, or the influx of younger miners and outward migration of older miners (Merchant, Taylor et al. 1986). The latest reports indicate that the prevalence of CWP in the US has been reduced to around 3 percent. This rate and earlier prevalence rates, however, are (mostly) from a NIOSH X-ray surveillance program where participation by the miners has been very low. While the reasons for the dramatically low participation rates remain unknown, inferences to the population of interest (all miners) are likewise questionable due to the potential for serious selection effects. Thus, the true prevalence of CWP in the US mining population is unknown. Inferences based on participation rates as low as 30% (and even lower) are plainly unreliable, especially in the absence of post-evaluation samples of non-respondents.

The first exposure-response study of CWP using gravimetric sampling of respirable coal mine dust was in the UK (Jacobsen, Rae, et al. 1969). There were 10-years of observation of 4,122 coal face miners in 20 collieries selected in 1953. The results suggested negligible risk of CWP ILO Category 2/1 over a working lifetime where coal mine dust levels were below 2.0 mg/m^3. Smoking was not associated with CWP prevalence. These results were the basis of the current MSHA dust standard of 2.0 mg/m^3.

A 20-year follow-up of this same cohort confirmed the original exposure-response relationship except the long-term risks were slightly greater with negligible risk of 2/1 occurring below 1 mg/m^3. Large variations in colliery results were not accounted for by quartz, rank, or other risk factors measured, and there was no pattern suggesting quartz affected the probability of developing simple CWP (Hurley, Copland, et al. 1979) (Figure II-23 below from Merchant, Taylor, et al. (1986). A relationship between quartz and PMF was reported by Jacobsen and Maclaren (1982).

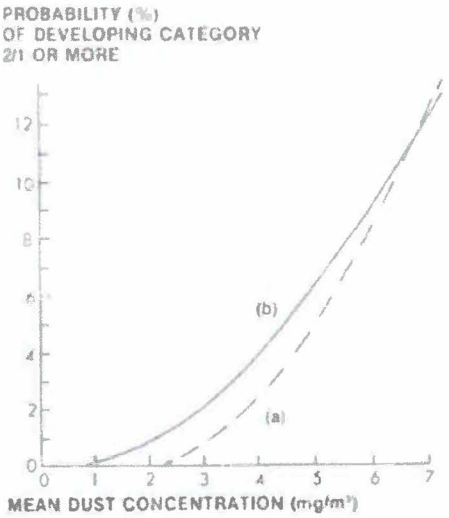


Fig. II-23. Lines (a) and (b) are estimates of probabilities of developing Category 2 or 3 of simple pneumoconiosis over an approximately 35-year working life at the coalface, in relation to the mean dust concentration experienced during that period. (a) is based on 10 years of data, Interim Standards Study, Pneumoconiosis Field Research. (b) is update of (a), based on 20 years of data, Pneumoconiosis Field Research.

It is clear that several factors can produce CWP under certain conditions. Conditions amenable to the occurrence of CWP include high coal mine dust concentrations, higher ranks of coal, and combinations of coal dust and high percentages of quartz admixed in the coal. The combinations of CMD and high quartz can present as CWP, but is more likely to be mixed dust CWP and silicosis. Under some conditions background prevalence is as high as CMD-attributable CWP, so it is important to adjust for it. Based on Attfield and Seixas (1995) we have used 5% as reasonable background prevalence for all radiographic categories.

CWP 2+ is considered a reliable diagnosis to consider as the response variable.

Exposure-response associations of radiographic CWP 2+ and cumulative coal mine dust exposures are displayed in Figure 1. No exposure-response associations between CWP and cumulative respirable coal mine were apparent for Colliery Q (Hurley, Copland et al. 1979; Hurley, Burns et al. 1982), Rank 5 coal (Attfield and Morring 1992b) and non-quartz coal mine dust (Miller, Hagen et al. 1998).

The horizontal line at 5% prevalence indicates the estimated background prevalence, and exposure-response curves above this indicate greater observed radiological abnormalities than expected. There are eight curves showing a greater than expected prevalence of CWP at some level of cumulative exposure. These include four curves for coal ranks 1-

(Attfield and Morring 1992b) ; two groups of examined and unexamined miners (Soutar and Hurley 1986); high rank coal from Attfield and Seixas (1995); and the eight collieries from Hurley et al (1982).

The vertical line at 80 mg/m^3-years indicates a 40-year working lifetime at 2.0 mg/m^3. Any part of the exposure-response curves to the right of 80 mg/m^3-years indicates coal miners are working at lifetime exposures above the standard of 2.0 mg/m^3. There are six exposure-response curves indicating mining conditions where CMD exposures are above the 2.0 mg/m^3 standard and prevalence is greater than the standard. These conditions in the upper right quadrant are out of compliance with the standard, but are not relevant to setting a new standard as the excess occurred at working levels above the standard. These include three curves for CWP 2+: eight collieries from the UK (Soutar et al, 1979) and coal ranks 3 and 4 (Attfield and Morring 1992b).

The data in the lower right quadrant also relate to working at exposures above the standard of 2.0 mg/m^3 and cumulative exposures above the 80 mg/m^3-years. The prevalence of CWP is not elevated above expected, or above background. These data are not relevant data for lowering the standard. They suggest that under some conditions exposures greater than the standard do not produce an increased risk of radiographic CWP. These include Rank 5 (Attfield and Morring 1992b), Colliery Q (Hurley, Copland, et al. 1979) and CMD in a Scottish mine containing unusually amounts of quartz (Miller, Hagen, et al. 1998).

The data in the lower left quadrant show conditions where exposure is below the cumulative standard and the workplace is not above the 80 mg/m^3-years allowable cumulative exposure and the prevalence of CWP is not above expected. A proportion of all miners from all studies have worked under these conditions.

It is the upper left quadrant that provides data suggesting that the 2.0 mg/m^3 standard is possibly too high and should be lowered. There are five examples in this quadrant where cumulative exposures are below the standard and there is an excess prevalence of CWP 2+. These are the high rank curves (ranks 1 and 2) from (Attfield and Morring 1992b), one high rank curve from (Attfield and Seixas 1995), and curves for examined and unexamined miners from the UK(Soutar, Maclaren et al. 1986).

The most obvious characteristic of these studies in the upper left quadrant is that three of the five involve exposure to high rank coals. The remaining seven curves do not show excess prevalence of CWP 2+ below the current standard considering background prevalence (Figure 1). The US data are shown separately in Figure 2 to more easily visualize the associations in these data.

Figure 1

Summary of Exposure-Response studies of radiographic CWP category 2 with cumulative respirable coalmine dust (mg/m3-years) in US and UK Hurley (1979); Attfield-Seixas (1995); Attfield-Morring (1992); Soutar et al (1986); Miller et al, 1998)

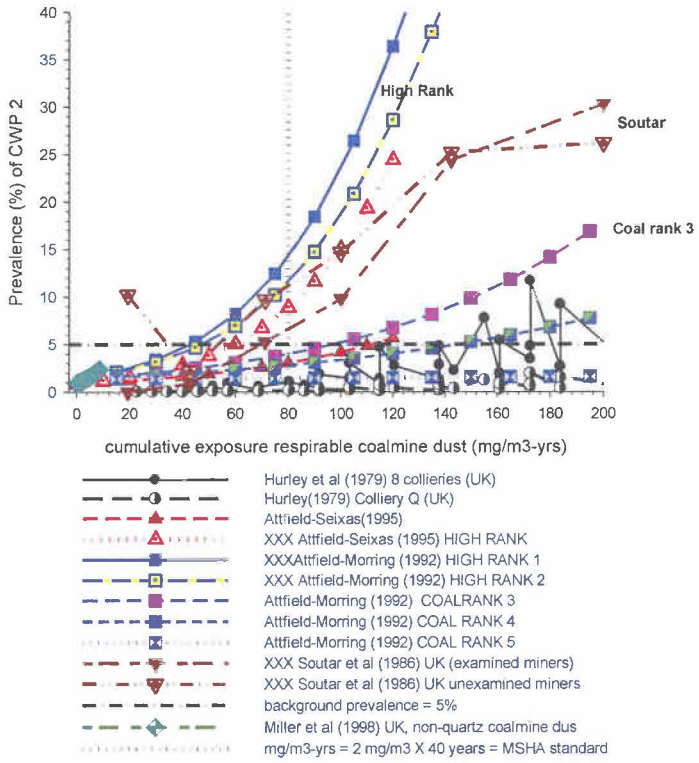
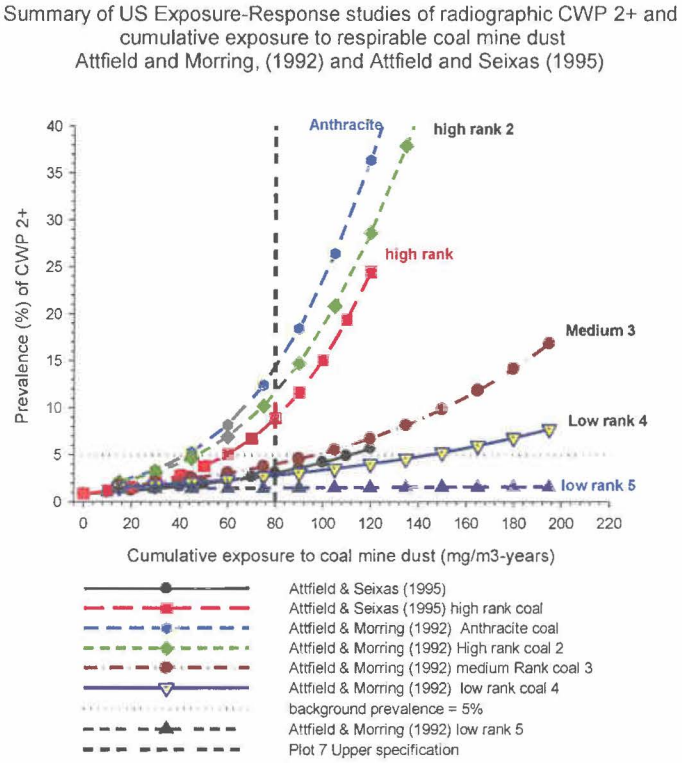


Figure 2

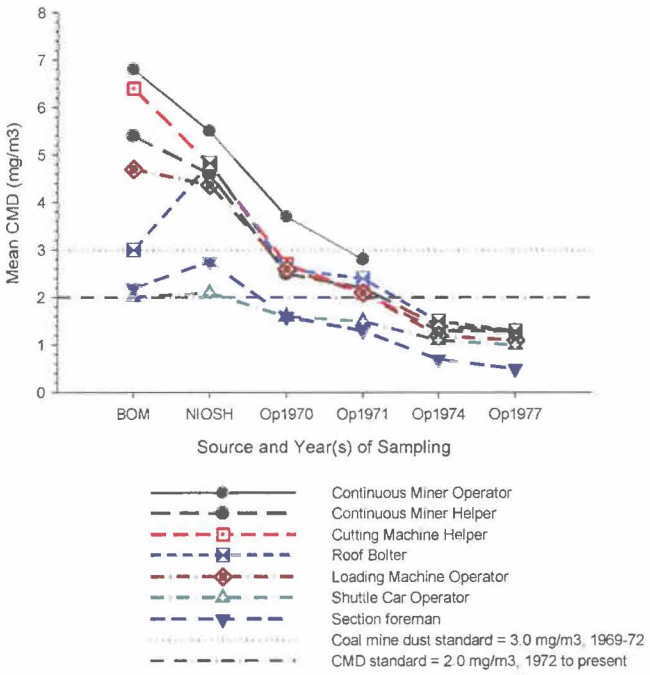


There are two US exposure-response studies in this group of coal worker cohorts (Attfield and Morring 1992b; Attfield and Seixas 1995) (Figure 2). These studies have two limitations unique to NIOSH cohorts. One is the low participation in later rounds of the NSCWP. This potential selection bias applies to the more recent study where workers participating in the first and second rounds of the NSCWP were re-examined in the fourth round (Attfield and Seixas 1995). Low participation in rounds 2 and 4 could result in selection bias. If there was selection bias, there is inadequate information to determine its magnitude or direction. This limitation is relevant only for Attfield and Seixas where participation involved coal miners from rounds other than round 1 of the NSCWP (Attfield and Seixas 1995).

The second major limitation is systematic bias in pre-1970 exposure estimates where a mean adjustment factor was used to back-extrapolate 1970-72 compliance data to the miners pre-1970 work experience. This procedure produced over-estimates of risk in high exposure jobs and under-estimates of risk in lower exposure jobs and exposure-response that are biased upward. These biases are explained in Section III of this report in the summary of Attfield and Morring (1992a). Another view of differences in CMD exposure is displayed in Figure 3.

Figure 3

Mean dust concentrations (mg/m3) by job, year (pre-1970 to 1977), and data source. Attfield and Morring (1992) = BOM samples, 1968-69; NIOSH adjusted estimates = (Mean Operator samples 1970-1971) x 2.3; Parobeck and Jankowski (1979) Operator samples 1974 and 1977



2. Summary and Comments on Studies of Exposure-Response Studies of Radiographic CWP

Hurley, J., J. Burns, et al. (1982). "Coalworkers' simple pneumoconiosis and exposure to dust at 10 British coal mines." Brit J Ind Med 39: 120-127.

and

Hurley, J., L. Copland, et al. (1979). Simple pneumoconiosis and exposure to respirable dust: relationships from twenty-five years' research at ten British coalmines. Report TM/79/13. Edinburgh, Scotland, Institute of Occupational Medicine.

Summary and Comments

These are studies of 2,600 British coal miners in 10 collieries with at least 20-years exposure and category 2/1 or greater CWP. Most attended the 1st, 3rd and 5th surveys of the PFR. Estimated cumulative exposure was derived from the 20-year sampling results beginning at the first survey. Pre-1953 exposure was based on averages for each work group from the post-1953 sampling results. Exposure samples in the first 10 years were measured with an early sampling device, the Standard Thermal Precipitator, with concentrations expressed as ppcm (particles per cubic centimeter) for particles 1-5 μm in size. Side-by-side sampling with the MRE gravimetric sampler were conducted to convert ppcm units to gravimetric units (mg/m^3). The MRE sampler was used in the second 10 years of the study. Individual results for cumulative exposures assumed a 1740 working hours/year and were in gh/m^3 units.

One year at 1 gh/m^3 = 0.57 mg/m^3-years cumulative exposure. Averages years worked were 33-years. This conversion is used subsequently so units are presented as mg/m^3-years rather than gh/m^3 as in the paper.

Mean cumulative exposure to coal dust was 104 mg/m^3-years and 14% of the cohort had exposures >100 mg/m^3-years (or average exposure of 3.2 and >5.2 mg/m^3 respectively based on average tenure of 33 years). There are two notable features of the cumulative exposure data. First, there is high variability overall and within each colliery, indicating a wide range of individual exposures and some very high exposures for some miners. Second, there are evident differences in mean exposure levels between collieries. Quartz exposures are much less variable within a colliery, and differences in quartz exposure are usually due to differences between mines rather than within mines.

The prevalences of CWP 0/1+ and 2/1+ were 13.5% and 3.1% respectively using the independent randomized method for classifying X-rays. The prevalence ranged from

0% in Colliery P to 13.8% in Colliery T. There is a clear overall exposure-response trend for all ten coal mines and many of the individual collieries had the same general pattern. The authors pointed out two collieries with divergent patterns. Colliery T showed high risk with an overall prevalence of 13.8% and a threshold at about 55 mg/m^3-years. Prevalence was 20% or higher at exposures ranging from 120-190 mg/m^3-years, but there was only one miner in the highest exposure group. Colliery Q was an outlier with very low risks. The overall prevalence was 0.8% with two cases at the highest exposure category of >205 mg/m^3-years and a threshold at about 180 mg/m^3-years not considering background prevalence (Figure 4). The authors indicated similar relationships were observed for CWP 1+ but these data were not shown.

Exposure-response trends for the eight combined collieries, excluding T and Q, shows a higher threshold (100 mg/m^3-years) and steeper slope compared to the combined exposure-response trend from all ten collieries (Figure 4). Similar relationships are observed for average exposure for 35 years, with no apparent excess below the standard of 2.0 mg/m^3 for Colliery T or the other collieries (Figure 5a, 5b).

Mean cumulative quartz exposure was 5.02 (SD = 3.3) mg/m^3-years and was highly correlated (r = 0.77) with mixed dust overall. The authors suggest there was little evidence quartz influenced CWP development overall. Mineral characteristics at each mine were similar. Quartz content at Colliery T was the same as the overall average (5%), while it was 6.4% at low risk Colliery Q. The comparison of quartz and CMD alone is suggestive of a general effect of quartz exposure. For example, the exposure-response trend for quartz is not linear but at exposures >6 mg/m^3-years quartz and >150 mg/m^3-years CMD the quartz effect appears to be associated with about a 5% prevalence of CWP 2+. At lower exposure levels of quartz and CMD the associations with prevalence appear to be equivalent. On the other hand, the correlation is so high (r = 0.77) it may not be possible to distinguish the separate effects of CMD and quartz alone, except at dust levels <150 mg/m^3-years (Figure 5a, 5b).

There may have been selection bias at Colliery T as many miners left before the fifth survey because of imminent closure of the mine. Also, the "excess at colliery T was inflated by an underestimation of the miners' exposures accumulated before the first medical survey."

The authors conclude there are very large variations in medical responses between collieries despite similar dust exposures. The reasons for these differences are "not yet known," but they do not seem explicable on the basis of different quartz levels at the collieries. There is a subset of miners that show rapid progression over a short time-period (ten years) that is related to high quartz exposure (Hurley, Copland, et al. 1979). The issue of rapid progression of CWP 2+ in a small subset of miners is discussed in Section II of this report. Finally, radiographic classifications (categories 2/1 and greater) were "clearly associated" with measures of CMD exposure.

Additional Comments and Critique of Hurley, Copland, et al. (1979); Hurley, Burns, et al. (1982)

All coal miners had >20-years latency and adequate time to develop CWP. There were generally clear exposure-response trends for all collieries, although Collieries Q and T did not fit the general pattern with unusually low and high risks respectively. There was a clear threshold above about 100 mg/m^3-year cumulative exposure for eight collieries, excluding collieries Q and T. With an average working life-time of 33 years underground in this cohort, the threshold for development of CWP 2+ was about 1.8 mg/m^3 (60 mg/m^3-yrs/33-years) for all collieries and about 3 mg/m^3 (100 mg/m^3-years/33 years) for the eight collieries (excluding Q and T) in this study.

The low risks found in Colliery Q had been expected based on earlier results (Walton, Dodgson et al. 1977). Evidence was presented of bias with regard to Colliery T. Selection bias occurred because many miners left prior to the fifth survey because of imminent closure of the pit. The remaining "survivor" population may be the result of an "unusual pattern of selection." The authors also note there was evidence exposures were under-estimated prior to the first survey. Thus, it seems plausible that the data considered should exclude Colliery T because of bias. The reason for excluding Colliery Q is less obvious, perhaps on the basis of being an outlier. At any rate, the data from the remaining eight collieries appear to be the least biased and most reliable. These data show a threshold at 100 mg/m^3-years and no excess prevalence of CWP below about 2.5 mg/m^3 exposure for 40 years (Figure 5a, 5b).

Statistical analyses using logistic models were used to present different ways of presenting exposure-response to better assess the effect of various factors. One model confirmed that miners working longer had a higher prevalence of CWP 2+ than those at the same cumulative exposure category but with shorter tenure. Adding quartz did not substantially improve the model and is consistent with a general lack of response to quartz in CMD in this study. This does not appear to be consistent with the (green) quartz exposure-response trend observed in Figure 6.

This study mostly evaluates the chance of developing category 2/1+ by exposure estimates. Air samples were available for a 20-year period for each occupational group. The work history prior to the first survey was obtained by interview, and average concentrations based on samples collected from 1953-1973 were used for estimating pre-1953 CMD exposures. As a result a potentially large portion of a workers' cumulative exposure could be under- or over-estimated, most likely under-estimated. Note that it was the authors who indicated there was evidence of under-estimation for these exposures for Colliery T. For example, on average the miners had about 13 years of dust exposure prior to the start of surveys, or about 40% of their cumulative dust exposure is estimated from samples collected after the initial 13 years of underground work. It is quite likely early exposures were really higher than estimated -- thus resulting in an over-estimate of CWP risks. The authors acknowledge this. Nonetheless, it appears that an exposure-response trend does exist, but it may not be as severe as indicated. This bias is also likely to further reduce the threshold to some level greater than 2.5 mg/m^3.

It is important to note that the (implied) dust threshold relates to category 2/1+ and this threshold might be quite different if related merely to the development of category 1/0+. Attfield et al., however, showed no apparent difference in an implied threshold for categories 1+ and 2+ overall (Attfield and Seixas 1995). Adding the effect of high ranked coal, however, produced a higher threshold for CWP 2+ than for CWP 1+, which is an expected result. The apparent lack of a quartz effect in this study and the authors' comment that CWP 2+ and CWP 0/1+ had generally similar results are suggestive that thresholds may also be similar.

Like most studies of this type, much depends on the dust exposure estimates. However, the British Surveillance Program exposure estimates are thought to be the most complete in the coal industry. Like the US studies, portions of the work history are based on extrapolations backward to high exposures early in the work life of the miners and before the initial medical surveys.

In summary, this study indicates no apparent excess prevalence of CWP below about 2.5 mg/m^3.and less

Figure 4

Exposure-response of CWP 2+ and cumulative exposure to mixed respirable coalmine dust of 2600 coalminers in 10 British coalmines (Hurley et al, (1982))

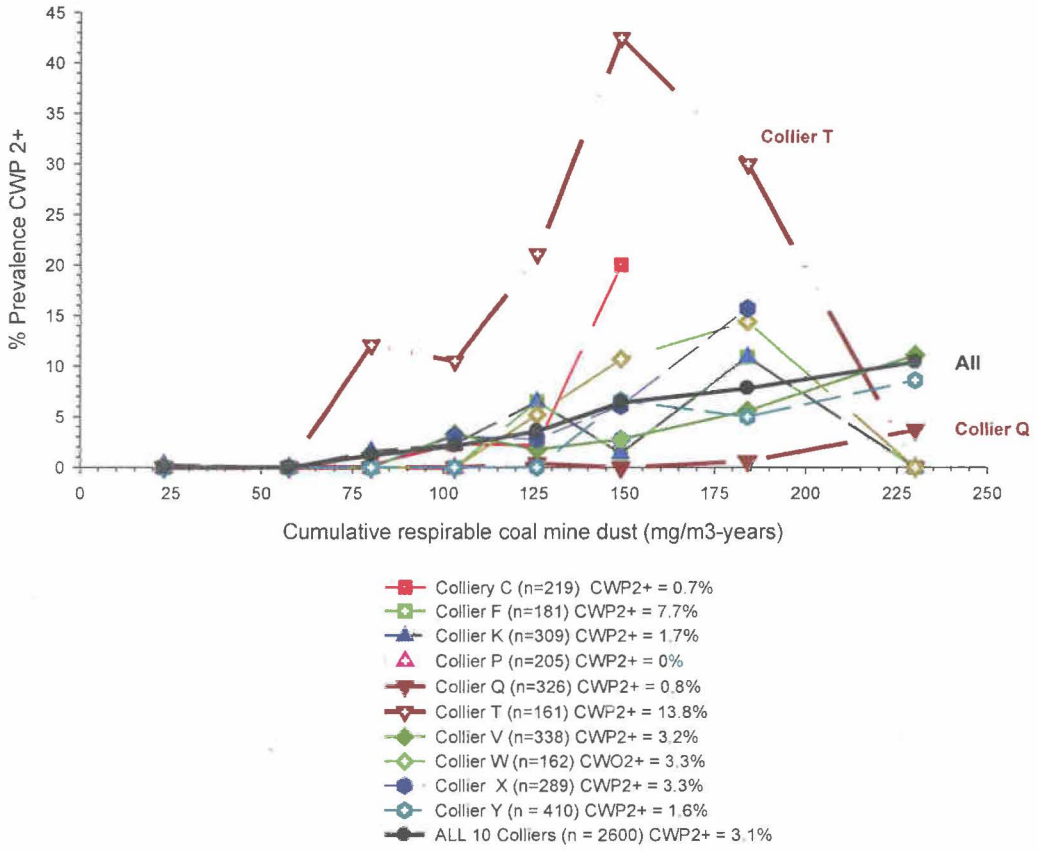


Figure 5a

Approximate estimates of probabilities of developing category 2/1 or more simple CWP over roughly 35 years (Hurley et al, 1982)

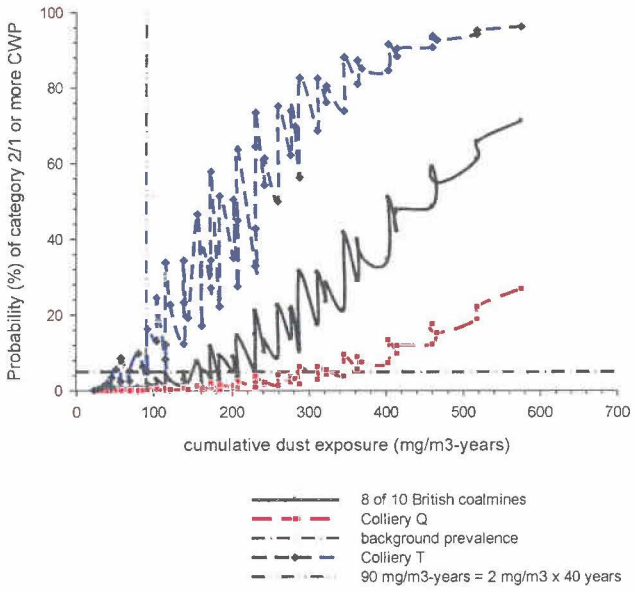


Figure 5b

Estimated probability (%) of CWP 2+ in relation to mean dust concentration assuming about 35 years for 8 British coalmines and colliery T and Q from logistic model (Hurley et al, 1979)

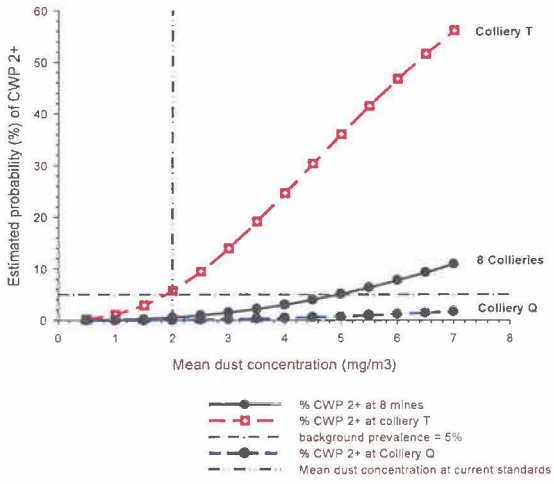
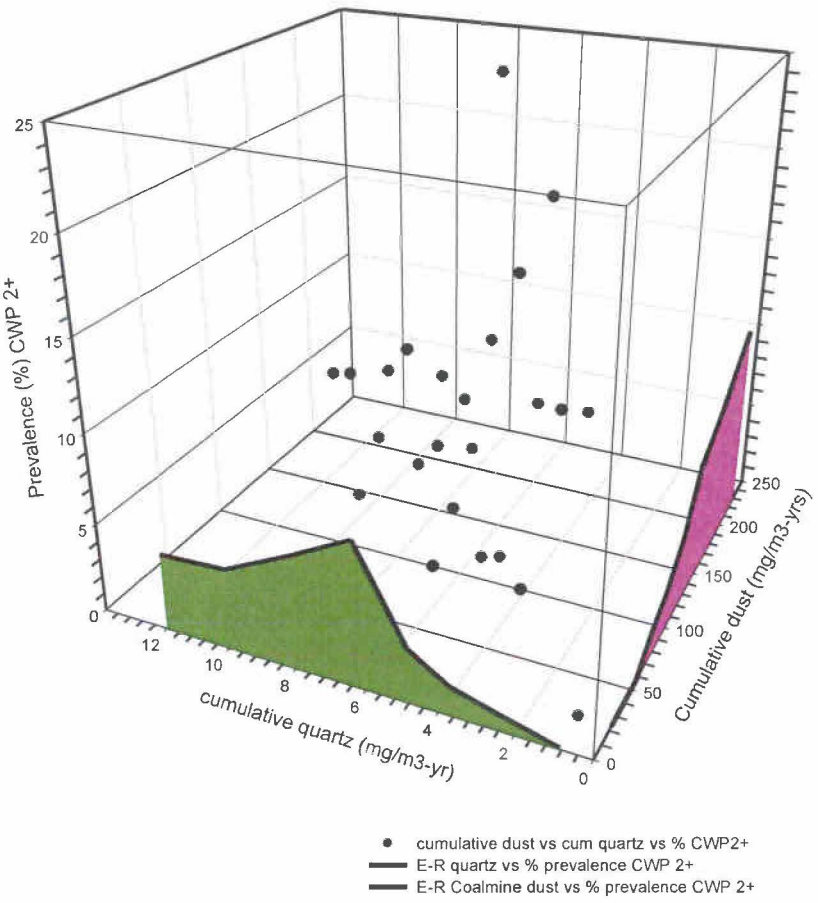


Figure 6

Percentage (%) CWP 2+ in relation to dust and quartz
cumlulative exposure in mg/m3-years in 10 British coalmines
Hurley et al (1982)



Soutar, C., W. Maclaren, et al. (1986). "Quantitative relations between exposure to respirable coalmine dust and coalworkers' simple pneumoconiosis in men who have worked as miners but have left the coal industry." Brit J Ind Med 43: 29-36.

Summary and Comments

Previous studies had examined exposure-response associations among working miners without consideration of miners who left the industry (ex-miners) (Jacobsen, Rae, et al. 1971; Hurley, Burns, et al. 1982). The ex-miners left the industry for various reasons, some of which could be for health reasons or because they had greater responses to coal dust than working miners.

The purpose of this study was to assess whether ex-miners' exposure-response associations of CWP and CMD exposure were similar to those of working miners.

The sample of miners was selected from men examined at the first round survey 1953-1958 at 24 collieries. All 3,645 miners with category 1 or greater CWP and 14,093 miners randomly selected from the remaining participants were selected for inclusion in the study. After 22 years follow-up there were 2,255 miners and 3,896 ex-miners still alive and who attended follow-up medical exams, including X-ray and work history. This is the cohort that was assessed for exposure-response relationships between CWP and coal dust exposure.

The results of these analyses indicated no "systematic or statistically significant difference between men who stayed and men who left in the quantitative relations between dust exposure and simple pneumoconiosis. Present estimates of risk of simple pneumoconiosis in relation to exposure to mixed respirable dust in working miners adequately describe the relation found in men who have been miners but have left the industry."

This conclusion is consistent with Figures 7a and 7b that show no substantive differences between exposure-response curves for miners and ex-miners for different age groups for CWP 1+ and CWP 2+.

Additional Comments and Critique of Soutar, Maclaren, et al. (1986)

This study may be the only study of ex-miners, and it suggests that exposure-response of miners and ex-miners are similar enough that exposure to CMD did not pose any greater risk to ex-miners than it did to miners. Thus, there appears to be no reason for a lower standard because of this potentially more susceptible population. The issue becomes clear in Figures 7a and 7b where it is shown that exposure-response curves for miners and ex-miners were fairly parallel and mimicked each other closely. These curves support the authors' conclusions that indicate "whatever standard is adequate to protect miners, should also apply to ex-miners".

Interpretation of the two sets of figures is problematic. Figure 7b (= Figures 1 and 2 from Soutar, et al.) are the observed prevalence of CWP vs. dust exposure by age group under 65. Figure 7c (= Figures 3 and 4 from Soutar, et al.) are logistic regressions of predicted prevalence for smokers only and adjusting for collieries. It appears the predicted prevalence would be the adjusted model for exposure-response curves displayed in Figure 7b, which are not adjusted for potential confounding. If so, the predicted exposure-response curves in Figure 7c are extrapolations beyond the data because maximum exposure levels are greater (= 600 gh/m^3) than in the observed data where the maximum values for different groups ranges from <200 to 450 gh/m^3 in Figure 7b.

Figures 7b and 7c suggest a possible threshold of about 100 gh/m3 (57 mg/m^3-years) for CWP 2+. The usefulness of category 0/1+ is questionable because a diagnosis of CWP below, for example, category 1/1 or 2/1 is not reliable, has high background prevalence, and "could be the result of disease other than pneumoconiosis, since in other, non-mining populations, age related small rounded opacities of low profusion may be shown." This reference is to a cohort of polyvinylchloride workers where two readers found no association of category 0/1+ with dust but a background prevalence of about 2%. If the third reader is included, the background would be higher (Soutar, Copland, et al. 1980).

The gh/m^3 units used by the British to estimate exposure remain confusing. The authors only refer to "dust exposure," making it unclear whether the exposure-response relationships refer to average shift air concentrations or to cumulative exposure. Mean dust exposure ranged from 73 to 140 gh/m^3 (and SD from 71 to 118) in Table 1 among the categories of miners, ex-miners and unexamined. The maximum exposures are in the range of about 600 gh/m^3, which seem high for mean levels (intensity) and low for cumulative exposure levels.

Furthermore, X-rays were interpreted by a panel of "self-trained readers." Readings from such a panel are reproducible and adequate for the purposes of this study. In fact, this procedure was followed at NIOSH's Appalachian Laboratory for Occupational Safety and Health years ago when lay readers were used. In this study a test comparison was conducted with a subset of the lay readings compared to readings from a panel of three experienced and medically qualified readers. Results showed that the self-trained panel recorded higher prevalences of simple CWP. This difference, thus, may have affected the CWP category 0/1+, but not category 2+ and the relationships with dust.

Figure 7a

Prevalence (%) of CWP 2+ at first survey by dust exposure up to first survey and whether or not coalminers were examined at follow-up survey
Soutar et al (1986)

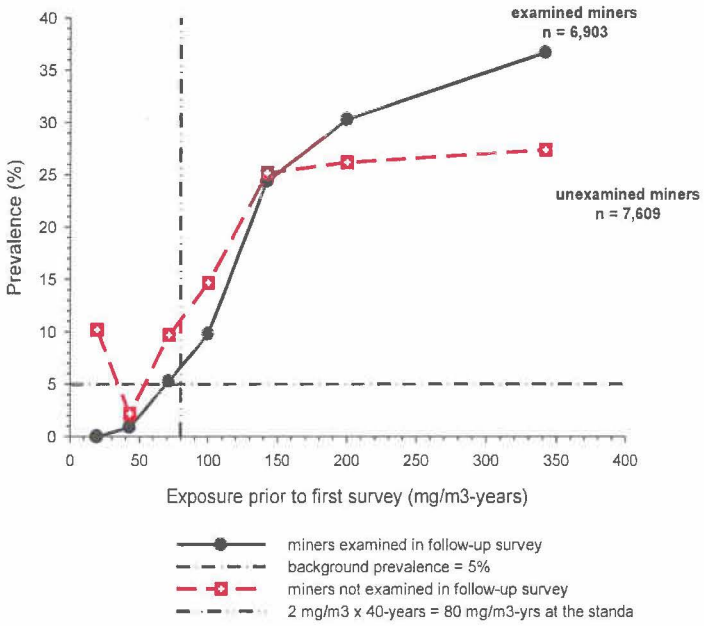


Figure 7b

Exposure-Response for Observed Prevalence of CWP 0/1+ and CWP 2/1+ versus dust exposure (gh/m3) for miners and ex-miners by age groups. From (Soutar, Maclaren, et al. 1986).

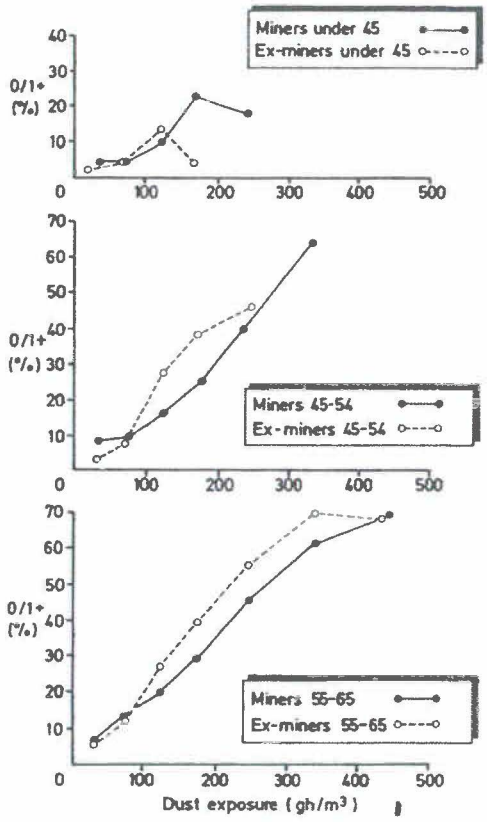


Fig 1 *Observed frequencies of small rounded opacities category 0/1 or greater in miners and ex-miners under 65, within three age groupings.*

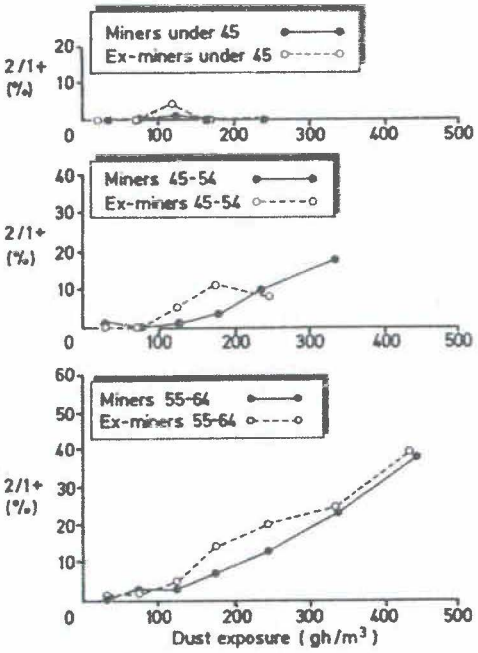


Fig 2 *Observed frequencies of small rounded opacities category 2/1 or greater in miners and ex-miners under 65, within three age groupings.*

Figure 7c

Predicted prevalence of CWP 0/1+ and 2/1+ in relation to dust exposure (gh/m3) and by age group using logistic regression for miners and ex-miners who smoke. From Figures 3 and 4 from (Soutar, Maclaren, et al. 1986).

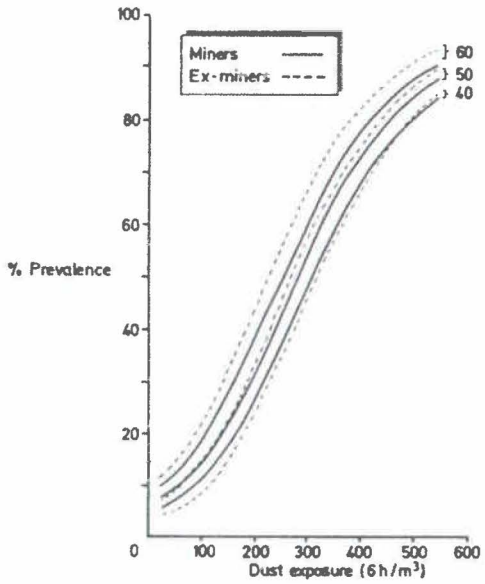


Fig 3 *Predicted prevalence of small rounded opacities category 0/1 or greater in relation to dust exposure and for three ages (men aged 40, 50, and 60) in miners and ex-miners under 65. These curves are averages of fitted logistic curves for smokers only, over collieries, using equal weights for both miners and ex-miners.*

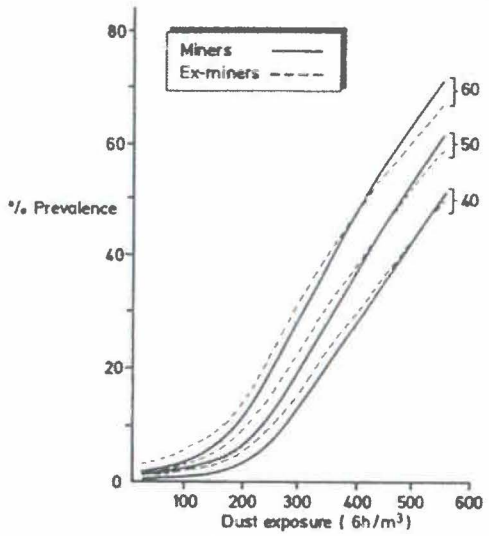


Fig 4 *Predicted prevalence of small rounded opacities category 2/1 or greater in relation to dust exposure and for three ages (men aged 40, 50, and 60) in miners and ex-miners under 65. See caption to fig 1 for further description of derivation of curves.*

Attfield, M. and N. Seixas (1995). "Prevalence of pneumoconiosis and its relationship to dust exposure in a cohort of U.S. bituminous coal miners and ex-miners." Am J Ind Med 27: 137-151.

Summary and Comments

This is a cohort study of 7,281 US underground miners and ex-miners who participated in Rounds 1 and 2 of the NSCWP begun in 1970. There were 3,194 (44%) participants selected for study who were <59 years old in 1985 and were examined in Round 4. Miners were excluded from the study for a variety of legitimate reasons.
Cumulative exposure ranged from 0 to 211 mg/ m^3-years with a mean of 34 and standard deviation of 32 mg/m^3-years. Most (75%) of the cohort had low exposures between 13-41 mg/m^3-years.

The overall prevalence of CWP 1+ (all major categories) was 4% (n = 131). For CWP 2+ (categories 2, 3) prevalence was 0.7% (n=23) and for PMF was 0.8% (n= 28).

Age and cumulative dust exposure were significant factors affecting prevalence of CWP 1+, CWP 2+ and PMF, with clear exposure-response trends of increasing CWP with increasing cumulative coal dust exposure (Figure 8).

Additional Comments and Critique of Attfield and Seixas (1995)

These data show clear exposure-response trends for CWP to increase with increasing cumulative exposure. The logistic regression models suggest no excess prevalence of CWP 2+ and PMF for low rank coal at exposures below the standard. There was excess prevalence of CWP 1+ when exposed to high rank coals. There is a clear and large effect of rank, with high rank coal showing strong steep trends, while lower ranks generally had shallow slopes except for CWP 1+ (Figure 8 and their Figure 3).

There are categorical analyses of CWP 1+ and 2+ in the authors' Figure 2, which suggests a threshold for median readings of CWP 1+ at about 30 mg/m^3–years and about 80 mg/m^3-years if the 5% background prevalence is taken into account and about 30 mg/m^3–years if it is not. These data are suggestive of no measurably increased risk of CWP at coal dust exposures less than about 30 mg/m^3–years without consideration of background prevalence.

The authors reported a predicted prevalence of 5% category CWP 1+ among zero exposed coal miners. Predicted prevalences were 0.9% for CWP 2+ and 0.5% for PMF (their Table V). From the categorical analysis (the authors' Figure 2 & 3) prevalence is 2-3% up to about 30 mg/m^3–years. Citing unpublished work of Castellan, et al., the prevalence of category 1/0 among unexposed blue collar workers about 56 years old was 1.4% (SE = 0.8%). The upper confidence limit of this prevalence is 3%. The authors cite Figure 2 of Collins, et al. (1988) as showing among 60-year smokers a 5% prevalence of category 0/1+ small irregular opacities (90% being 1/0+). Prevalence of small rounded opacities was 3%, suggesting a prevalence of category 1/0+ of around 5% or more.

Meyer et al. (1997) conducted a literature analysis of prevalence of category 1/0+ among workers with no exposure to dust. There were nine study populations in Europe and North America that had unexposed workers or control groups for analysis. The population prevalence was 5.3% (2.9-7.7%), and was significantly greater in Europe than North America where the contrast was 11.3% (10.1-12.5%) vs. 1.6% (0.6-2.6%). The prevalence among males was 5.5% (3.4-7.6%). Prevalence remained higher in Europe than North America by age category >50-years, being 11.7% vs. 2.3%. Age, gender and smoking did not explain these differences in prevalences. Reader variability and environmental or unaccounted occupational exposures were considered as possible causes of the large differences between Europe and North America.

Based on these data, a background prevalence of 5% for category 1/0 appears reasonable in the absence of a non-exposed control group in the studies reviewed. The authors'

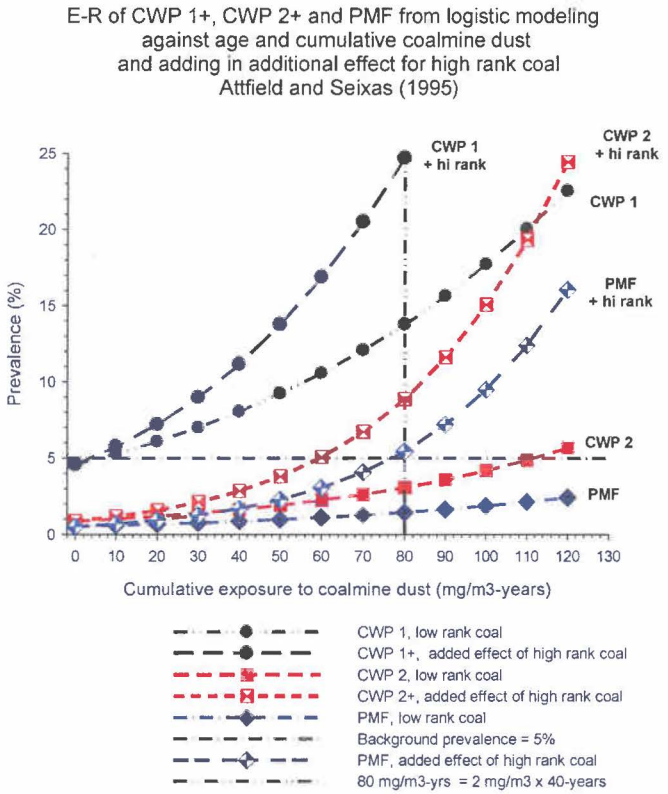
background prevalence level of about 5% agrees reasonably well with the Collins, et al. data regarding small irregular opacities for CWP 0/1 for men aged 60 years with zero dust exposure. From the categorical analysis (the authors' Figure 2), prevalence is less than 5% up to about 30 mg/m^3–years. Presumably background for CWP 1+ would be less than about 5%. But these data are quite variable and the authors' data from Figure 5 suggests a background prevalence of 5% or more.

Potential limitation in the exposure estimates noted by the authors include potentially incomplete work histories based on interviews and "deficiencies in recalling work history." Mine operator samples (especially from mines with <125 miners) tend to underestimate exposures. However most of the mines in this study were larger than 125 miners so this bias may not be large. Both of these biases, however, can produce over-estimates of the pulmonary fibrogenicity of CMD and produce radiographic changes at lower exposure levels than actually occur.

A probable limitation relates to exposures prior to 1970 which were included in the overall estimates of cumulative exposure. Both pre- and post-1970 time periods contributed to the development of CWP 1+ in the combined low and medium coal rank groups. However, there is convincing evidence that pre-1970 exposure estimates may be seriously underestimated (data from Doyle 1970 shown below).

Occupation	No of mines	No of samples	Range (mg/m3)	Mean (mg/m3)
Continuous miner operator	21	178	0.02-21.44	4.08
Continuous miner helper	19	131	0.44-18.90	3.47
Cutting machine operator	15	98	0.71-15.42	3.69
Cutting machine helper	8	37	0.77-14.70	4.45
Coal drill operator	9	59	0.42-12.94	3.55
Loading machine operator	18	97	0.25-39.56	3.75

Figure 8



Miller, B., S. Hagen, et al. (1998). "Risks of silicosis in coalworkers exposed to unusual concentrations of respirable quartz." Occup Environ Med 55: 52-58.

and

Buchanan, D., B. Miller, et al. (2003). "Quantitative relations between exposure to respirable quartz and risk of silicosis." Occup Environ Med 60: 159-164.

These studies are summarized and commented on in Section II of this report where they clearly show the effects of high quartz exposure producing rapidly progressing silicosis. There were strong associations with quartz exposures but no associations of CWP and CMD exposure.

Morfeld, P., J. Ambrosy, et al. (2002). "The Risk of Developing Coal Workers' Pneumoconiosis in German Coal Mining under Modern Mining Conditions." Ann Occup Hyg 46(Supplement 1): 251-253.

Summary and Comments

This is an inception cohort of 1,369 coal miners who began work underground at two large German collieries during the period from 1974-1979 and had at least 0.5 years exposure underground. Miners were about equally divided between the Heinrich Robert Colliery, mining high rank coking coal used in steel production and the Walsum Colliery mining low rank gas and flaming coal used in energy production. By law each miner must receive a chest radiograph every other year and smoking histories are available on each miner. Over 36,000 stationary (or area samples) gravimetric dust measurements were collected from 1974-1998, which is the same time period as the follow-up.

Exposure was dissimilar between the two collieries:

	Coal dust Intensity (mg/m^3) Mean (max)	Quartz Intensity (mg/m^3) Mean (max)	Time UG (yrs) Mean(max)	Approximately cumulative exposure = Intensity x yrs UG = mg/m^3-yr Mean (maximum)	
				Coal Dust	Quartz
Low rank coal(n = 699)	1.68 (6.91)	0.063 (0.88)	14.6 (23)	24.5 (159) 0.92 (20.2)	0.92
High rank Coal(n = 670)	2.06 (6.00)	0.038 (0.31)	14.9 (24)	30.7 (144) 0.91 (7.4)	

Average CMD exposure in the low rank mine was below 2.0 mg/m^3 and less than the 2.06 mg/m^3 of the high rank coal. Intensity of quartz exposures were reversed with the higher average (and maximum) values in low rank coal compared to high rank coal. Years underground were similar in the two mines, so there is little difference in cumulative exposure between miners.

There were no chest radiographs showing category CWP 1+ indicating no association between CWP and CMD.

Additional Comments and Critique of Morfeld, Ambrosy, et al. (2002)

This study shows no association between exposures to CMD at mean levels above the MSHA standard in high rank coal. In low rank coal, the mean was slightly below the MSHA standard, but a proportion of miners had exposure levels above 2.0 mg/m^3. Because there are zero cases of CWP 1+ the best one can say about exposure-response is that the 2.0 mg/m^3 standard appears to be protective in this cohort, and quartz exposures at the concentrations experienced also do not produce pneumoconiosis.

A limitation of this study is that latency may be too short for development of pneumoconiosis. The maximum latency was 24 years with an average of 15 years. The relatively short latency for CWP may be an explanation for the absence of any apparent risk of developing CWP 1+.

Three percent of the miners developed category 0/1, and all cases of 0/1 at the Walsum Colliery were either smokers or ex-smokers. These may be cases of the so-called "dirty lung syndrome" attributed to cigarette smoking and is the approximate baseline prevalence for 0/1 in this study. These data tend to support the German concept for considering category 1/1+ a definite CWP category. Categories 0/1 and 1/0 are fraught with much variation and depending on how film reading is done can seriously affect outcomes in studies. Incidence of category 0/1 was not analyzed further in this study.

It is interesting that the authors compare their low risk estimates with US estimates and note the gross disparity in risk. They indicate that if personal dust sampling had been done it would have sharpened (increased) the discrepancy between the US and German findings. This refers to the general finding that area samples often are less than personal sampling results, and thus may underestimate individual exposure results.

Scarisbrick, D. and T. Quinlan (2002). "Health surveillance for coal workers' pneumoconiosis in the United Kingdom 1988-2000." Ann Occup Hyg 46)((Suppl. 1): 254-256.

Summary and Comments

This study reports on CWP occurrences for the colliery population in the UK under the Periodic X-ray ("PXR") scheme for the years 1998-2000. Since the beginning of this program in 1959 the prevalence of CWP 1 and CWP 2+ has dropped dramatically, until the last survey when prevalence increased (Table, Figure 9).

Prevalence of CWP in UK from 1959-2000 under the Periodic X-ray (PXR) Scheme (Scarisbrick and Quinlan 2002)

Round	Years	No. X-rayed	Category 1		Category 2+		All Categories	
			No.	Prevalence	No.	Prevalence	No.	Prevalence
1	1959-63	462999	32608	7	23401	5	56009	12.1
3	1969-73	238759	16389	6.9	7888	3	24277	10.2
5	1978-81	198055	6256	3.2	1902	1	8158	4.1
7	1986-89	76802	453	0.6	65	0.1	518	0.7
8	1990-93	36970	138	0.4	10	0.01	148	0.4
9	1994-97	6378	13	0.2	0	0	13	0.2
	1998-2000	4647	26	0.6	9	0.2	35	0.8

The increased prevalence occurred primarily in two collieries where prevalences for all categories were 1.3% and 2.3%. For category 2+, prevalences were 0.5% and 1.2% respectively. Possible causes for these increases in the last years of the 20th Century focused on the two collieries designated as A and B. Characteristics of each are listed.

Main findings from focused investigation on Collieries A and B (Scarisbrick and Quinlan 2002)

Characteristic	Colliery A	Colliery B
Use of respiratory protection equipment	Slightly > national average	Significantly < national average
Dust Levels	Not excessive over last 10 years but some increase last 10-years	Dusty
Places of Work		Most of those affected had worked in geological faults & cutting through stone may have led to increased quartz exposure
Mining methods		Recent introduction machinery to cut through rock previously removed by explosives requiring removal of miners when firing, & lower exposures.
Working hours	Cases worked longer than non-cases & standard work week. Work week time doubled in extreme cases & 7 days/wk, 12 hr shifts common. Considered most significant factor leading to increased CWP incidence in collieries A & B.	

Age changes in the UK coal mine population may also have produced some changes in CWP. In the early part of this 40-year period most miners retired at age 65. As the industry got smaller and pits closed the older miners tended to leave so the average age decreased. In the last few years the trend has reversed with age increasing because miners are tending to stay longer and ex-miners are returning. Up to 1997 at least, dust control was the cause for the decreases in CWP prevalence, and a younger age distribution was not a major cause for decreasing CWP because prevalence reductions were similar in all age categories.

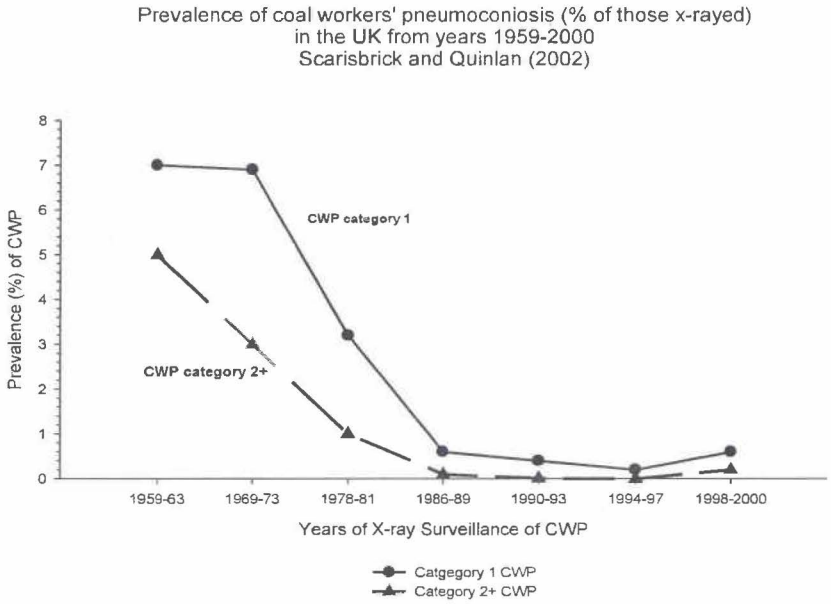
Additional Comments and Critique of Scarisbrick and Quinlan (2002)

This study may be useful in assessing possible reasons for the recent increases in incidence and rapid progression of CWP. In these two pits the primary possible causes for increased CWP included:

- Much longer working hours and, therefore, higher cumulative exposures;
- Increased quartz exposure in Colliery B due to increased cutting through stone; and
- Change in mining methods employing new mining equipment that can cut through rock that in the past was removed by explosives (Colliery B)

This study is consistent with findings in the US of reduced prevalence of CWP and a recent but slight increase in rapidly progressive pneumoconiosis. It may be useful in explaining possible reasons for the recent increase in CWP prevalence. This study is not useful for assessing exposure-response or developing a standard.

Figure 9



Naidoo, R., T. Robins, et al. (2004). "Radiographic outcomes among South African coal miners." Int Arch Occup Environ Health 77: 471-481.

Summary and Comments

This is a cross-sectional exposure-response study of a cohort of 684 current bituminous coal miners in the Mpumalanga province of South Africa. It is the first study to document the prevalence of CWP in a living South African cohort of coal miners.

The miner cohort consisted of all 684 current miners in three mines and excluded all workers at or above grade 13, junior management level, administrative positions, etc. This is a cross-sectional study design in that only the most recent chest X-rays were used. Ex-miners were recruited for the study but because of the small number of former employees and the 11% non-participation rate this is not a major focus of this analysis. The cumulative respirable CMD variable was categorized into terciles of low exposure (0.62-20.1 mg/m^3-years; n = 278), medium exposure (20.1-72.8 mg/m^3-years; n = 285), and high exposure (72.8-259 mg/m^3-years; n=294). Pack years was adjusted for in the exposure-response analysis.[7] Average intensity of exposures was 0.2-0.3 mg/m^3 on the

[7] Pack years is a term used in public health to measure the amount a person has smoked over a long period of time. It is calculated by multiplying the number of packs of cigarettes smoked per day by the number of years the person has smoked. For example, one pack year is equal to smoking 20 cigarettes per day for one year, or 40 cigarettes per day for half a year, and so on. A smoker who smoked one pack a day for 40 years would have a 40 pack year smoking history.

surface and 0.9-1.9 mg/m^3 at the face. Among mechanical miner operators, mean concentrations ranged from 1.2-2.8 mg/m^3. Percent silica ranged from 1.2-2.8% at the face.

There was a clear exposure-response trend of CWP 1+ and cumulative respirable CMD (trend test p=<0.001), but no trend with radiological emphysema (Figure 9). The exposure-response trend for CWP 1+ was also significant using cumulative exposure as a continuous variable.

Additional Comments and Critique of Naidoo, Robins, et al. (2004)

These data show a clear association of CMD and CWP 1+, but low prevalence that is below 5% at high exposures. The mid-point of 165 mg/m^3-years as the high exposure range and average tenure of 10 years for face workers suggest an average intensity exposure of about 16 mg/m^3. The average intensity over a 40-year working lifetime would be 4 mg/m^3. At an intensity of about 2.0 mg/m^3 there would be a prevalence of <1% CWP 1+ assuming 40 years tenure. While intensity of exposure is high, the prevalence of CWP is likely to be below background levels.

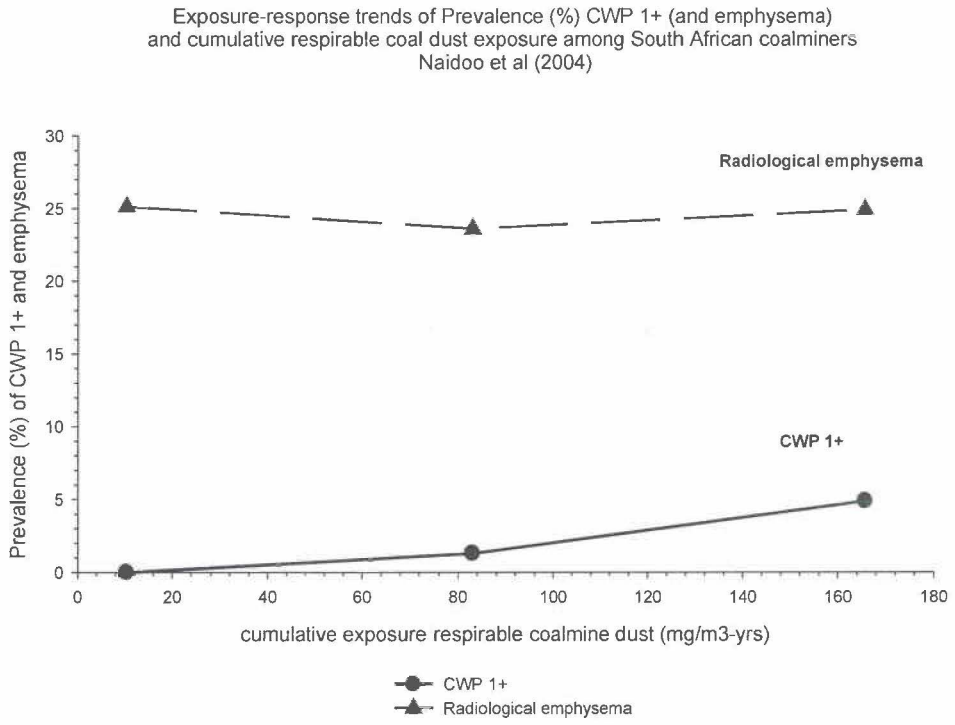
Such a low prevalence at high exposures may be due to inadequate latency for CWP to develop. Miners were classified into three groups by exposure, with the most exposed group being miners with 10+ years at the face. Maximum intensity of mean exposure at the face for all three mines was 1.9 mg/m^3. A cumulative exposure of 165 mg/m^3-years and maximum intensity of 1.9 mg/m^3 leads to an implausible tenure of 87 years. Maximum intensity of exposures (as opposed to mean) must have been well above the 2.0 mg/m^3 MSHA standard.

The authors comment that the low 4.2% prevalence of CWP in South African miners is similar to the 4.5-6.8% reported in the US (Atffield and Seixas 1995), but with about 50% lower average exposures in the US (34 mg/m^3-years) than this study (57 mg/m^3-years).

These data indicate an association of CWP 1+ and cumulative respirable CMD exposure in this South African cohort. Prevalence is low even at high CMD exposure (and relatively low quartz exposure). At 2.0 mg/m^3 intensity, these data suggest no increased prevalence; the finding of three cases (1.4%) at 20-73 mg/m^3-years (or 0.5-1.8 mg/m^3 for a 40-year working lifetime) could be due to chance. This chance finding could include a much higher intensity for relatively short periods at the face where it appears there are some individual exposures that could be 4 mg/m^3 or more. If background prevalence is taken into account there are no significant excesses of CWP 1+ at concentrations well above a 2.0 mg/m^3 standard (Figure 10).

Prevalence of radiological emphysema was quite high, but showed no relationship with cumulative respirable CMD (Figure 10).

Figure 10



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V. COAL MINE DUST EXPOSURE-RESPONSE RELATIONSHIPS WITH PULMONARY FUNCTION

1. Summary of Exposure-Response Studies and Pulmonary Function

It has been noted that exposure to respirable CMD can result in a respiratory abnormality, independent of CWP, characterized by obstruction to airflow on exhalation (Soutar and Hurley 1986; Atffield and Hodous 1992; Coggan and Newman-Taylor 1998; Cowie, Miller, et al. 2006). Such a pattern of function loss is referred to as chronic obstructive pulmonary disease ("COPD"), which is a chronic lung disease that includes two main illnesses: chronic bronchitis and emphysema. COPD is characterized as an obstructive pattern of airflow and is measured using a spirometer to assess the volume of air exhaled during the first second of a forced expiratory maneuver (FEV_1). A spirometer is an instrument for measuring lung volumes and flow rates. A forced expiratory maneuver is the basic maneuver of spirometry where the subject takes the deepest possible breath and blows into the mouthpiece as hard, fast, and completely as possible. Spirometry also provides estimates of forced vital capacity ("FVC") and FEV_1 to FVC ratio ("FEV1/FVC%") which is the FEV_1 expressed as a percentage of the FVC and is the fraction of the total air that is exhaled in the first second. Sometimes FVC and FEV_1/FVC% are reported in these studies. Decrements in FVC are one measure of restrictive lung disease, which is not of primary concern in COPD. FEV_1/FVC% is another measure of obstruction, but is considered less reliable as the ratio is dependent on the value of FVC. Cigarette smoking is the most common cause of COPD. In the occupational setting exposures to dusts, chemicals and fumes may also cause or contribute to COPD. COPD is classified as an occupational disease in Germany, while chronic bronchitis and emphysema (examples of COPD) are considered occupational diseases in the United Kingdom (UK).

However, questions have been raised whether coal dust causes "clinically important loss in lung function in the absence of complicated pneumoconiosis" (Lapp, Morgan, et al. 1994). Two ways to evaluate this question and also to determine exposure-response associations for use in setting standards include: 1) study lung function among miners according to their exposure to CMD exposure; and 2) analyses of relations between emphysema in coal miners at necropsy and their exposure to coal dust (Coggan and Newman-Taylor 1998). The first issue we will discuss is exposure-response associations between FEV_1 and CMD exposure. The second issue regarding emphysema is not generally useful because of the inability to relate pathology findings (i.e., autopsy emphysema score) with CMD air concentrations and airborne exposure to CMD.

Two study designs are used in these types of studies. One is a cross-sectional design where at one point in time miners willing to participate are examined using spirometry for lung function (FVC, FEV_1), and, as part of the examination, a questionnaire is filled out by the miners providing information on work history, respiratory symptomatology, and other risk factors for reduced lung function such as smoking history, age, height and

sex. Retrospective exposure to CMD is the sum of tenure in these jobs multiplied by estimated CMD concentrations in that job. Analysis consists of determining whether reductions in lung function (FEV_1) are associated with higher exposures after adjustments for age, height, sex, and smoking.

A prospective or longitudinal study design is where a cross-section of workers are examined and then re-examined some time (or times) later, such as every three to five years for a decade or more. The study population comprises miners that were examined at both the initial examination and the last examination. Response is the change in FEV_1 between round one ("R1") and the last round of examination ("years (R*n*)"). It can be measured in losses in milliliters (ml) of air or as change in percent predicted ("% predicted"). In the longitudinal study design each individual is his own control, unlike the cross-sectional design where the referent is an external (and sometimes internal) population for estimating % predicted. Air samples collected between R1 and R2 (or succeeding rounds) are used to estimate cumulative exposure during the study interval, and to estimate loss in FEV_1 (ml) attributed to CMD exposure, aging, and smoking by the statistical regression models.

A period of years between examinations are necessary because changes in lung function over short time periods are small and variability in serial measurements are great enough that four or five years may be the minimum number of years required to detect a meaningful change.

Expected reductions in FEV_1 are associated with aging and smoking. These estimates may vary between cross-sectional and longitudinal designs. For example, Seixas, et al. have both designs and some data are listed to indicate some differences in results between designs and to help judge yearly and cumulative losses in FEV_1 associated with some risk factors (Seixas, Robins, et al. 1993).

		Unit risk (ml) (pre-R2)	FEV_1 loss (pre-R2)
(Seixas, Robins, et al. 1993)	Cross-sectional design		
	Age (years)	- 44.5 ml per year	45-years = -1904 ml
	Smoking	- 44.7 ml (ex-smoker)	-44.7 ml
	Pack-years	- 9.4 ml per pack year	40 pack-years = -376 ml
	Longitudinal design		
	Age (years)	-4.9 ml per year	45-years = -220 ml
	Smoking	-8.7 ml	-8.7 ml

Breathlessness is one health measure associated with clinically significant deficits reductions in FEV_1. In a study of 7,000 miners (Cowie, Miller et al. 1999; Cowie, Miller

et al. 2006), clinically important measured deficits in FEV_1 were defined in relation to breathlessness. A three-fold relative risk ("RR") of breathlessness ("walking slower than other people on level ground because of their chest") was associated on average with a 0.993 liter deficit in FEV_1. A two-fold RR is associated with a deficit of 627 ml, with a 1.5-fold RR at 367 ml deficit in FEV_1. These data suggest that a deficit of over about 300 ml FEV_1 may be associated with a clinically significant adverse effect of breathlessness.

The probability of such deficits is increased with high exposure to CMD, but note that probabilities are high even at zero exposure to CMD as shown in the following table (Soutar, Hurley, et al. 2004). These data suggest a high background rate (at 0 exposures) of clinically significant breathlessness and deficits in FEV_1.

	0 mg/m^3	6 mg/m^3	0 mg/m^3	6 mg/m^3	0 mg/m^3	6 mg/m^3
	-933 ml FEV_1 % risk (probability)		-627 ml FEV_1 % risk (probability)		-367 ml FEV_1 % risk (probability)	
Non-smokers	10%	19%	25%	40%	41%	55%
Smokers	22%	36%	44%	60%	62%	75%

If these data are representative, a loss of >300 ml may be a clinically significant effect as a lower limit and that >40% of nonsmoking and >60% of smoking miners would have >300 ml deficit in FEV_1 at zero exposure and therefore have impairment that is not attributable to coal mine dust exposure.

We now present the data regarding reductions in FEV_1 associated with CMD. These are expressed in terms of unit risk in ml, cumulative risk at 90 mg/m^3-years, or an equivalent of working 45 years at 2 mg/m^3. This figure is on the conservative side since it is more plausible that a miner's work life is shorter than 45 years, and for currently retired workers it is more commonly a 35- to 40-year work history. Unit risk is the estimated reduction in FEV_1 at 1 mg/m^3 for 1-year that is attributed to CMD exposure in multiple regression models. Unit risk can be multiplied by the number of years worked to calculate cumulative risk. The cumulative risk (in ml FEV_1) can be used to assess an average clinically significant response based on the association of FEV_1 and breathlessness.

Another measure of clinically significant COPD is % predicted FEV_1. In spirometry, 80% and 65% predicted values are commonly used as individually significant declines in lung function. We have calculated an average % predicted based on an initial FEV_1 of 4.4 liters, or 100% predicted for comparisons between studies. Average loss in FEV_1 over the study period is subtracted from 4.4 liters FEV_1 to estimate average % predicted in the study population attributed to CMD exposure. This is a high average FEV_1 but was the approximate value reported found at R1 in a United States study (Seixas, Robins, et al. 1993). Based on unit risk readers can calculate their own cumulative loss, or loss in % predicted if different comparisons are desired.

Finally we have calculated exposure estimates so they are in the same metric of mg/m^3 and mg/m^3-years. The UK data commonly use gram hours per cubic meter (gh/m^3) assuming 1,600 or 1,740 hours/year. We have used 2,000 hours work per year and 45 years to change gh/m^3 to mg/m^3-years because this is the conversion used in Table 4-5 (CDC 1995) to convert coefficients in mg/m^3-years to gh/m^3 coefficients. The coefficients are the same as unit risks, or loss of FEV_1 (in ml) per exposure unit (mg/m^3-year).

The formula for converting gh/m^3 to mg/m^3–year is:

$$gh/m^3 \div (\text{hours/year}) \times [1000(\text{to change g to mg})] = mg/m^3\text{-year}$$

For example, a coefficient of -0.00036 L per gh/m^3 → 0.00036 L per (2000 hours) x (1000) = -0.00018 L/mg/m^3-year, or -0.18 ml per mg/m^3-year (Love and Miller 1982). Exposure for 45-years at 2 mg/m^3 (= 90 mg/m^3-years) produces a loss of -16 ml FEV_1 attributable to coal mine dust for a working lifetime. The results from a study of coal miners in the United States (US) with a similar study design (Atffield 1985) showed a coefficient of -0.028 L per mg/m^3-year (unit risk = -28 ml), which over a working life-time is predicted to produce a calculated loss of 1,261 ml FEV_1. This formula produces coefficients that are slightly different than the calculations using 1600 hours (Coggan and Newman-Taylor 1998) but similar to the NIOSH conversions (CDC 1995).

The overall scientific evidence from cross-sectional and longitudinal studies is summarized below. Summaries and comments on each individual study of COPD are included in paragraph 2. a., b., c., and d. of this section.

a. Cross-sectional Studies

There are nine cross-sectional studies (Table 1) and 13 exposure-response analyses of cohorts or sub-sets of the cohort shown in Figure 1. All but one analysis shows negative associations of FEV_1 loss with increasing exposure to CMD (Figure 1). Average losses in FEV_1 at 90 mg/m^3-years generally do not suggest clinically significant deficits as all but two exposure-response trends show mean FEV_1 above 95% predicted and with a less than 300 ml loss in FEV_1. Lifetime losses of this magnitude are, on average, not associated with symptoms of breathlessness nor functional loss related to COPD. Eleven of 13 exposure-response curves (85%) reported **no** clinically significant reductions in FEV_1 at or below the current standard of 2 mg/m^3 (i.e., 90 mg/m^3 for 45 years). Figure 1 shows that all but two exposure-response associations had greater than 95% predicted FEV_1 after 45-years exposure at 2 mg/m^3.

The steepest declines in FEV_1 were among new US miners exposed prior to Round 2 (< 1970) before federal regulation of coal mine dust levels; FEV_1 was reduced to 44% of predicted with a unit risk of -28 ml per mg/m^3 (Seixas, Robins, et al. 1992). The second largest declines were from the same cohort with post-1970 exposures and a unit risk of -

5.9 ml per mg/m^3. These steep declines are inconsistent with results from other cross-sectional studies, and in particular are inconsistent with the two other studies of US miners who also were from the NSCWP. In these studies where exposures occurred before 1970 (Round 1), unit risks were 50 times less at -0.4 ml (Atffield and Hodous 1992) and -0.5 ml per mg/m^3 (Henneberger and Attfield 1996) compared to Seixas, et al. Post-1970 unit risks were 17 times less (-0.35 ml) and 23 times less (-1.2 ml) for Attfield & Hodous and Henneberger & Attfield compared to Seixas, et al. There is some overlap in these studies as all participants were samples from the 7,139 miners examined in Round 1 (Atffield and Hodous 1992) or 1,915 miners in R1 and R2 (Henneberger and Attfield 1996), or 977 miners in both R1 and R4 (Seixas, Robins, et al. 1993). Reasons for these inconsistent findings are unclear given the data were collected in the same manner by the same technicians from miners in the same NSCWP cohort.

Cross-sectional exposure-response analyses consistently show small reductions in FEV_1 associated with CMD exposure after adjustments for age, smoking, and height. Figure 1 and Table 1 show 12 of 14 studies with average cumulative losses of less than 300 ml in FEV_1 during a working life time at standard exposure levels. The deficits in FEV_1 are, on average, **not** clinically significant where clinical significance is considered to be a loss of more than about 300 ml in FEV_1. Available data suggest that at age 60 in the absence of exposure to CMD there is about a 40% chance that a non-smoker will show a comparable deficit and 60% probability for smokers. A 35-year exposure to 6 mg/m^3 increases those probabilities to 55% and 75% (Cowie, Miller, et al. 1999; Soutar, Hurley, et al. 2004; Cowie, Miller, et al. 2006). CMD exposure appears to add relatively little increased risk to these high probabilities.

These data suggest that, on average, when exposure is under the MSHA standard of 2 mg/m^3 for 45 years, there will be few clinically significant declines in FEV_1 or increased incidence of COPD.

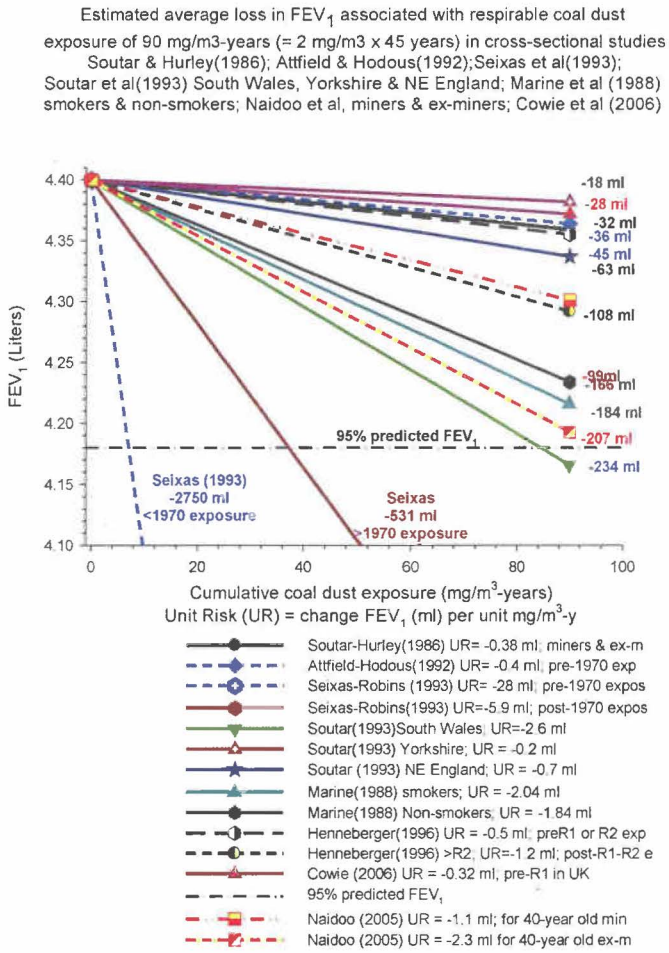
There is one study of open-cast coal mining (or surface mining) in the UK (Love, Miller, et al. 1997). There were 1,224 men and 25 women with all dust levels below 1 mg/m^3 and 99% of quartz samples were below the maximum exposure level of 0.4 mg/m^3. Lung function (FEV_1, FVC, $\%FEV_1/FVC$) were "close to predicted values and showed no relation to time worked in opencast occupations."

Table 1: Average Estimated loss in FEV_1 associated with respirable coal mine dust in cross-sectional studies.

Reference	UR per mg/m^3-y (ml)	Change FEV1 @ 90 mg/m^3-y (ml) (% predicted FEV_1)	Notes
(Hurley and Soutar 1986) bronchitic sub-set of (Soutar and Hurley 1986)	-1.2 ml	-108 ml (97.6%)	199 ex-miners + symptoms of chronic bronchitis
(Atffield and Hodous 1992) US	**-0.35 ml**	**-31 ml (99.3%)**	**7,139 pre-R1 (pre-1970 exposure)**
(Seixas, Robins, et al. 1993) US	**-27.5 ml** **-5.9 ml**	**-2750 ml (43.8%)** **-531 ml (87.9%)**	**997 miners, Pre-1970** **1997 miners, post-1970**
(Soutar, Campbell, et al. 1993) UK	**-0.52 ml** **-0.04 ml** **+1.4 ml**	**-46.8 ml (98.9%)** **-3.6 ml (99.9%)** **+126 ml 102.9%)**	**South Wales** **Yorkshire** **NE England**
(Marine, Gurr, et al. 1988) re-analysis of (Rogan, Atffield, et al. 1973) UK	**-2.04 ml** **-1.84 ml** -1.7 ml -1.5 ml	**-184 ml (95.8%)** **-166 ml (96.2%)** -153 ml (96.5%) -135 ml (96.9%)	Total cohort **2837 smokers** **543non-smokers** Impaired <80% FEV_1 827(29%) smokers 92(17%) non-smokers
(Henneberger and Attfield 1996) US	**-0.5 ml** **-1.2 ml**	**-45 ml (99.0%)** **-108 ml (97.6%)**	**1915 Pre-R1 / R2** **1915 post-R1 / R2** **(15.2 yrs)**
(Carta, Aru, et al. 1996) Sardinia	upward trend by tertiles	Data not shown in table, "significantly dependent on…cumulative dust exposure"	cumulative exposure too small to assess risk, 50% <2.1 mg/m^3-yr
(Naidoo, Robins, et al. 2005) SA	**-1.1 ml** **-2.3 ml**	**-99 ml (97.9%)** **-207 ml (95.3%)**	**670 miners** **197 ex-miners** Predictions for 40-yr old
(Cowie, Miller, et al. 2006) UK	**-0.32 ml**	**-28.4 ml (99.4%)**	**7188 miners, late 1970s**

Units in gh/m^3 were recalculated to mg/m^3-years based on 2000 hours/year. Based on FEV_1 = 4.40 liters before CMD exposure, percent predicted change in FEV_1 attributed to CMD is calculated. (Also presented in Figure 1) **Bold results are included in Figure 1.**

Figure 1



b. Longitudinal Studies

There are eight cohorts studied prospectively with ten exposure-response curves shown in Figure 2. Coggon and Taylor (Coggan and Newman-Taylor 1998) had described results earlier from 5 longitudinal studies as less clear-cut than from cross-sectional studies. They suggested associations of FEV_1 with CMD exposure were of similar magnitude as those seen in cross-sectional results. They thought the most reliable indicator of exposure-response relationships was the UK study of miners and ex-miners (Soutar and Hurley 1986) with a unit risk of -0.38 ml per mg/m^3, which is quite similar to two of the US studies (Atffield and Hodous 1992; Henneberger and Attfield 1996). Reasons for selecting this risk as representative and reliable were because it had the best exposure data, included both miners and ex-miners, had data on smoking, and were consistent with general findings from other studies (Coggan and Newman-Taylor 1998).

A unit risk of -0.38 ml per mg/m^3 does not produce clinically significant reductions in FEV_1 or increased COPD at lifetime exposure of 45 years at 2 mg/m^3.

We have added two studies to this list, both of which show no associations (Wang, Wu, et al. 2005; Morfeld, Noll, et al. 2010). Two studies showed clinically significant or nearly significant declines (Atffield 1985; Carta, Aru, et al. 1996). Four groups of miners showed positive slopes suggesting improvements in FEV_1 with increasing exposure (Seixas, Robins, et al. 1993; Henneberger and Attfield 1996; Morfeld, Noll, et al. 2010). In all instances FEV_1 is above 90% predicted, except for Carta (1996).

The weight of the evidence from the seven longitudinal cohorts and ten groups of coal miners with exposure-response curves show a consistent lack of association (eight of ten groups) between CMD exposure and clinically significant mean reductions in FEV_1. The range of mean non-significant changes is +252 ml to -64 ml at 90 mg/m^3-years. There is one apparent outlier where there is a negative unit risk of -7.6 ml per mg/m^3 or a loss of about 700 ml attributable to 90 mg/m^3-year CMD exposure (Carta, Aru, et al. 1996).

Our results are more heterogeneous and vary somewhat from Coggon and Taylor. We found 2 studies showing clinically significant deficits of around 300 ml or greater (Atffield 1985; Carta, Aru, et al. 1996); 4 studies showing no significant deficits (losses ranging from -64 ml to 0 ml) attributable to CMD or increased performance with increased exposure (Love and Miller 1982; Soutar and Hurley 1986; Henneberger and Attfield 1996; Wang, Wu, et al. 2005; Morfeld, Noll et al. 2010); and 3 subsets of miners showing no apparent losses in FEV_1 (the unit risk is positive) attributable to CMD exposure at concentrations above the current standard (Seixas, Robins, et al. 1993; Henneberger and Attfield 1996).

The greatest difference in our results is in the Attfield study. Coggon and Taylor reported a unit risk of -1.6 ml per gh/m^3. At 1,600 hours/year, which they used as a conversion factor, this is a unit risk of -1 ml per mg/m^3. At 2,000 hours/year the unit risk is calculated as -0.80 ml per mg/m^3. The coefficient from the study (Atffield 1985) is reported as -0.028 liter, or a unit risk of -28 ml per mg/m^3 (Table 4, Model III). This appears to be incorrect. Based on a prediction cited in the text the unit risk is calculated to be -2.55 ml per mg/m^3, which is believed to be the correct value and is more consistent with results from other studies. (See summary below for further discussion.) The source of the data in Coggon and Taylor is unclear. Their unit risk is consistent with general trends observed in other studies, but is less than our calculated risk based on extrapolations from the text.

Three US studies (see below) had both longitudinal and cross-sectional components and risks estimated for both pre-1970 and post-1970 exposures. The results are both heterogeneous and inconsistent thereby reducing their reliability for use in determining a standard of consistent pattern of exposure-response.

	(Atffield 1985; Atffield and Hodous 1992)		(Seixas, Robins, et al. 1993)		(Henneberger and Attfield 1996)	
	Pre-1970 UR/mg/m^3	Post-1970 UR /mg/m^3	Pre-1970 UR/mg/m^3	Post-1970 UR/mg/m^3	Pre-1970 UR/mg/m^3	Post-1970 UR/mg/m^3
cross-section	-0.35 ml		-28 ml	-5.9 ml	-0.5 ml	-1.2 ml
Longitudinal		-2.55 ml (estimated)	+0.7 ml	+2.8 ml	-0.07 ml	+2.0 ml

The largest inconsistencies are found in Seixas, et al. Strong negative associations are reported in the cross-sectional analyses but positive trends in the longitudinal design. Henneberger et al show small declines in all exposure-response slopes except for a positive trend in the longitudinal analysis of post-1970 exposure. The Attfield, et al. studies are different publications, but are consistent in that trends at least are in the same direction for both pre- and post-1970 exposures.

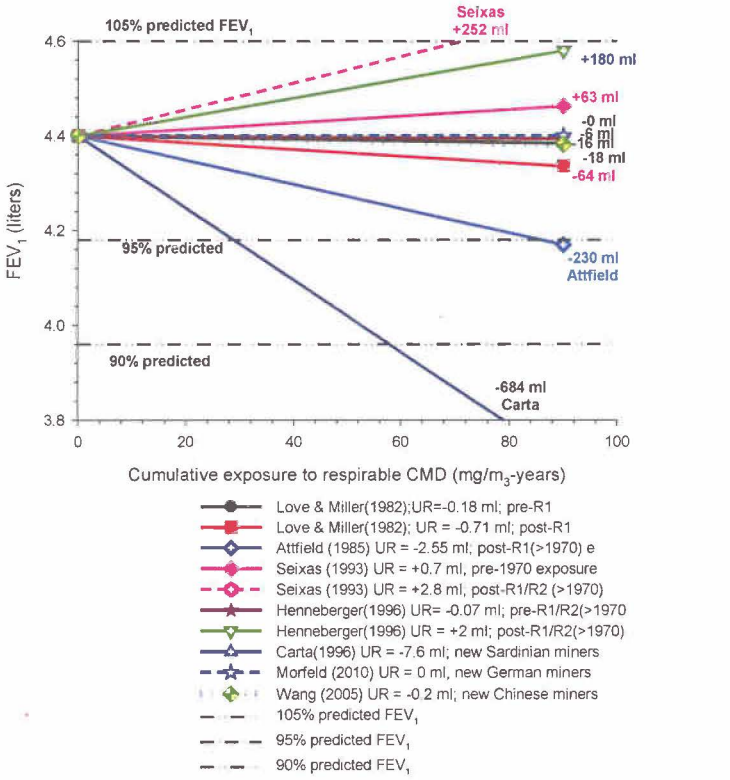
The predominant pattern emerging from the longitudinal studies pictured in Figure 2 is small changes with clinically insignificant declines in FEV_1 (< 300 ml) and no apparent losses in FEV_1 attributable to CMD exposure.

Table 2. Average estimated change in FEV_1 associated with respirable coal mine dust in longitudinal studies. (See Table 1 for calculation of cumulative exposure.)

Reference	UR per mg/m^3-y (ml)	Change FEV_1 @ 90 mg/m^3-y (ml) (% predicted FEV_1)	Notes
(Love and Miller 1982)	**-0.18 ml** **-0.71 ml**	**-16.2 ml (99.6%)** **-64 ml (98.6%)**	**1677 UK miners(11 y follow-up)pre-R1** **Post-R1 exposure at maximum likely of 11 mg/m^3 under current conditions**
(Soutar and Hurley 1986)	**-0.38 ml**	**-34.2 ml (99.2%)**	**4059 miners/ex-miners adjusted age, height, weight, smoking, mine**
(Atffield 1985)	**-2.55ml(est)**	**-230 ml (94.8%)**	**1072 miners Concurrent 11-y exposure**
(Seixas, Robins, et al. 1993)	**+0.7 ml** **+2.8 ml**	**+63 ml (101%)** **+252 ml (105.7%)**	**977 miners , pre-1970 exposure** **977 miner, R2-R4 exposures**
(Henneberger and Attfield 1996)	**-0.07 ml** **+2.0 ml**	**-6.3 ml (99.9%)** **+180 ml (104.1%)**	**1915 Pre-R1/R2** **1915 Post-R1/R2 (15.1 years)**
(Carta, Aru, et al. 1996)	**-7.6 ml**	**-684 ml (84.5%)**	**909 new Sardinia miners (10 y follow-up)**
(Morfeld, Noll, et al. 2010)	**-0 ml**	**- 0 ml (100%+)**	**1369 new German miners (24 y follow-up)**
(Wang, Wu, et al. 2005)	**-0.2 ml**	**-18 ml (99.6%)**	**317 newly hired, (3 y follow-up)**

Figure 2

Estimated average change in FEV_1 associated with cumulative exposure to respirable CMD of 90 mg/m^3-years (=2 mg/m^3 x 45 years) in ~~longitudinal studies~~
Love & Miller (1982); Attfield (1985); Seixas et al, (1993);
Henneberger & Attfield (1996); Carta et al, 1996); Morfeld et al (2010);
Wang et al, (2005)



While not totally consistent, both cross-sectional and longitudinal studies show findings of significant associations between CMD exposure and reduced FEV_1. However, deficits in FEV_1 attributed to CMD exposure are, with few exceptions, not clinically significant at maximum exposures allowed under current standards (2 mg/m^3) and for close to maximum hours worked (2,000 hours/year for 45 years).

Hill's guidelines (Hill (1965)) suggest a causal association between CMD and reduced FEV_1 in part because there are consistent findings of negative biological gradients (exposure-response trends). However, these are weak associations in that the reductions in FEV_1 are not generally of clinical significance, and in some cases are positive. This can be interpreted as meaning that no effect can be attributable to CMD. And if the trends are not statistically significant an apparent effect may be due to chance. Consistency is an important guideline for causality, but consistent findings of weak associations are not very supportive of causality because results from such studies are more susceptible to bias and confounding. Smoking is a common confounding variable,

but smoking is adjusted for in all these studies, and where examined, smokers may be less susceptible to decreases in CMD-attributable FEV_1 than non-smokers.

The most probable biases appear to be selection and information biases that are of greatest concern in the US studies.

Information biases relate to misclassification of exposures. This bias is of particular concern in pre-1970 exposure estimates because these appear to be over-estimates for high exposures and under-estimates for low exposures. The effect is to produce a spuriously reduced exposure-response slope that over-estimates risk. Post-1970 exposures are based on operator samples that may be biased low in some mines. Potential effects produced by this bias is similar to the pre-1979 exposure estimates in that the result may be spuriously steep declines in exposure-response slopes suggesting excessive reductions in FEV_1 attributed to CMD.

Selection bias occurs in studies where miners had to be participants in rounds two through four of the NSCWP. Participation rates were >90% in round 1 so there should be no selection bias, but participation rates were well below 90% in rounds 2-4 and could bias results in an unknown direction. It is not clear whether or not these biases are the cause of outlier results in the US studies. The probability of these biases appears to be of much less magnitude and less concern in cohorts of UK miners.

The most reliable results are considered to be those from the PFR studies in the UK, where for many years there was a program to measure exposures and examine miner periodically. In the UK, miner participation in the medical surveys was required so participation rates were high and the probability of selection bias virtually non-existent. In the US, NSCWP study participation was voluntary and participation rates considerably less than 90% after round 1 so there is a high potential for the occurrence of selection bias.

The crux of our conclusions can be found in Tables 1 and 2 and Figures 1 and 2. Both cross-sectional and longitudinal designs show mostly weak and clinically non-significant mean reductions in FEV_1. These data are suggestive that CMD exposure at the current standard is unlikely to be an important cause of COPD or clinically reduced FEV_1 in current coal miners. The incidence of COPD appears to be elevated generally due to high background levels of COPD at zero exposure levels as reported in the UK. Increased incidence of COPD potentially attributable to CMD is relatively small and only slightly above measurement error or bias. Background prevalence of COPD in the US is needed for more reliable interpretation of US studies. We conclude that CMD does not appear to cause appreciable reductions in FEV_1 in coal miners at current exposures and less than 45-years tenure underground.

2. Summary and Comments on Individual Cross-sectional and Longitudinal Pulmonary Function Studies

a. Cross-Sectional Studies

Hurley and Soutar (1986): "Can exposure to coalmine dust cause a severe impairment of lung function?" Brit J Ind Med 43: 150-157.

This is a companion work of Soutar and Hurley (Soutar and Hurley 1986) which was published in the same volume at a conference in Bochum, Germany. Coggon and Taylor did not comment on this work since it was a sub-set of the main effort with overlap in the same miners in both studies. For our review this paper is relevant because it relates to the importance of severe changes of pulmonary function loss.

From the main study (Soutar and Hurley 1986) there were 453 ex-miners < 65 who appeared to suffer larger effects dues to dust exposure and who had symptoms of chronic bronchitis. Of these 453 ex-miners, 158 left mining and did not take other jobs, 199 left mining and took other work, while the remaining 96 could not be classified regarding their future employment. The 199 ex-miners were the subject of this report. The characteristics of these 199 men were compared with 2 groups of similar age from the main body of 4,059 men, 1) ex miners <65 years, and 2) active miners. It is unclear why group 1 (ex-miners <65) were used for comparison as this group included the study group of 199. The authors note the higher proportion of smokers among the study group (77%) and the comparability of the unadjusted FEV_1 with the ex-miners <65 from the main study group. Had the 199 ex-miners not been included in the one comparison group, perhaps the proportion of cigarette smokers in the study group would have been even more disparate and the FEV_1 might have shown a different pattern. That aside, the main analysis rested with the 199 ex-workers with bronchitis who left and took other work. The authors' table 2 shows an obvious trend by age (at follow-up survey) between FEV_1 and dust exposure -- especially in the older age categories. These trends, however, did not account for smoking. However, the authors' regression treatment of the data does account for smoking as well as region, and the effect of dust exposure for these 199 ex-workers was clearly strong (unit risk = -1.2 ml), with higher statistical significance than other variables considered (their table 3). When the authors utilized exactly the same regression model on the main body of 4,059 workers, the estimate relating to the dust/FEV_1 relationship was confirmed (but more conservatively). Various alterations were made in the smoking variable and regressions re-run. In all instances the coefficients for dust did not differ very much from the original dust coefficient of -1.2 ml per mg/m^3. The data indicated that 35 of the ex-smokers had a rather severe dust effect and the dust regression coefficient in this case was -1.55 ml per unit exposure or -140 ml over a working lifetime compared to -34 ml overall in all 4,059 miners and ex-miners. Among the 199 ex-miners with bronchitis there was a -108 ml loss in FEV_1.

In this study the authors are (implicitly) cautious. They view it as somewhat of a case study of unhealthy miners which indicates that a few cases do show a clinically important effect relating to dust. They say the overall effect is modest and severe declines are likely to be rare.

Atffield and Hodous (1992): "Pulmonary function of U.S. coal miners related to dust exposure estimates." Am Rev Respir Dis 145: 605-609.

This is a sound study methodologically -- except for the exposure estimates which are biased to increase the exposure-response slope of the study group of pre-1970 miners exposed to high and unregulated CMD levels.

This is a cross section analysis of miners from the first round of the NSCWP and the first attempt to use quantitative estimates of exposure in US miners. Of the 9,078 miners examined, the study was restricted to 7,139 miners age 25 or older. This is a sound restriction because of increasing FEV_1 until about age 25. Pulmonary function parameters visited were the FEV_1, FVC, and $FEV_{1/}$ FVC%, but FEV_1 was the primary response variable. Exposures prior to 1970 were estimated by the procedures of Attfield and Morring (Attfield and Morring 1992a). Although the authors did counsel caution and noted some potential problems with the dust estimates, we documented the over- and under-estimates of lower and higher exposures respectively in the section on CWP. The authors note in their estimates of exposure that unknown temporal changes between 1950 and 1970 made it impossible to ascertain if their back extrapolation method was valid.

The authors converted all CMD to gh/m^3 using 1,740 hours worked per year. Basic multiple regression techniques were used with response variables of age, height, smoking status, pack-years, and estimated cumulative dust exposure. They also included terms with and without regional effects. The effects from further models were explored; i.e. separate models for smoking groups, and interaction terms for smoking multiplied by dust exposure. Other models were employed related to the group without CWP and also a sub-set of miners from the 17 mines visited by the Bureau of Mines to gain survey data which were common to the NSCWP mines -- i.e. the mines the BOM used in their 1968-69 dust surveys plus further models mostly dealing with interaction terms.

The authors Figures 1-3 relate FEV_1 to age for low, medium, and high dust categories and for non-smokers, ex-smokers, and current smokers. The effects of age and smoking are obvious and also there appears to be an additional effect for dust -- especially for the non-smokers and ex-smokers. The dust effect for the smokers is not so obvious. For the main model, the regression coefficient for FEV_1 and CMD is -0.69 ml per gh/m^3 (or -0.35 ml in mg/m^3 and 2,000 hours/year) and is highly significant. The basic model was also used to evaluate FVC and the FEV_1/FVC% ratio. Again, a dust effect was seen relating to the FVC (-0.25 ml mg/m^3) and was significant. When the basic model was re-run without adjustments for regional effects, the negative trend became even steeper with dust coefficients of -0.35 and -0.40 ml per mg/m^3 respectively. As noted, region is

correlated highly with type (rank) of coal and adjusting for regional effects could remove some of the effects due to dust exposure in the regression analysis.

The authors estimated that over a 40-year working life under the current 2 mg/m^3 standard, there would be a loss of 2-3 ml/year or a 100 ml loss of FEV_1 due to dust exposure. The calculation seems incorrect. Using the coefficient of -0.35 ml per mg/m^3–year from this study, the loss in FEV_1 associated with 90 mg/m^3-year would average about -28 ml, or about 3.2 ml/year.

The authors indicate a loss of about 5 ml/pack-year among smokers. While a small average loss for smokers, this average hides a more severe chronic effect for a majority of smokers. As the authors themselves questioned "Could it then be that the average decrement of 5 to 9 ml associated with dust exposure also hides some severe dust exposure effects?" A problem is that these data suggest dust exposure produces on average -0.34 ml loss in FEV_1 per mg/m^3. At cumulative exposures of 90 mg/m^3-years, this unit risk suggest total loss in FEV_1 due to dust will be about -31 ml for 45 years, or less than 1 ml/year (= -0.69 ml/year). Thus the estimated effect of smoking 1 pack of cigarettes per day produces about 7 times greater loss in FEV_1 than CMD exposure at 2 mg/m^3.

The author's summarization suggests that for miners working in fairly dusty conditions (e.g. 6 mg/m^3), the dust effect is similar to that seen for smokers. On the basis of the regression coefficients, the dust effects appear substantially less than smoking effects. Notwithstanding limitations relating to exposure, there is a separate and independent dust effect. However, the effect (say at 2 mg/m^3 for 45 years) appears quite minor (-31 ml) compared to 45 years aging (-1,395 ml) and smoking 20 pack-years (-308 ml).

Seixas, Robins, et al. (1993): "Longitudinal and cross sectional analyses of exposure to coal mine dust and pulmonary function in new miners." Brit J Ind Med 50: 929-937.

This is a cohort of 977 US coal miners who began mining 1969 or later and had acceptable spirometry at Rounds 2 and 4. All participants began mining 1-5 years before R1 and 15-18 years before retesting in R4. Tests included spirometry (FEV_1, FVC, FEV_1/FVC%), job and smoking histories, and estimated cumulative coal mine dust exposure based on personal operator samples. Exposure-response results were adjusted for age, height, smoking (category and pack-years), race, mining state (current, ex) and years worked in non-mining dusty occupations. The study design was both cross-sectional (R2 and R4) and longitudinal (changes R2 to R4 counting both pre-and post-1970 exposures).

Mean age at R4 was about 40-years with 39% smokers, 33% ex-smokers and 28% never smokers. Average cumulative exposure was 15.4 (6.2) mg/m^3-yrs, with 3.8 mg/m^3-years for pre-R1 exposures and 11.6 mg/m^3-years occurring between R2-R4. Average exposure during the post-R2 era was 0.92 (0.38) mg/m^3. Percent Predicted FVC was

above 103.7% at R2, with a loss of about -624 ml that reduced FEV_1 to 97.0% predicted at R4. Average FEV_1 was 98.3% at R2 with a loss of about -592 ml and reduction to 92.4% of predicted at R4. Losses were greatest among smokers with similar changes for ex-smokers and never smokers.

The longitudinal (or prospective) analyses was said to perhaps "provide a more sensitive design for the detection of low level effects and for temporal effects of the exposure-response relation." The results unexpectedly showed non-significant increases in FEV_1 in the pre-R2 period when exposures were highest as well as increases during lower exposures between R2 and R4 (unit risk = + 0.7 ml and +2.8 ml per mg/m^3 respectively). There were significant expected decreases associated with age (-4.9 ml per year) and smoking over the same study period. FVC was significantly increased (+1.2 ml per mg/m^3, $p = 0.006$) during the pre-R2 exposure period, and showed a non-significant (-1.8 ml per mg/m^3, $p>0.2$) decrease during R2-R4.

Because of these unexpected findings that are contrary to cross-sectional results from R4 miners (Seixas, Robins, et al. 1992), further cross-sectional analyses were undertaken in this cohort (*see* our Table 1, Figure 1). These cross-sectional results showed FEV_1 was significantly associated with cumulative CMD exposures for both exposure periods; the slope was -27.5 ml per mg/m^3 at R2 and -5.9 ml ($p = 0.03$) at R4. These models showed r^2 values of 0.39 and 0.44 respectively. We note the authors comment these data show that "much of the dust related decline in ventilatory function evident at R4 must have occurred before the start of the longitudinal follow-up period…before R2."

Further Comments on Seixas, Robins, et al. (1993)

Note that the 3 mg/m^3 standard went into effect in 1970 and the 2 mg/m^3 standard in 1973. Pre-R2 data were collected 1972-5, so all or some of pre-R2 exposures would likely be greater than 2 mg/m^3; post-R2 exposures occurred when the 2 mg/m^3 standard was operative.

The cross-sectional data showed overall losses in FEV_1 over the 18 years of this study. These losses are associated with smoking and aging. There is **no** association of reduction in FEV_1 with CMD exposure in the same coal miners as determined in the longitudinal portion of this study. Actually CMD exposure is associated with slight increases in FEV_1 during both the pre-R2 (slope = +0.7 ml (-0.08 to +1.48)) and post-R2 exposure periods (+2.8 ml (-5.2 to +8.29) per mg/m^3 CMD exposure. FVC shows a similar slight increase in pre-R2 (+1.2 ml)) and slight decrease in post-R2 exposure periods (-1.8 ml) (Figures 3, 4).

For some reason the authors used cumulative exposure in the pre-R2 analysis but mean CMD in the post-R2 analysis for the longitudinal portion of this study. This is noted in the methods but the rationale is not provided. Only cumulative exposure is used in cross-sectional analyses for both pre- and post-1970 analyses.

The cross-sectional data show a rapid loss of about -28 ml per mg/m^3 FEV_1 during the one to five year period between 1970 and R2 (1972-5) when exposures were highest and presumably mostly above the current MSHA standard. After R2 the losses in FEV_1 associated with CMD exposure were nearly five-fold smaller (-5.9 ml), but still significant (p =0.03). The authors described the findings at R4 as "although the mean FEV_1 and FVC as a percent of prediction declined (Table 1), no additional loss associated with continued exposure was detected." The meaning of this statement is unclear, as it appears from the data that there were losses for FEV_1 associated with both % predicted and exposure to CMD.

The authors' characterizations of these data are repeated because of the contradictory findings for longitudinal and cross-sectional results, and the lack of clarity and apparent mixing of results we got when reading this paper and trying to understand the data. The distinction between longitudinal and cross-sectional is not readily apparent from their text or tables. [Their Table 2 = longitudinal data, Tables 3 & 4 = cross-sectional data.]

Longitudinal analyses:

- There was a "small but statistically significant increase in FVC and FEV_1 with higher pre-R2 cumulative exposure" [But the authors' Table 2, shows the increase is significant only for FVC (p=0.006) but not FEV_1 (p=0.066).]

- "No statistically significant associations were found between post-R2 average exposure and pulmonary function changes.". [the authors' Table 2 shows -1.8 ml decrease in FVC (p>0.2) and +2.8 ml increase in FEV_1 (p>0.2).]

Cross-sectional analyses:

- Post-R2 analyses showed FEV_1 was associated with cumulative exposure with a loss of -5.9 ml per mg/m^3 (p 933; p=0.03). There was a loss of -2 ml per mg/m^3 for FVC (p>0.2; authors' Table 2).

- Because longitudinal and cross-sectional results were different, as the authors noted, "it seems" much of the cross-sectional decline must have occurred before R2. This is confirmed by the "strong association" and losses of about -27.5 ml per unit cumulative exposure in FEV_1 and -30 ml for FVC during pre-R2 exposures (p. 933).

- There were large losses in lung function pre-R2 largely before federal regulations reduced CMD exposures (cross-sectional results). But the authors stated during post-R2 "mean FEV_1 and FVC as a per cent of predicted declined (table 1), no additional loss associated with continued exposure was detected." Their tables show losses associated with pre- and post-1970 exposures in the cross-sectional analyses, but increases in FEV_1 in both pre- and post-1970 exposures in the longitudinal analyses. This statement is not supported by data reported in tables (p. 934, 1st paragraph in discussion).

• 3rd paragraph of p. 934: The strong associations with CMD and large losses in pre-R2 and smaller declines post-R2 might plausibly be explained, the authors commented , as "a recovery after the initial exposure related decrements. That is, miners with heavy initial dust exposure and pulmonary decrements may have a subsequent recovery or slowing of loss and seem to have a positive pre-R2 exposure to post-R2 change in pulmonary function relations." (These are cross-sectional findings and suggest recovery of FEV_1 occurs at CMD exposures below 2 mg/m^3.)

• 4th paragraph of p. 934: With a standard deviation ("SD") of 32 ml/year for FEV_1, a change of less than 2-3 ml/year can probably not be detected. The source of this statistic is unclear as standard error ("SE") for age ranged from 1.8 to 3 ml/year.

The authors then discuss cross-sectional results only, presumably because only positive changes (or increases in lung function) were associated with longitudinal data at exposures levels above or at the current standard.

The following paragraphs attempt to explain the cross-sectional findings. Several potential biases including selection bias, hyper-reactive airways, greater measurement errors in pre-R2 versus post-R2 exposures were not considered likely to explain the large differences in strength of association between pre- and post-R2 associations. Reversible inflammation was suggested as a possible cause of initial decrements in lung function that were reduced or reversed as dust concentrations declined. But it seems clear inflammation could not be the cause for the inexplicable increased function during the pre-1970 exposure period.

The summary conclusion of the authors is unclear, and is based on cross-sectional results. They suggest CMD concentrations at the current standard "seem to have a substantial effect on pulmonary function" during the initial years of high exposure. For subsequent years when exposure is regulated, loss of lung function continues (as indicated by reductions in % predicted), but the "loss was apparently not related to exposure." But the next sentence appears to contradict the lack of association with CMD, when the authors say "the loss of FEV_1 in relation to exposure to dust persists."

A reason for doing this longitudinal study was because "longitudinal studies may provide a more sensitive design for the detection of low level effects and for examination of temporal aspects of the exposure-response relation." The reader should note that each miner acts as his own control, so that changes are based on actual observations and not on statistical adjustments of different groups at different points in time. For these reasons the longitudinal analyses is considered the better study design providing the most relevant and precise data for assessing exposure-response and cumulative effects of CMD on lung function or COPD. Therefore the longitudinal results in Figure 2 are considered the most reliable, and they indicate no associations between CMD and FEV_1 over the 18 years of this study among relatively new coal miners working mostly below the 2 mg/m^3 standard.

A limitation of the longitudinal analysis is the poor correlation (low r^2 values) indicating much unexplained variability suggesting the models may be unreliable. In a case-control

study of miners followed about 11-years for changes in FEV_1, the potential role of other plausible risk factors other than smoking and age were investigated (Wang, Petsonk, et al. 1999). They found 2+-fold increased risks of clinically important decrements in FEV_1 for miners not using respirators, working as roof bolters, having exposure to shot-firing, and childhood domestic exposure to passive smoke (or environmental tobacco smoke). There was also a regional effect (OR = 1.78). The coefficients from these risk factors were used to estimate declines in FEV_1 extrapolated to 13 years for the average time between R2 and R4. These calculations indicate their combined effect could produce a loss of about -460 ml FEV_1. The mining region effect estimate was a loss of about -12 ml. The average difference in FEV_1 is -460 ml between R2 and R4. Since none of these risk factors were included in the statistical models, much of the unexplained variability in the statistical models used might be explained by these factors alone.

Figure 3

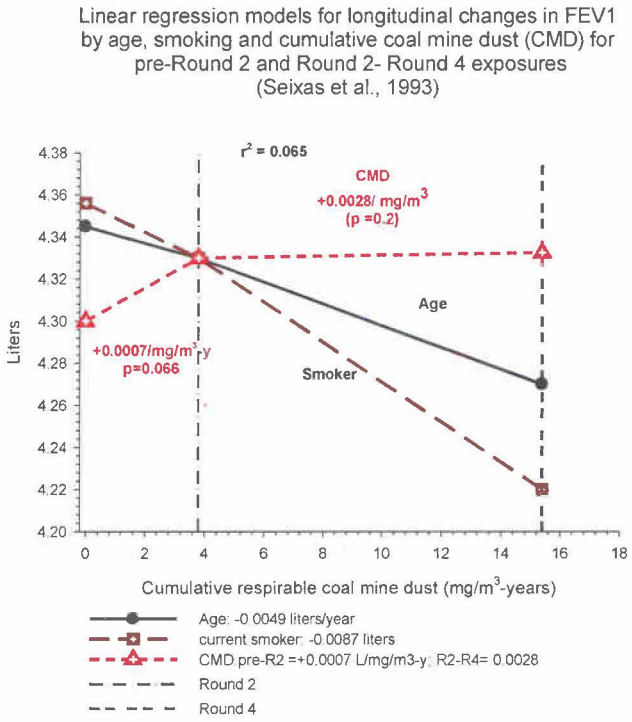
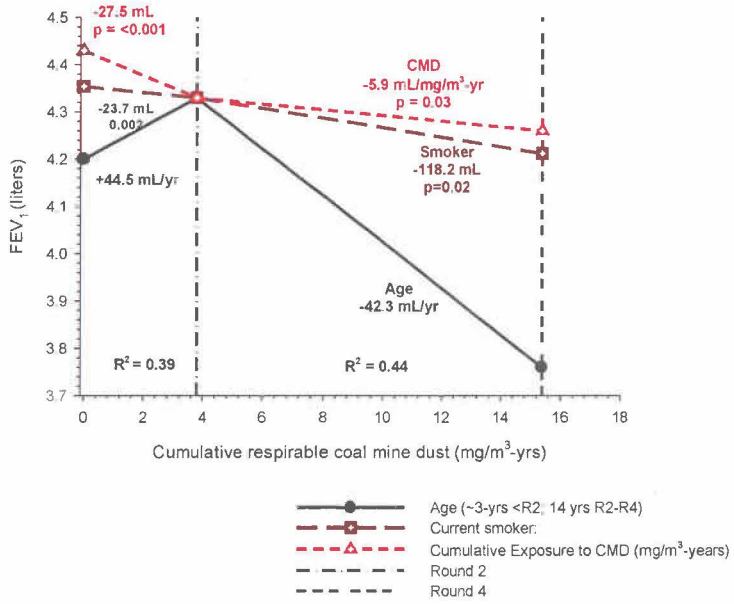


Figure 4

Linear regression models for cross-sectional changes in FEV_1 associated with CMD exposures in pre-Round 2 (3.8 mg/m^3-years) and post-Round 2 (13-15 years R2-R4; (11.6 mg/m^3-years), age and smoking of new miners in NSCWP (Seixas et al., 1993)



Soutar, Campbell, et al. (1993) "Important deficits of lung function in three modern colliery populations with dust exposure." Am Rev Respir Dis 147: 797-803.

This is a cross-sectional study of 1,671 miners and ex-miners who had worked at any of three collieries (South Wales, Yorkshire, Northeast England) between 1970 (time of introduction new coal mine dust standard) and medical surveys conducted from 1981-1986. The 1970 British coal mine dust standard was 8 mg/m^3 at the long-wall face, which was considered equivalent to a colliery-wide concentration of 4.3 mg/m^3. This regulation was introduced in 1970 and became law in 1975; in 1978 it was revised downward to 7 mg/m^3 and colliery mean coal-face concentrations of 3.8 mg/m^3.

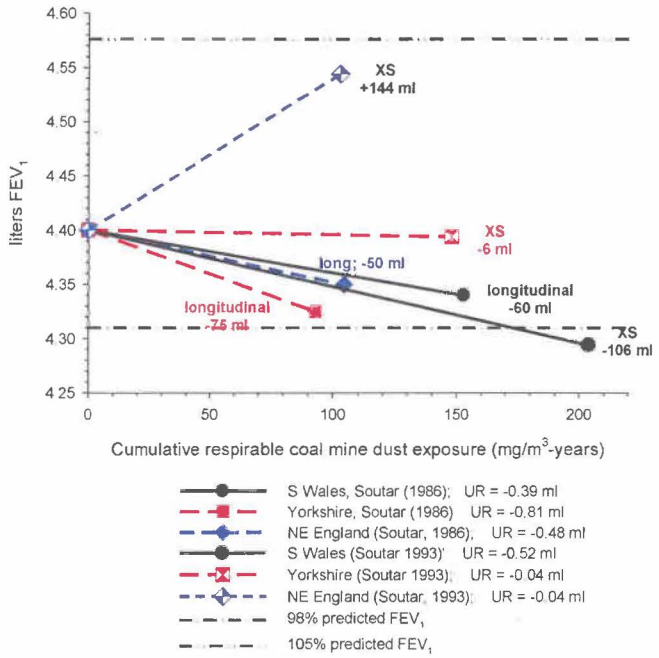
Logistic regression analyses were conducted to assess exposure-response relationships between cumulative CMD exposure and changes in FEV_1 by colliery and with adjustments for height, weight, smoking category, age, and miner/ex-miner status. Because of the lack of associations in Yorkshire and Northeast England collieries, they also compared the associations in the current study with those the same collieries studied in the 1950s and followed for 22 years (Soutar and Hurley 1986). These results are converted to mg/m^3 units and summarized in the following Table and Figure 5.

Regression results in UK for three collieries in UK (Soutar, Campbell, et al,., 1993)

	South Wales	Yorkshire	North East England
22-year follow-up study (Soutar and Hurley 1986)			
Mean cumulative exposure (mg/m^3-yrs)	153	93	104.5
Unit risk (ml change in $FEV_1/mg/m^3$)	-0.39 ml	-0.81 ml	-0.48 ml
Delta FEV_1 @mean cumulative exposure	-59.7 ml	-75.3 ml	-50.2 ml
Delta FEV_1 @ 90 mg/m^3-years)	-35.1	-72.9	-43.2
Current cross-sectional study (Soutar, Campbell et al. 1993)			
Mean cumulative exposure (mg/m^3-yrs)	204	148	103
Unit risk (ml change in $FEV_1/mg/m^3$)	-0.52 ml	-0.04 ml	+1.4 ml
Delta FEV_1 @mean cumulative exposure	-106 ml	-5.9 ml	+144 ml
Delta FEV_1 @ 90 mg/m^3-years)	-46.8 ml	-3.6 ml	+126 ml

Figure 5

Estimated average change in FEV1 associated with cumulative exposure to respirable CMD at average cumulative exposure in 3 collieries (S Wales, Yorkshire, NE England) in a longitudinal study design with pre-1972 exposures (Soutar & Hurley, 1986) and a cross-sectional design with mostly post-1970 CMD exposures (Soutar, Campbell et al., 1993)



These data from both the cross-sectional and longitudinal study designs are analyzed for both pre-1970 and post-1970 exposure periods. They indicate that average cumulative

exposures are well above US standards. Trends are consistently similar with the exception of the Northeast England colliery where FEV_1 values increase with increasing exposure in the cross-sectional analysis. All the prospective trends are negative with FEV_1 decreasing as CMD exposure increases as expected. However, FEV_1 reductions are generally not statistically or clinically significant. Despite high average exposures, mean FEV_1 values are above 98% predicted levels at exposures more than two-fold greater than the US standard.

Data from these two cohorts and exposure-response analyses and after adjustments for known confounders suggest no apparent clinically important declines in FEV_1 performance with regard to group averages.

There is a non-significant negative coefficient for Yorkshire in the current study, but the correlation is 0.81 and the authors indicate the effects of age and coalmine dust exposure cannot be separated. Nevertheless, there is no apparent exposure-response association as the combined effect of both age and CMD variables do not indicate a significant association.

Marine, Gurr, et al. (1988): "Clinically important respiratory effects of dust exposure and smoking in British coal miners." Am Rev Respir Dis 137: 106-112.

This is a cross-sectional study of British coal workers. It involves 3,380 miners from 20 mines in the Pneumoconiosis Field Research ("PFR") who participated in all three of the first three surveys studied over a roughly 10 year period. Workers excluded from the analysis were those over 65 at the third survey, ex-smokers, and those with PMF. Most all of the evaluations were made separately for smokers and non-smokers. The aim of the study was to determine the separate and independent effects of dust exposure and smoking on certain measures of respiratory dysfunction. CMD was determined from the ordinary PFR environmental surveys during the inter-survey periods round one to round three, but estimates prior to round one were reviewed and corrections made to previous estimates. An evaluation of the corrected dust measures was made to ensure that the negative associations of dust on FEV_1 remained (as previously determined). This was performed with new regressions adjusting for the ordinary co-factors and confirmed the negative association, but found it a bit more severe for smokers and non-smokers alike, being -94- and -102-ml losses for every 100 ghm^3 among smokers and non-smokers, respectively. When these are converted to unit risks for a 2,000 hour/year, the estimated losses in FEV_1 are -1.84 ml and -2.04 ml per mg/m^3 for smokers and non-smokers in this study population. There were four clinically important factors that change (often increase) unit risks for smokers, but often decrease unit risk for non-smokers. Unit risks for FEV_1 for four categories of impaired miners are listed for smokers and non-smokers respectively and shown in Figure 6:

- 1) Miners with FEV_1 < 80% predicted: Unit risks are -1.7 ml and -1.5 ml per $mg/m^3$for smokers and non-smokers respectively;

- 2) Miners with bronchitis: Unit risks are -5.1 ml and -2.1 ml per mg/m^3;

•3) Miners with bronchitis and FEV_1 < 80% predicted: Unit risks are -5.39 ml and -2.8 ml per mg/m^3; and

•4) Miners with FEV_1 < 65% predicted: Unit risks are -5.8 ml and -1.3 ml per mg/m^3.

The predicted equations were from an internal group of 451 non-smoking workers without bronchitis. The negative relationship between dust exposure and FEV_1 was shown for this apparently healthy sub-group of subjects for two broad age groups. By admission, the authors indicate that the correlation between age and exposure was fairly high, being over 0.4 for both smokers and non-smokers. The authors imply that the separate effects (aging and exposure) would be "taken care of" via suitable regression techniques, although the ability to totally "untangle" these effects is often questionable. The percentage data from the authors' table 3 show a cross-tabulation of the four measures of pulmonary dysfunction by age and CMD groupings separately for smokers and non-smokers. While a general trend of increases across CMD (gh/m^3) for the four groups with respiratory dysfunction existed for both smokers and non-smokers, it was a consistent trend only on an overall basis for all age groups combined. The trends were clearly not totally consistent by age grouping. Thus, broadly speaking, these data indicate (in a proportionate sense) an overall independent dust effect on indicators of dysfunction.

The more formal evaluation involving logistic regression regarding the prevalence of bronchitis and loss of FEV_1 are shown in relation to age, dust exposure, and smoking status (separately). Where appropriate, interaction terms for age multiplied by dust were included. These analyses (authors' Table 4) demonstrate (as in their table 3 percentages) increased likelihoods of the response to indicators of dysfunction by dust exposure. Nearly all of the coefficients are significantly greater than zero. However, the effect for non-smokers with FEV_1 < 65% predicted did not reach statistical significance. In these health-impaired miners the FEV_1 losses attributed to dust get larger as impairment increases. In smokers, losses for miners with <80% FEV_1, chronic bronchitis, FEV_1 <80% + chronic bronchitis, and FEV_1 <65% had reductions in FEV_1 per mg/m^3 CMD of 1.1, 2.4, 1.9 and 4.5 times greater than losses among non-smokers.

The prevalence of all four measures of pulmonary dysfunction by smoking status at two broad levels of CMD (set at 47 years of age) show increasing proportions of miners with dysfunction as exposure to CMD increases for both smoking categories. The author's Table 5 (partially constructed below), coupled with the tabular data in their Tables 3 and 4, and their probability graph in Figure 2 suggest a significant dust effect on the lung function response parameters. Note that the prevalences are also high for workers with zero exposure.

Prevalence (%) of respiratory dysfunction by smoking status at selected cumulative CMD at age 47-years

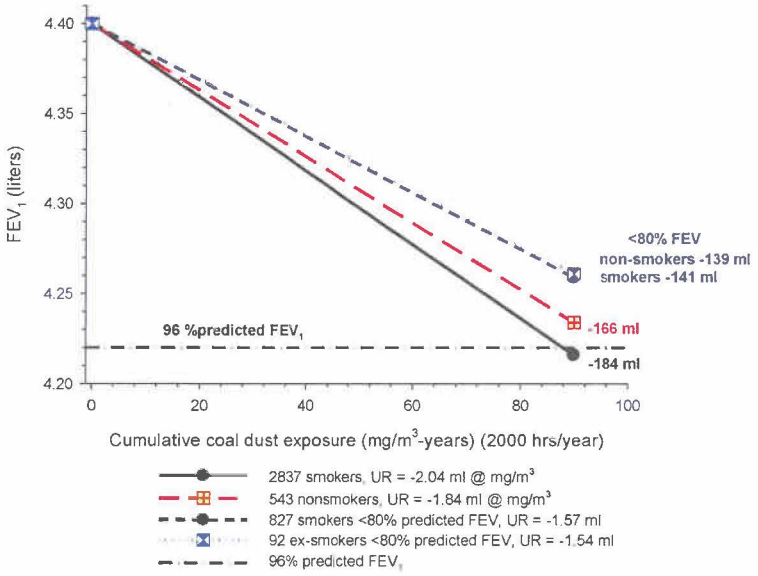
Respiratory dysfunction	Zero Exposure 1740 h/year		Intermediate Exposure ~100 mg/m^3-year ~30-yrs at 3.1-3.7 mg/m^3		High exposure ~200 mg/m^3-year ~30-yr at 6.1-7.2 mg/m^3	
	Smokers	Non-smokers	Smokers	Nonsmokers	Smokers	Non-smokers
FEV_1<80%	17.1%	9.7%	27.2%	15.5%	40.0%	23.9%
FEV_1<65%	5.0%	3.2%	8.5%	5.0%	14.2%	7.7%

These data show about a two-fold greater loss in FEV_1 among smokers than non-smokers. The dust effect is about three-fold greater at high exposures relative to low exposure and is similar for smokers and non-smokers. The smoking and dust effects are similar among these impaired miners as approximated by the formulas where dust effect = [(% in non-smokers at high exposure) (% in non-smokers at 0 exposure) and smoking effect = (% in smokers at 0 exposure). At <80% predicted FEV_1 the smoking vs. dust effect is 17% vs. 14%; for <65% predicted FEV_1 smoking and dust effects are the same at 5% vs. 5%. These data indicate an effect similar to smoking at high dust exposures.

While this is a sound study which is methodologically "tight" and well controlled, there are a few issues which may "mute" the results to some degree. The possibility of selection effects are always troublesome with a working population, but adequately discussed in the article with some clarity. Perhaps the largest concern might be what is noted in the authors' Table 5 where very broad categories of CMD are given, i.e. 87 and 174 mg/m^3-years for an average 47 year old. These are very high levels of CMD, equating to about 3.5 mg/m^3 for the lower level exposures and about 7 mg/m^3 for the higher exposures calculated for 25 years tenure. In the US and in the UK (now), these average cumulative dust concentrations would be considered astoundingly "off the chart" exposures. The proportions shown in this table should be considered in light of the high background prevalences which are observed for those with zero exposure. Also, the true exposures involved may even be higher than calculated, in that some workers were employed 20 to 30 years prior to the first survey and their exposure estimates were extrapolated from estimates obtained between the first and second survey periods of the PFR.

Figure 6

Estimated average loss in FEV1 associated among UK coal miner cohort with all smokers and nonsmokers and impaired smokers and non-smokers with <80% predicted FEV1 and exposed to respirable coal dust exposure of 90 mg/m3-years (= 2 mg/m3 x 45 years)
Marine, Gurr et al., (1988)



Henneberger and Attfield (1996): "Coal mine dust exposure and spirometry in experienced miners." Am J Resp Crit Care Med 153: 1560-1566.

This study was done basically because of the unusual effects noted earlier by Seixas, et al. (new miners) which initially showed declines in pulmonary function followed by at least partial recovery (Seixas, Robins, et al. 1993). The analysis was similar to Seixas, et al., but for experienced miners rather than new miners. Two questions were addressed:

1) What changes in lung function of experienced coal miners are associated with higher exposures before regulation and after government mandated reductions in mine dust levels (pre- and post-1970)?
2) How do the changes in experienced miners compare to those observed in new miners?

The study period and subjects were from rounds one, two, and four of the NSCWP. There were 4,048 miners who participated in R4. Of these, 1,270 were new miners first hired after 1970 and studied by Seixas, et al., but excluded from this study. This left 2,778 miners examined at R4 and also working prior to R1 or R2. Of the 2,778 remaining, 31% (n = 863) were also excluded, some for reasons that seem due to poor field work, interview techniques, or participation. Reasons for these exclusions include:

51 females, 62 with incomplete spirometry, 672 not participating in R1/R2, 30 with incomplete questionnaires, and 42 who had contradictory information regarding work during R1, R2, and R4. This left 1,915 workers for evaluation.

Exposure data prior to R1 were estimated by the usual methods (Attfield and Morring 1992a) that we have demonstrated to be biased so as to produce spuriously steeper exposure-response slopes. Exposures after R1 are taken from the MSHA data base. FEV_1, FVC, and the ratio of the two were evaluated. Three sets of standard linear regression models were utilized, which for the most part mimicked Seixas, et al. The cross-sectional analyses were at R1/R2 and R4. The longitudinal analysis involved differences between R1/R2 and R4.

For the first cross-sectional analysis at R1/R2 there was a non-significant negative coefficient for FEV_1 (unit risk = -0.5 ml per mg/m^3), but a positive one for FVC (unit risk = +0.6 ml per mg/m^3). The FEV_1 results are in the same direction as Seixas, et al., but the decline in FEV_1 among new miners was 55 times greater than among experienced miners (unit risk = -27.5 ml vs. -0.5 ml respectively) despite the much lower exposure for new miners. The differences in FEV_1 are inconsistent with the differences in exposure. Experienced miners were older (50 vs. 40 years), and had more mining experience (average of 10.9 years with maximum of 36 years versus <5-years). These differences are most evident in the ten-fold difference in mean cumulative exposure, 38.5 mg/m^3-years for experienced miners versus 3.8 mg/m^3-years for new miners. This unexpected mismatch between reductions in FEV_1 and CMD exposure are inconsistent with an exposure-response association and are suggestive that other unmeasured factors are affecting these findings.

The second cross-sectional evaluation at R4 showed negative associations of lung function and dust, with unit risk of -1.2 ml per mg/m^3 for FEV_1 and non-significant -0.7 ml for FVC. The negative associations with FEV_1 were stronger among new miners than experienced miners (-5.9 ml versus -1.2 ml per mg/m^3). In this instance exposure occurring between R1/2 and R2 were the same for old and new miners (0.90 and 0.92 mg/m^3 respectively).

There were no statistical differences between pre- and post-1970 unit risks, but it is surprising that the coefficient is 2.4 times larger for exposures <1 mg/m^3 than at pre-1970 exposures >3 mg/m^3 (Henneberger and Attfield 1996). These trends are in the opposite direction from the "rebound" effect hypothesis, and may be suggestive of random variation around no change, or selection effects in the opposite direction of the "healthy effect" hypothesis where the more susceptible, less healthy miners remain in the workforce.

The first longitudinal evaluation for pre R1/R2 exposures showed negative dust associations with unit risks per mg/m^3 = -0.07 ml for FEV_1 and -0.10 ml for FVC. These results for old miners are in the opposite direction observed in new miners who showed a slight improvement in lung function during the high exposure years. These results are directly counter to the hypothesis of greater susceptibility of younger new miners.

However, unit risk for both new and old miners estimated from pre-1970 exposures are similar and are suggestive of essentially zero change (unit risk is +0.7 ml versus -0.07 ml for new and old miners respectively) during these times of high concentrations of CMD.

The second longitudinal assessment between R1/2 and R4 showed no associations of reduced lung function and CMD exposure. Unit risks were +2.0 ml for FEV_1 and +0.4 ml for FVC. Associations with age and smoking remained strong and negative as usual. These findings are similar to those for new miners, both showing improvement in FEV_1 of +2-3 ml per mg/m^3. (*See* our Table 2, Figure 2)

In summary, results from cross-sectional studies for new miners indicated that at high pre-1970 exposure levels there is a strong negative association with large declines in FEV_1, and smaller but significant losses at lower exposures (Seixas, Robins et al. 1993). Among older miners the findings are dissimilar as associations are non-existent (-0.5 ml) and weak (-1.2 ml) at low post-1970 exposures and high pre-1970 exposures respectively. Another way of saying this is that there were strong negative associations among new miners, and no associations among older miners in the cross-sectional studies.

The longitudinal data are surprising in that there are no association of reduced FEV_1 during either high exposure periods or low exposure periods in both studies (Seixas, Robins, et al. 1993; Henneberger and Attfield 1996) (*See* our Table 2 and Figure 2).

Carta, Aru, et al. (1996): "Dust exposure, respiratory symptoms, and longitudinal decline in lung function in young coal miners." Occup Environ Med 53: 312-319.

This is another study with both cross-sectional and longitudinal study designs. The cohort consists of new miners in Sardinia employed 1977-1993. Initial exposures began when lignite and brown coal mines were first opened in 1977.

The cross-sectional data indicate significant association between reduced FEV_1 and CMD, but the data (coefficients) are not shown. This study is discussed in the section on longitudinal studies.

Naidoo, Robins, et al. (2005): Differential respirable dust related lung function effects between current and former South African coal miners." Int Arch Occup Environ Health 78(4): 293-302.

This cross-sectional study had two aims: 1) to determine exposure-response relationships among current and former miners, and 2) to examine the dust-related relationships controlling for smoking and a history of tuberculosis ("TB"). From a sample of 900 likely black participants, 684 current miners and 188 former miners were selected from three mines. All workers were interviewed regarding their job history and company records were extracted relating to the duration, job, and seam worked at the mine in question. Apparently, several sources of data were used in determining worker exposure,

including historic dust sampling data available at the mine site. While not stated specifically, onsite sampling was performed to augment existing data. Cumulative exposure was calculated for each worker in mg/m^3-years. The primary health variables evaluated were percent predicted FEV_1 and FVC and the primary exposure variable was CMD. Ordinary co-variates such as smoking and work status were considered plus a history of TB and a host of interaction terms used in the regression analyses. The cumulative exposure index ("CMD") was sub-divided in three exposure categories of low, medium, and high mg/m^3-years.

It was clear that the former miners in the high exposure category had lower % predicted FEV_1 values than those in the medium exposed group and low exposure categories. There was no apparent exposure-response trend for miners, and all mean % predicted FEV_1 values were above 100% (the authors' Figure 1a). For the former miners, there appeared to be a large difference in lung function at high and low exposures, but the differences were not significant owing to the small number of former miner participants in the low exposure category. The coefficients in the authors' table 4 show significant associations with CMD and a history of TB.

The positive effects of being a current miner and current smoker (and negative effect of ex-smoking) may indicate the healthy worker syndrome. Regarding the CMD/lung function relationships, the regression evaluations definitely show a dramatic difference for both FEV_1 and FVC between the current and former miners, with former miners showing around twice the reduction in FEV_1 as current miners.

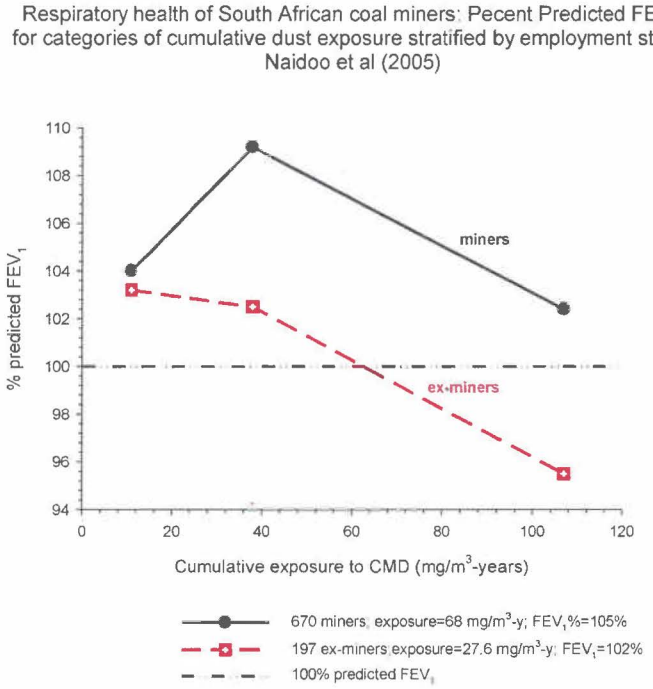
Former miners also showed more serious declines in the FEV_1 predicted values than current miners with nearly 6% of the former miners having <65% predicted compared to around 3% of current miners. While the major health outcome variables were percent predicted FEV_1 and FVC, the authors converted these values to absolute values for a 40 year old worker and found a -1.1 ml decline per mg/m^3 for FEV_1 among current workers and a -2.2 ml decline per mg/m^3 for former miners. Note that just small percentages of current and former miners showed marked reductions, which might have clinical importance. Moreover, a goodly amount of the decline was due to a past history of TB.

These were nicely done and well controlled analyses which show some overall and sub-group relationships between CMD and losses of lung function, while controlling for various extraneous factors, especially amongst ex-miners. These data seems to "track" well with other cross-sectional studies with an admitted limitation regarding lack of comparable information from prospective evaluations.

These data based on % predicted values are shown in our Figure 7 (below) for miners and former miners, and show the greater loss of lung function among the former miners. There is no exposure-response association for miners as the middle exposure category has the highest risk while low and high exposure groups have similar values. The regression analysis using % predicted metrics indicates negative and straight slopes, a function of the regression model.

UR for FEV_1 & CMD	Loss in %predicted FEV_1 after 90 mg/m^3-years exposure	Sub-groups studied
-0.036 % predict -0.033 % predict -0.065% predict	-3.24 % predicted -2.97 % predicted -5.85 % predicted	857 miners & former - miners (Table 4) 670 current miners (Table 5) 197 Former-miners (Table 5)

Figure 7



Cowie, Miller, et al. (2006): Dust related risks of clinically relevant lung functional deficits." Occup Environ Med 63: 320-325.

Data are from the PFR in the UK for the fifth round of exams conducted in the late 1970's. The study group involved 7,188 workers from nine mines who had a high prevalence of chronic bronchitis (31%), and 7% prevalence of simple CWP. The major aim of the study was to determine CMD-related risks of clinically relevant lung functional deficits. Standard questionnaire data on miner characteristics, symptoms, smoking, and work history were collected in all PFR surveys. A key symptom for this study is breathlessness, as taken from the questionnaire. CMD exposures up to the time

of the fifth survey were determined from PFR dust measures which were part of the original PFR study design. However, some estimation was made for workers employed prior to the PFR (early 1950s), and their exposures were assumed equal to that measured in the first ten years of the PFR. Observed FEV_1 among the miners was compared to predicted values determined from an internal group of asymptomatic non-smokers adjusted for age and height. Apparently, factors for determining these predictions did not consider CWP, dust, mine, or any factor other than age and height. These predictions were used rather than those from the European Coal and Steel Community values. FEV_1 was standardized by using the observed FEV_1 minus the predicted FEV_1.

Relationship between breathlessness and FEV_1 were expressed as odds ratios and used to determine levels of FEV_1 that might represent clinically important deficits, which were based on the odds of reporting breathlessness at certain levels of FEV_1. The authors choose three levels of dyspnea; losses of 0.367 liters with an odds ratio of 1.5; -0.627 liters with an odds ratio of two, and -0.993 liters with an odds ratio of three. This procedure is a bit unclear in that the levels and ratios are not presented in tabular form from analyses and it is not clear why these levels were chosen by the authors. By calculating (from regression) the estimated FEV_1 x CMD (adjusted for age and smoking), probability estimates were made that an individual would have an FEV_1 below the specified levels.

Not all workers had satisfactory lung function maneuvers, but all were included in the analyses as it was felt that excluding workers who could not perform well would result in a loss of (presumably ill workers) men of particular interest. But inclusion of spirometry results that do not meet criteria for inclusion (such as inability to take a full breath or less than maximum exhalation) will reduce the average performances and potentially bias results. Only 18% reported having shortness of breath ("SOB") while 31% reported having bronchitis. A relationship between breathlessness and FEV_1 was clearly observed in the study. The logistic regression relating to breathlessness and smoking were clearly significant relative to non-smokers, but the odds were barely significant for FEV_1 per 100 ml decline. The important deficits (noted above) were subtracted from individual predicted FEV_1's (adjusted for age and average height) to obtain absolute levels of FEV_1 whereby probabilities of dust related effects could be obtained.

These FEV_1 values are noted in the authors' Table 2, which shows the coefficients for the regression model of lung function in relation to age and dust. Per gh/m^3 of exposure, the average deficit in FEV_1 is -0.63 ml (statistically significant), or -0.32 ml per mg/m^3. All of the above noted evaluations lead to the pertinent "bottom line" calculations which are contained as probabilities (the authors' Figure 2 and illustrated as an example in their Table 4).

The authors' Figure 2 indicates the probability (the estimated percentage of the study group with FEV_1 below the small, medium, and high levels noted above) of relevant deficits of FEV_1 x CMD, separately for age categories and smoking status. The probabilities by various CMD in gh/m^3 are difficult to determine graphically and also

difficult to compare them by age group, smoking status, and level of deficit. However, the data in the authors' table 4 are very clear showing precise estimates of the percentage of miners with values less than predicted (i.e. by average lifetime (35 year) dust concentration multiplied by smoking status for a 60-year old worker).

For non-smokers the probability of a small deficit of 0.367 liters FEV_1 at 2 mg/m^3 is 41% at zero exposure, 44% at 1 mg/m^3, and 47% at 2 mg/m^3 (or cumulative exposures of 0, 35, and 70 mg/m^3-years respectively). This is about a 7% differential between 2 and 0 mg/m^3 exposures levels. The proportions of current smokers with these deficits are 62%, 64%, and 67% respectively, or a differential of 5% at 0, 1, and 3 mg/m^3. Perhaps most relevant is that increases of 1 mg/m^3 average exposure are associated with about 1.5% to 2.5% increased prevalences of FEV_1 deficits as exposure increases going from zero to 2 mg/m^3.

The authors compare the predicted effects for a 60-year smoker using these probability data. At an average lifetime exposure of 4 mg/m^3 there is a 54% probability of a medium deficit (-627 ml) of which 9.3% is estimated to be related to dust, 20% related to smoking, and 21% related to background.

This is a well-designed study employing a new strategy for interpreting the data based on probabilities of small, medium and large deficits in FEV_1 at different exposure levels. After removing background effects, the probabilities of deficits increase from 0 to 1 mg/m^3 and 0 to 2 mg/m^3 by 2.8% and 5.4% for a 60-year old non-smoker with a 35 year working life. Probabilities for a smoker are essentially the same as non-smokers with probabilities of 2.7% and 5.1% respectively, although background probabilities for smokers are 20% higher than non-smokers (41.3% and 61.5%).

The high prevalences of clinically significant losses in FEV_1 among these miners is not expected, and especially so at zero or background exposure levels.

b. Longitudinal Studies

Love and Miller (1982): "Longitudinal study of lung function in coal-miners." Thorax 37: 193-197.

This is a longitudinal study with the objective to re-examine earlier cross-sectional findings (Rogan, Atffield, et al. 1973) showing reductions in FEV_1 related to CMD exposure in excess of that attributable to age and smoking. Cross-sectional study designs are limited in that measurements are made on different individuals at the same time, so any inference "concerning loss of FEV_1 can therefore only be indirect." Since longitudinal studies directly measure lung function and exposure in the same individuals over time (10-12-years in this study), inferences about loss of FEV_1 are based on direct observations.

Three medical surveys measured FEV_1, FVC, symptoms and smoking from 1957-1973 in five collieries in the UK. Both work histories and coal mine respirable dust measurements were also collected over this same period. Cumulative exposures were estimated from these data and assuming prior conditions were similar.

Participation was >95% at all collieries with 6,191 miners attending. Miners under 30-years or with PMF were excluded, leaving 1,677 (27%) miners in the study population. The prevalence of current smokers was 66%, with 13% non-smokers, 4.6% ex-smokers, and 16% intermittent smokers.

Multiple linear regressions were run to estimate changes in FEV_1 assessing effects of age, height, smoking, mine, concurrent (during surveys) and past exposures. Losses in FEV_1 were associated with increasing age, height and smoking, with similar and greater losses for intermittent and current smokers compared to non-smokers; ex-smokers were intermediate. Mean cumulative past exposure was 2.5 times greater than concurrent exposures and was significantly associated with losses in FEV_1 (unit risk is -0.18 ml per mg/m^3) but was not associated with concurrent exposures when colliery differences were adjusted for (unit risk is -0.70 ml per mg/m^3).

Comments on Love and Miller (1982)

The best fitting multiple regression models never explain more than 7% of the total variation in the data. Suspects for the cause of this high amount of variability include measurement error and short-term variability from such factors as temporary illness, circadian changes, and variations in effort and technique. If the regression is not significant, then none of the variables in the model should be considered significant or important.

It may be that high unexplained variability is a feature of longitudinal analyses, as the authors cite other longitudinal studies with large unexplained variability.

Another limitation of longitudinal studies is the high dropout rate, which was more than a third and may be high enough to limit inferences from this study. A follow-up study of non-participants if completed may ameliorate this limitation.

There was a statistically significant loss in FEV_1 associated with *previous* CMD exposure at an average of -0.18 ml per mg/m^3. [This estimate is calculated from the published results on the assumption the miner works 2,000 hours per year.] The average *previous* exposure was said to be 117 gh/m^3 (or about 5.32 mg/m^3) in their Table 5, but it is unclear whether this is previous exposure or whether it is the average over the 11-year follow-up period. If the latter it would be concurrent exposure. Whatever the correct exposure time is, the predicted loss is -42 ml FEV_1 over 11-years, or a loss of -3.8 ml FEV_1 per year.

There was *no* association with *concurrent* dust exposure when adjustments are made for colliery differences. Maximum likely *concurrent* exposure is about 11 mg/m^3. This

evidence shows that at exposures 2.65 times the US standard there is a statistically significant loss, but not significant clinical loss, in FEV_1. Mean CMD exposures at the level of the current US standard showed no apparent association with FEV_1.

At this point, the data results become confusing in this paper. Predicted results from *concurrent* CMD exposures (11-years of follow-up) refer back to the authors' Tables 4 and 5. But coefficients presented in these tables appear to be for *previous* exposures of 117 gh/m^3 as discussed in the 2nd paragraph above. There appear to be no coefficients or exposures presented for *concurrent* exposures. The data in the authors' Table 3 suggest *concurrent* exposures are about 40% those of *previous* CMD exposures.

Our interpretation of these results suggest a threshold effect such that below some coal mine dust exposure level there is no significant loss of FEV_1. It also suggests that cross-sectional studies may be useful in assessing coal mine dust and FEV_1 losses (or COPD), as the results of this longitudinal analyses were similar to such cross-sectional surveys in this population of coal miners (Rogan, Attfield, et al. 1973).

Concurrent exposures were during five medical surveys over the period from 1957-1973. The current UK standard is 3.8 mg/m^3 (CDC 1995) so these data suggest no association of reduced FEV_1 below that exposure level.

Soutar, C. and J. Hurley (1986): "Relation between dust exposure and lung function in miners and ex-miners." Brit J Ind Med 43: 307-320.

This study had two aims:

1) Confirm previous findings of associations between coal mine dust and lung function with a more representative group, improve exposure estimates, and provide additional measures of lung function.
2) Determine if former miners had different lung function and a different response to coal mine dust than current miners. This required a consistent finding in subgroups showing more severe effects than average.

This is one of the most comprehensive studies relating to CMD exposure and changes in FEV_1. The two major aims of the study have clearly been satisfied. The study population is a sample of 1,867 current British coal workers and 2,192 former miners out of a total of 17,738 miners from 24 collieries examined beginning in the 1950s and followed for 22 years. This is a 77% drop-out rate due largely to death. Thus, lung function and cumulative exposure were evaluated for miners still working and for former miners. This latter group was divided into those <65 and those >65 years of age. There was ample division of information according to cigarette smoking and for those with and without bronchitis (and even further sub-groups). The various sub-groups evaluated were numerous and in all cases, extraneous effects were accounted for in their evaluation.

The overall association of FEV_1 with dust showed losses of -34 ml overall at 90 mg/m^3-year cumulative exposure. The loss was greatest for ex-smokers (-41.9 ml), intermediate

for non-smokers (-40.5 ml) and least for smokers (-29.3 ml). The authors offered no opinion as to why smokers had the smallest losses in FEV_1.

Ex-miners <65 years of age showed the strongest association with dust exposure (-0.445 ml per mg/m^3), ex-miners >65 years the next strongest association (-0.37 ml) and current miners the weakest association (-0.34 per mg/m^3).

On balance, this study demonstrates a clear relationship between decrements in pulmonary function and cumulative dust exposure. The relationship is likely a causative one -- as all of the known extraneous factors have been considered in the analyses. Whether or not the changes seen are of a magnitude leading to disability is questionable, and the clinical importance of the reductions in FEV_1 at concentrations below the lower US standard are not demonstrated by the small overall average reductions of less than -42 ml of FEV_1 over a working lifetime.

Atffield (1985): "Longitudinal decline in FEV_1 in United States coalminers." Thorax 40: 132-137.

The analysis presented in this study is similar to Love and Miller (Love and Miller 1982) as an objective of this study was to determine whether the findings from British mines are relevant to the US experience.

The data source is NSCWP rounds one and three (a nine year interval) from 24 mines involving (originally) 1,470 workers common to both rounds out of 9,078 in the first round. Participation was poor after the first round. Decline in FEV_1 was assessed over the survey time interval of nine years. Dust exposures were constructed from the MSHA database used for compliance purposes. For comparison purposes with the Love and Miller 1982 data, the "delta" FEV_1 values were standardized to an 11 year interval by the formula [(1^{st} FEV_1 - last FEV_1) x (11 years) / 9 years (between surveys)].

The original cohort of 1,470 was restricted to 1,161 miners age 20-49 to remove differences between "stayers" and "leavers," thereby allowing "extrapolation to miners other than those in the stayers group." With these age restrictions there were no notable differences between the groups on demographic, health, or exposure variables (except leavers worked primarily pre-1970 and stayers primarily post-1970). Similarity in "leavers" and "stayers" reduces the likelihood of selection bias because of systemic exodus of miners, such as those with poorer health. The number was further restricted to 1,072 miners by excluding miners from three mines where <10 survivors existed or where there were missing pulmonary function maneuvers. While this group (1,072) was used in the initial evaluation, there was a further restriction reducing the usable number of workers to 957 for the evaluations regarding exposure-response estimates. Thus, the evaluation relates strictly to a survivor group, although as indicated extrapolation may be valid to leavers (or ex-miners).

The characteristics of the main study group are given in the authors' table 2 and appear to be unremarkable. The 11 year adjusted changes (first to third survey) in FEV_1 by smoking and age are shown in the authors' Table 3 and reveal nothing new -- older workers and smokers had larger declines FEV_1.

Four separate regressions were run depending each time on the inclusion of a different exposure-related variable. Other co-factors considered were similar to what had been used previously (Love and Miller 1982). The four exposure indices and exposure coefficients for delta FEV_1 were:

1) -- Inter-survey work underground (years): -3.4 ml /year (p=0.29)
2) -- Inter-survey work at face (years): -7.3 ml / year at face (p=0.01)
3) -- Inter-survey dust concentrations (mg/m^3): -28 ml / mg/m^3 between 1st and last FEV_1, (p = 0.12)
4) -- Prior tenure underground (years): -2.4 ml / years UG pre-1970 (p = 0.15)

The significance of the coefficients is mixed. Age, height, mine, and smoking were consistently and significantly associated with reductions in FEV_1, while the only significant exposure variable was inter-survey work at the face. Nonetheless, the equations from the authors' Table 4 were used to obtain predicted declines in FEV_1 for dust exposure and smoking. For smoking, the excess reduction over an 11 year period was around -100 ml, while for dust exposure the reductions varied between -36 and -84 ml. Note that for model two (with a significant coefficient for dust) the predicted decline was -80 ml, while for smokers the decline was -96 ml and was always greater than for other indicators of exposure.

The calculated losses in FEV_1 and coefficients for work and exposure do not appear to agree with the authors' comment in the last paragraph before the discussion that "work in coal mining or dust exposure was variously estimated at levels from 0.036 to 0.084 l" as indicated in FEV_1 deficits calculated from their Table 4:

- Inter-survey underground work: (mean years = 9) x -0.3.4 ml per year = -30.6 ml loss in FEV_1 (p =0.29);

- Inter-survey at face: (mean years = 3) x -7.3 ml per year = -21.9 ml loss in FEV_1 (p =0.01);

- UG work before initial survey: (mean years = 11) x -2.4 ml per year = -26.4 ml loss in FEV_1 (p = 0.15);

- Inter-survey concentration (mean mg/m^3 = 1.2) x -28 ml per mg/m^3 = -33.6 ml loss in FEV_1 (p = 0.12).

The authors' Table 5 shows predicted average effect of dust exposure over an 11-year period that was calculated from unit risks shown in Table 4. The predicted decline in FEV_1 was calculated to be -56 ml associated with exposure of 2 mg/m^3 for 11-years.

This association is reduced to a unit risk as follows: FEV_1 loss is -56 ml at 2 mg/m^3 x 11-years; or -56 ml at 22 mg/m^3-years; or -2.55 ml per mg/m^3. The coefficient in Table 4 is 11-fold greater than the calculated unit risk. We suggest the coefficient is a typo as this large a value would surely be statistically significant, which it is not. The calculated unit risk of -2.55 ml is more consistent with the declines associated with years worked and the statistically non-significant p-value of 0.12. This calculated unit risk is the value used in our Table 2 and Figure 2 in the summary of results.

The author suggests there is a similarity in results with regard to "general decline in FEV_1 standardized to 11 years", age specific FEV_1 changes, and smoking effects in the study of Love and Miller.

However, the associations of FEV_1 and CMD in this study do **not** mirror the unit risk of Love and Miller (Love and Miller 1982). The -28 ml unit risk standardized to 11 years (Atffield 1985) is 155 times greater than that of Love and Miller (-28 ml versus -0.18 ml). The calculated age-specific unit risk for FEV_1 is 11 times greater (-2.55 ml versus -0.18 ml). Exposures are also dissimilar, with an average exposure for men at each colliery of 47.2 gh/m^3 (or 23.6 mg/m3 for a 2000 hour/year). If this average is for the 14-year follow-up period, the un-weighted average exposure is 2.1 mg/m^3 in Love and Miller, while it is 1.2 mg/m^3 in the Attfield study.

Thus, the US data show larger declines in FEV_1 and lower coal mine dust exposures (Atffield 1985) relative to the similar study in the UK (Love and Miller 1982).

The author discusses potential biases and limitations and cites differences and agreements with the comparison with the Love and Miller evaluation. The results from this study are limited in scope and nothing much new is learned from the evaluations made. There appears to be little of clinical importance in the reductions of FEV_1 across the adjusted 11 year period. Methodologically speaking, this is a well-designed study using data with limitations (dust and otherwise) which was available, but providing meager results.

Carta, Aru, et al. (1996): "Dust exposure, respiratory symptoms, and longitudinal decline in lung function in young coal miners." Occup Environ Med 53: 312-319.

This was a somewhat difficult study to evaluate in that parts of it were cross-sectional while a portion dealt with yearly decline. The health indicators of interest were respiratory symptoms, and lung function parameters FVC, FEV_1, expiratory flow rates at 25% and 50% of FVC, and the CO transfer factor. Over 900 miners were evaluated between 1983 and 1993 at seven different survey periods. Most were newly hired and survey periods and participants relative to the total work force can be seen in the authors' Figure 1. The above noted health indicators were compared with past and current exposures to respirable coal mine dust. There did appear to be good control regarding health examinations as they were performed in the same manner at the same location by the same staff. The issue is not totally clear regarding results from 193 non-

symptomatic, non-smoking miners who were not exposed to dust or fumes (prior to being hired) and who had higher than expected lung function relative to predicted normal. Apparently, they served (in part) as an internal reference group whereby their residual standard deviations for age and height were applied, and standardized residuals (observed - expected) were obtained for each member of the cohort for all lung function parameters. While this is not totally clear, it is clear that annual decline in each functional parameter was obtained at each survey period and compared to those from the previous period and expressed as either increments or decrements.

During the study period, the mean respirable dust concentrations varied considerably between 1.73 and 3.05 mg/m^3 at the face, but elsewhere were somewhat constant at less than 1.0 mg/m^3. Details of mg/m^3-years prior to the first survey and during the follow-up period are outlined on pg. 315. Details of the smoking and CMD effect on both lung function and symptoms are contained in the authors' Figures 2A and 2B. All are adjusted for age, height and smoking. Exposure-response involved tertiles of exposure and associations were weaker for symptoms than for lung function parameters. It is unclear in either of these illustrations that the effects of dust (in Figure 2A) and the effects of smoking (in Figure 2B) have been neutralized. In the cross-sectional analysis, the lower bound of all odds ratios relating to symptoms vs. dust percentiles does not encompass unity. While interesting, clearly the odds ratios relating the 75th percentile (3.74 mg/m^3-years) for all symptoms indicate exposure-response trend. The authors' Table 4 included only significant variables affecting annual declines in pulmonary function parameters.

As has been noted in other studies, the amount of unexplained variation in the regression results is very high. Nonetheless, after allowing for the effect of other variables, there remained an annual effect of CMD during follow-up on the FVC, FEV_1, and CO transfer factor. The regression results in the authors' Table 5 for absolute changes in lung function at follow-up show consistent negative coefficients for all lung function parameters. An attempt was made in this review to duplicate, confirm, or reconcile the ratios between smoking and dust (during the longitudinal evaluation) but was not successful. Nonetheless, FEV_1/FVC% is consistent with other studies indicating (not proving as these authors indicate) a different pathological response (obstruction) for cigarette smokers. The odds ratios shown in the authors' Table 6 provide added strength to the finding that annual exposure is a good predictor of symptoms after adjusting for extraneous factors. It does not appear in this study that the effects of dust on lung function are great, but negative coefficients exist in most instances. Smoking is the most important exposure variable but moderate dust exposure also produces an effect.

This was a difficult and somewhat complex article to review and evaluate. Convincing evidence exists that CMD does have an effect (as the data show). But the magnitude of the effect seems minor and possibly of small clinical importance. Whether CMD exposure leads to permanent disability and premature death cannot be determined from this study.

Morfeld, Noll, et al. (2010): "Effect of dust exposure and nitrogen oxides on lung function parameters of German coalminers: a longitudinal study applying GEE regression 1974–1998." Int Arch Occup Environ Health 83: 357-371.

This longitudinal study was conducted from 1974 to 1998 at two German mines for newly hired workers in the period 1974-1979. There were 1,369 miners evaluated who, on average had nine measurements of lung function during the follow-up period. These new hires were free of prior dust exposure and were relatively young. Around 90% were below the age of 25 when hired, but lung growth up to about 25 years was adjusted for in the analysis. The major outcome variables of concern were the FVC, FEV_1, and ratio of the two relative to their percent predicted values. NO and NO_2 were also of concern because of blasting and diesel vehicle use. Exposure data were collected throughout the length of the evaluation. The German exposure limit for respirable coal mine dust was 4 mg/m^3. However, on average, exposures at the two mines in question were quite low (the authors' Figure 1). While details of the exposures are stated in the body of the article, Figure 1 indicates that from about 1975 to 1986, levels were between 2 and 2.5 mg/m^3, and thereafter until after 1995 were below 2 mg/m^3. Overall, the average dust concentrations were 1.89 mg/m^3 but varied a bit by mine, from 2.10 mg/m^3 for one mine to 1.67 mg/m^3 for the other. Respirable quartz was around 0.067 mg/m^3 and also varied by mine.

A major limitation in the study is the use of different spirometers and staff that were used at different survey times. This limitation was realized by the authors and attempts were made to adjust for these factors in regression. While dust exposures were relatively low, the relationship between dust and the pulmonary function parameters may not even have been needed (using various regression techniques) when one sees the values as a percent predicted between the first and last examination period. For example:

	FEV_1	$FEV_1/FVC\%$
First exam	106%	101%
Last exam	101%	99%

While these percentages seem to "speak for themselves", one must bear in mind that some confounding exists for workers <25 years when lungs are still developing.

Several regression models were employed; the first one mimicked the work of Rogan, et al. and showed negative coefficients for non-quartz respirable dust. This model, however, did not consider important extraneous co-variables. This issue was remedied in three different regression models (B1, B2, and B3). While exposure to non-quartz respirable dust since 1992 indicated a negative coefficient after controlling for co-factors, CMD was clearly a minor and non-significant factor in this study. Prior to 1992, the coefficient was positive but again non-significant. As expected, coefficients for the ordinary co-factors most often considered in regression were negative, i.e. age, weight,

smoking etc....some being significant and some not. Further regressions for the entire time period 1974-98 and for workers below 25 years of age were also performed, but these results added little to the overall picture.

In the concluding paragraph the authors suggest these results provide no basis for lowering the maximum coal mine dust standard of 4 mg/m ^{3}. While negligible effects were shown for oxides of nitrogen, all were minor and non-significant. Very minor negative changes occurred in all three lung function parameters, but they were clearly non-significant.

A fairly detailed longitudinal evaluation was conducted on this group of miners with no-to-negligible past respirable dust exposure. These data do not confirm results reported by others. Adjustments were made for still developing lung function of young workers and possible bias from use of different spirometers and staff at various times, and these factors may impinge on the results to some degree. Overall, this is a completely negative study relating to the effects of dust on lung function.

Wang, Wu, et al. (2005): "A prospective cohort study among new Chinese coal miners: the early pattern of lung function change." Occup Environ Med 62: 800-805.

This study involved 317 new Chinese miners and 132 unexposed referents enrolled in a mining technical school. Pre-employment exams included a questionnaire and spirometry conducted prospectively over three years with 15 medical surveys.

There were large age and smoking history differences between miners and controls with miners being older (22.3 years vs. 17.5 years) and having more smokers. None of the controls were smokers compared to 43% smokers and 1% ex-smokers among miners. Dust exposures were astoundingly high as two-thirds of the sampled exposures were four times the 2 mg/m^3 standard. Average exposures were 9 mg/m^3 respirable and 24 mg/m^3 total dust; 75th percentile exposures were 3.7 and 10.7 with maximums of 79 and 186 mg/m^3 respectively.

There was a small group of 30 non-smoking miners less than 20-years who were comparable to the controls. These miners showed yearly declines in FEV_1 of -22 ml compared to controls with an increase of +160 ml/year. The increases were linear, but the miners decreases in FEV_1 were not linear showing relatively sharp declines in the first year of mining, a plateau the second year, and partial recovery the third year. There were significant tenure trends associated with changes in FEV_1, but "a dose response relation...was not clearly observed." The mixed effects model showed a non-significant loss of -200 ml/ year ($p = 0.30$) for FEV_1.

The linear upward trend among controls is not unusual as they were young and the lung function patterns were still developing with peak performance being attained somewhere in the 20's. That smoking miners lost more function than the non-smokers is not

unusual. What is observed is possible CMD effect on the miners but no clear exposure-response association despite the very high CMD exposures.

Comment on Wang, Wu, et al. (2005)

This is an interesting article but it adds little to the issue at hand. Negative coefficients are to be expected given the very high dust levels to which the miners were exposed. Early in their exposure history, miners may experience decreases in lung function (FEV_1) and we agree with the authors' suggestion that it might be important to know about these early changes. But caution is advised in interpreting these early declines, and linear projections based in the first two years of exposures are likely to be inaccurate. Other studies have shown results similar to this study with very early declines in the FEV_1 and then upward changes and a tapering off effect (Hodous and Hankinson 1988; Seixas, Robins, et al. 1993).

Limitations include a short length of follow-up (which is ameliorated somewhat by the frequent surveys), not entirely comparable controls, excessive temperature variations during spirometry, and CMD exposures well above 2 mg/m^3. Thus, this study is of limited value.

c. Summaries of Individual Studies without Exposure-Response Analysis

Yang and Lin (2009): "Airway Function and Respiratory Resistance in Taiwanese Coal Workers with Simple Pneumoconiosis." Chang Gung Med J 32: 438-446.

This study involved 71 miners with CWP and 36 business men and students as controls who were given a battery of tests regarding airways limitations that included a rather non-standard test for respiratory resistance. Nothing very remarkable was shown. The major parameters measured showed no difference in the FVC between controls and even miners with category 2 and 3 CWP. The same was true for the FEV_1 but limited to miners with category 1 CWP. However, there appeared to be a slight decrease in the FEV_1 for miners with more advanced CWP (categories 2 and 3). The FEV_1/FVC ratio was decreased for this latter group (below 70%) for both smokers and non-smokers. The reduced ratios for this group however were very minor (barely below 70%) but still lower than for miners with category 1 CWP. Thus, there appears to be no real significant results regarding ordinary measures of obstruction. However, it appears there are slight indications that respiratory resistance at low frequency may be a more sensitive indicator for determining obstruction in miners with CWP. While there were no differences regarding smoking habits, there was a vast disparity between miners and controls regarding the percentage who smoked.

The authors show that non-conventional tests may be more sensitive than the age-old spirometry evaluations. These authors used the body box (plethysmograph) to measure

residual volume and total lung capacity. There was no relevant environmental information in this article. A factor of very minor relevance is whether "someone" wants to suggest that all miners with CWP should be given a complete battery of tests to determine airflow limitation (especially measures of respiratory resistance).

This article is not relevant for assessing exposure-response for CMD and FEV_1.

Sircar, Hnizdo, et al. (2007): "Decline in lung function and mortality: implications for medical monitoring." Occup Environ Med 64: 461-466.

This is a mortality study to assess the risks of mortality related to various cut-off points in yearly decline in FEV_1. There were 1,730 study participants selected out of an original cohort of 9,076 from the NSCWP who had performed two pulmonary function tests (spirometry) about 13 years apart. Follow-up was for an additional 12 years. The cohort consisted of coal miners with spirometry in the first round and also in either the third or fourth round. Several limiting factors narrowed the study group to 1,730. All confounding factors such as smoking, age, obstruction, restriction, and obesity were accounted for in the analyses. The authors indicated four cut-off points for FEV_1 decline and estimated mortality hazard ratios stratified by smoking and lack of obstruction/restriction at round one and adjusted for initial FEV_1, weight, age and height:

Initial Change FEV_1	HAZARD RATIOS			
	Cohort	Non-smokers	Smokers	No Obstructive / Restrictive Pattern
<30 ml/year	1.0	1.0	1.0	1.0
30-60 ml/year	1.07	1.08	1.04	1.17
60-90 ml/year	1.40	1.56	1.33	1.64
>90 ml/year	2.05	1.72	2.03	2.16

While the individuals with <30 ml/year loss in FEV_1 served as an internal comparison group, an external group of 7,309 from the first survey were used. There were 285 deaths in the cohort. Factors clearly influencing mortality were change in weight, pack years of smoking, initial FEV_1, % with patterns of obstruction and restriction, rate of FEV_1 decline in ml/year, and smoking status. The authors' Table 3 demonstrates convincingly that larger than expected FEV_1 decline is a fairly firm predictor of overall mortality as well as combined cardiovascular and non-malignant respiratory disease mortality. For example, the all-cause age-adjusted mortality rate per 1,000 person years by FEV_1 cut-off points was: 11.4 for FEV_1 <30 ml/year, 11.8 for FEV_1 30-60 ml/year, 13.2 for FEV_1 60-90 ml/year, and 24.0 for FEV_1 >90 ml/yr. The cardiovascular and non-malignant respiratory age-adjusted rates were equally astounding as workers with FEV_1 declines >90 ml/year had a death rate 3 times greater than others. The overall results suggest that the risk of death increases considerably amongst workers with FEV_1 declines of 60-90

ml/year and is even more significant for declines greater than 90 ml/yr. In the full cohort, the effects of smoking status are obvious with non-smokers showing a decline in FEV_1 of -37.6 ml/year, ex-smokers -42.5 ml/year, and smokers -51.6 ml/yr. Perhaps the major finding for this study group of coal workers was the significant mortality risk for non-smokers with >90 ml/year) decline in FEV_1 associated with occupational dust exposure.

This is a clear-cut tool for health care providers. However, this study is not relevant to determining a standard as there are no exposure-response analyses.

Beeckman, Wang, et al. (2001): "Rapid declines in FEV_1 and subsequent respiratory symptoms, illnesses, and mortality in coal miners in the United States." Am J Respir Crit Care Med 163: 633-639.

This article is a rather complex evaluation with the stated purpose of determining the long term health outcomes associated with rapid declines in FEV_1 observed among some underground coal miners. The authors evaluated symptoms, illnesses, and mortality among the study population from the NSCWP. 310 cases with accelerated loss of FEV_1 60 ml/year or greater were matched with 324 controls on the basis of age, height, smoking status, and initial FEV_1. Cases with reduced FEV_1 were at about double the risk of dying from cardiovascular and pulmonary causes and had over a three-fold risk of death from COPD. Similar findings have also been observed in non-occupational populations where pulmonary function loss has been shown to be related with mortality from cardiovascular disease and COPD.

On balance, we do not disagree with these results. However, the question of why there were major FEV_1 declines and the evaluation to determine the causes was not done. No environmental data were used.

Wang, Petsonk, et al. (1999): "Clinically important FEV_1 declines among coal miners: an exploration of previously unrecognized determinants." Occup Environ Med 56: 837-844.

This is the same cohort used in the authors' 2001 article on rapid declines in FEV_1 (Beeckman, Wang, et al. 2001). It is not relevant for evaluating the adequacy of the 2.0 mg/m^3 CMD standard although COPD is associated with very low FEV_1. 310 cases with >60 ml/year decline in FEV_1 were matched with 324 controls. Questionnaires were administered to gain information on mining and non-mining factors which might influence large FEV_1 declines. Of the 634 original participants, only 264 workers (or family members) completed a follow-up questionnaire. The authors indicated that the participants were representative because of the matching on controlling factors. Only 121 of the cases (39%) and 141 of the controls (44%) responded. Matching on some controlling factors is necessary, but the unknowns "gleaned" from the questionnaire do not guarantee a uniform pattern for the non-respondents. The 264 miners participating (121 cases and 141 controls) were from the original 344 matched pairs, but only 65 pairs were actually included. Therefore the matched pair design was abandoned in favor of group analyses. Ordinary statistical treatment was given the groups plus a couple of

multiple regression models. Whether or not statistical significance was achieved is somewhat irrelevant in this study as the results are common sense in nature. There are no dust data (per se) in this study, thus no exposure-response estimates of any type.

The conclusions were "Use of respiratory protection seemed to reduce the risk of decline in FEV_1. Other factors that were found to be associated with declines in pulmonary function include smoking, body mass, weight gain, childhood pneumonia, and childhood exposure in the home to passive tobacco smoke and possibly smoke due to wood and coal fuels. Miners with excessive decline in FEV_1 were less likely to be working in mining jobs at follow-up". It is quite possible this type of information might be helpful in on-going programs for the prevention of chronic respiratory disease. This information is clearly more suited to a clinical approach and would very likely not be used in surveillance and epidemiological research activities.

Thus, this study is not relevant for determining an exposure standard.

Kizil and Donoghue (2002): "Coal dust exposures in the longwall mines of New South Wales, Australia: a respiratory risk assessment." Occup Med 52(3): 137-149.

This article describes dust exposure in longwall mining operations in Australia. The predicted effect of these exposures on CWP and FEV_1 are inferred from the US and UK evaluations (Soutar and Hurley 1986; Attfield and Seixas 1995). There were nearly 12,000 valid dust measurements from 33 mines. Seven occupational groups were derived and using nearly all of the dust measurements. The mean respirable dust concentration across all jobs over about a 4-5 year time span was 1.51 mg/m^3.

This article is particularly applicable to and provides a nice review of longwall operations. One should note that longwall mining can produce up to five times more dust than conventional room and pillar operations using continuous mining equipment (which are more prevalent in the US). Australian health predictions based on the average dust concentrations of 1.51 mg/m^3 were derived for CWP using a US evaluation (Attfield and Seixas 1995), and a UK evaluation for FEV_1 (Soutar and Hurley 1986) which is generally agreed upon by Coggon and Taylor (Coggan and Newman-Taylor 1998).

Soutar and Hurley (Soutar and Hurley 1986) estimated the average loss in FEV_1 attributed to CMD was -0.76 ml /ghm^3. Kizil and Donoghue (Kizil and Donoghue 2002) assumed a 1600 hour working year and calculated -0.76 ml /gh/m^3 is equivalent to a -1.22 ml loss in FEV_1 per mg/m^3-year. Thus, over 40 years at exposure of 1.51 mg/m^3, lifetime FEV_1 loss would be about -74 ml. The authors noted that a loss of this magnitude over 40 years at a mean concentration of 1.51 mg/m^3 seems tolerable and unlikely to be of clinical importance after taking into account variation in the effects of smoking. The authors also note that use of respirators reduce the risk below the estimates they derived.

In a comparative manner, the Soutar and Hurley association of -0.76 ml /ghm^3 and assuming a 2,000 hour working year produces a loss in FEV1 of -1.52 ml per mg/m^3-

year. At our 2 mg/m^3 standard, the lifetime FEV_1 loss to US miners would be in the neighborhood of -106 ml (2 mg/m^3 x 35 years x -1.52 mg/m^3). This is a bit higher than the Australian estimate but is likely still quite manageable.

Naidoo, Robins, et al. (2006): "Respirable Coal Dust Exposure and Respiratory Symptoms in South-African Coal Miners: A Comparison of Current and Ex-Miners." JOEM 48(6): 581-590.

This is a cross-sectional study with emphasis on pulmonary symptoms (cough, phlegm, wheezing, etc.). 896 miners were evaluated -- 684 current workers and 212 former workers; 24 from the latter group not reporting for their appointment. Although the main aim of the study was to gain information on the relationship between dust and symptoms, there were some minor evaluations that also included lung function. The questionnaire used was adequate relating to symptoms, work history and smoking status. The details regarding pulmonary function parameters and dust exposure given were the same as from the earlier article (Naidoo 2005).

The authors' Tables 1 and 2 are merely descriptive statistics for various characteristics depending on whether the workers were current or former miners, or whether they had worked underground or on the surface. Nothing remarkable or noteworthy can be seen in the data. Perhaps the only noteworthy data from the whole study can be found in the authors' Figure 1, where all symptoms were statistically less prevalent amongst current workers than former workers. For all workers mean CMD exposure was 58.1 mg/m^3-yrs., with current workers having much more exposure than former workers (67.5 vs. 27.6 mg/m^3). These two descriptive facts make it intuitively clear that there were no overall dust-related associations with symptoms. The lone evaluation of pulmonary function parameters showed that reduced percent predicted FEV_1 was significantly associated with symptoms among former miners. The converse is true for those without symptoms. While the associations may be significant, they are of minor importance as nearly all miners (with and without symptoms) had % predicted FEV_1 values of 100% or more. To a slightly lesser degree, the same phenomenon exists for FVC and FEV_1/FVC% ratio. Odds ratios from the logistic regression models are contained in the authors' Tables 4 and 5 for current and former miners. Lower bounds of the confidence intervals indicated most results were statistically significant. There were few associations between dust and symptoms except for the dichotomous variable of ever underground or surface only. There were very weak associations of CMD exposure and symptoms of phlegm and wheezing - but that was. Based on odds ratios a history of TB and smoking were good predictors of symptoms.

The bottom line from this study can be found on page 588 (Table 6) of the article and on page 586 (Figure 1). Symptoms (generally) were not associated with dust exposure, and former miners had a greatly elevated prevalence of symptoms compared to current miners. Selection effects have likely (and greatly) influenced these results -- the fit workers remained and the more ill dropped out of the workforce.

Love, Miller, et al. (1997): "Respiratory health effects of opencast coalmining: a cross-sectional study of current workers." Occup Environ Med 54: 416-423.

This study was reviewed in earlier sections on CWP. This review involves exposure estimates, pulmonary function, and bronchitis symptoms.

This is a cross-sectional study of surface miners in the all areas of the UK. The objective related to respiratory health effects in that segment of the coal industry. Dust sampling appeared to be related only to a specific period of time and thus, cumulative exposures were absent. Workers were grouped (combined) according to jobs and the dust measurements relating to all (mostly all) groups were extremely low -- of 626 samples, none of the group means exceeded 1 mg/m^3 -- although group A was close. Likewise, quartz samples were also low (see figures on p. 419). Logistic regression techniques were used for evaluating the health indices. While bronchitic symptoms were present in 13% of the workers, the effect of smoking was overwhelming (*see* the authors' Table 4) and accounted for the majority of workers with symptoms. Aging did not appear to be a factor but time worked in other dusty jobs may have related to some of the bronchitic symptoms. Interactions between the effects of smoking and work in other dusty trades were not given. A similar and possibly expected result was evident regarding lung function. The authors' Table five shows an expected age and smoking effect and regression evaluations indicated that none of the lung function parameters were related to the job groupings within the surface mining industry -- or to dusty jobs outside of the industry. While some dust information was available in this study, the results are of only minor relevance.

Rogan, Atffield, et al. (1973): Role of dust in the working environment in development of chronic bronchitis in British coal miners." Brit J Ind Med 30: 217-226.

This is a cross-section study of British face workers from 20 different mines in the UK. The 4,122 workers were studied three times at roughly five year intervals and their pulmonary function FEV_1, grade of CWP, age, smoking history, etc. were obtained. The number of workers was reduced to 3,581 after excluding those with PMF, those <25, those >65, and ex-smokers. The results from the study relate to information from the third survey. Dust exposures were available and their accumulation to CMD has been described adequately (in this paper and elsewhere). Dust information prior to the first survey period was meager and was estimated by applying exposures between the first and second survey period to jobs from the workers' occupational history questionnaire. Some possibility exists for under-estimation of exposures due to these latter estimates. These analyses bear some resemblance to Morfeld (Morfeld, Noll, et al. 2010) in that the major changes that occurred and appear obvious are included in the authors' Table 1. Exposures were divided into three somewhat arbitrary categories (low, medium, high) and the Table shows unadjusted FEV_1 by exposure, age group, and smoking status. Height among the various groups was roughly equivalent. The independent effects appear for aging, smoking, and dust -- while the dust effect by smoking and age is of

prominent importance in this study. What remained was to determine through regression analysis (authors' Table 2) the significant effects for all variables in the model. All (save sitting height) were significant. While the coefficient for cigarette smoking (units of cigarettes/day) had no more significance than the dust exposures in gh/m^3. The authors' Tables 3, and 4 were compiled regarding CWP and bronchitis using % predicted FEV_1 derived from the main model. Regarding grade of CWP, nothing much can be said except that workers with category 1, 2, and 3 simple CWP were older and had more exposure. However, comparison of observed to expected FEV_1 was roughly equivalent. Not so for grade of bronchitis. As grade increased (save no bronchitis), the disparity between observed and predicted FEV_1 decreases. Calculating the average ratios yields values of 97%, 92% and 84% as bronchitis class increases. While this disparity was not obvious for those without bronchitis, a separate evaluation was made of this group and described in the appendix. The authors' Table 5 needs little attention as the trend is clear for bronchitis and not so clear for CWP (i.e. $FEV_{1\ obs} - FEV_{1\ exp}$). A separate regression (like in Table 2) was performed on the 2,272 workers with no bronchitis. The coefficient for dust was negative and minor but nonetheless significant. Among the smokers in this sub-group, the effect was slightly more.

In total, this study demonstrates an independent effect from cumulative dust on FEV_1 (controlling for other factors). Moreover, a relationship between dust exposure and grade of bronchitis was demonstrated. A minor effect was also noted from the separate analysis of 2,272 workers with no bronchitis. Aside from the possibility of under-estimates of exposure prior to the first survey period, the authors freely admit that there are potential selection effects with this evaluation which may limit its usefulness. It is noted that the ventilatory impairment shown in this study (example -- 150 ml with mean concentration of 4 mg/m^3 for a 35 year working life resulting in CMD of 240 gh/m^3) would be unlikely of clinical importance. This represents an average loss and it is reasoned that some miners thus exposed (upper end of the distribution) could develop significant and clinically important losses in FEV_1 due to exposure.

Overall, this is a reasonable study (with attendant shortcomings - admitted) demonstrating an independent effect from CMD on FEV_1 and grade of bronchitis.

Henneberger and Attfield (1997): "Respiratory symptoms and spirometry in experienced coal miners: effects of both distant and recent coal mine dust exposures." Am J Ind Med 32(3): 268-274.

This is an interesting and novel article whereby an original linear regression model used by the same authors a year earlier (which evaluated the relationship between dust (as a continuous variable) and FEV_1) was modified by substituting the continuous variable with layers (ranges) of exposure, thus making them categorical in nature. This study involved 1,866 miners who participated in either round one or two of the NSCWP and were again examined in round four. An objective was to determine if dust exposures (categorically) during an inter-survey period R1 to R4 or R2 to R4 were associated with the onset of symptoms, and whether prior or distant exposures had an influence on this onset. Initially, dust levels were categorized as either high (pre-first or second round) or

low (R1 to R4 or R2 to R4). However, a further categorical exposure "break-down" is noted (see authors' Table 2) for pre- and post-R1/R2 exposures producing a 2 x 3 design. We evaluated pre-1970 (pre-R1) exposure estimates with regard to CWP (Attfield and Morring 1992a; Attfield and Morring 1992b) showing there were biases. The inter-survey exposure estimates are from the MSHA data base. Symptoms of concern were chronic bronchitis, shortness of breath, and wheezing. The number of subjects in this work was reduced from what the same authors used a year earlier because of two additional criteria for entrance into the study, and the logistic regression techniques using a three-stage forward stepwise procedure to determine the best fit. The average pre R1/R2 exposures were 3.4 mg/m^3 while the post R1/R2 exposures were 1.0 mg/m^3. A slight deviation from the main aim of the study related to an evaluation of the FEV_1 vs. dust using a model similar to one used the previous year except the earlier continuous variable was removed and replaced with the categorical variables. Nothing in the summary or abstract of this paper relates to the FEV_1, presumably because only past exposures at level III had a significant effect.

Regarding symptomatology, the logistic model used shown in the authors' Table V is used for evaluating each symptom of interest. Overall, the odds ratios shown appear somewhat unremarkable. Some dust related effects are noticed (some significant) for both distant and the inter-survey periods, but they are overwhelmed by the more significant effects from symptoms at the initial round of exams, aging (to a lesser extent), smoking, and a factor related to those who left the industry by R4. The main risk that stands out is from the inter-survey period where SOB was highly significant with regard to the lowest prior exposures. Overall, there was no apparent increased risk of symptoms associated with current exposures or past exposures. The main finding relates to the increased risk of symptoms during the inter survey period where the average dust concentration was 1.9 mg/m^3; i.e. the effects of the low level post exposures (inter-survey R1-R4 or R2-R4) were evident for SOB and wheezing for miners who had low levels of exposure prior to 1970. As noted earlier, however, these effects were overwhelmed by other extraneous factors plus the estimated low exposure levels prior to 1970. It is quite likely pre-1970 risks are biased high because high exposures are biased high. This is a novel design with results of minor impact.

d. Emphysema, COPD, and Coal Mine Dust

Kuempel, Wheeler, et al. (2009): "Contributions of Dust Exposure and Cigarette Smoking to Emphysema Severity in Coal Miners in the United States." Am J Resp Crit Care Med 180(3): 257-264.

This is a study involving autopsies of coal miners from Southern WV and non-miners from WV and VT. There were 616 coal miner lungs from the Beckley, WV area and 106 non-miner lungs from WV and VT. Lung samples were evaluated for emphysema severity by two pathologists. Work histories, smoking histories, and other such data were gained from next of kin as well as from official records such as medical reports. Cumulative exposure was estimated according to a procedure detailed elsewhere (Attfield

and Morring 1992a). While a non-mining group was organized and their lungs evaluated, the main thrust of the article related to CMD and smoking among the miner population and the relative contribution they had on emphysema severity.

The autopsied lungs were of miners who died between 1957 and 1973 and the lung specimens were collected and prepared by Dr. Laqueur in Beckley (40 to 50 years ago). This particular period was critical regarding black lung legislation. The main purpose for the autopsies was for compensation purposes.

Comments on Kuempel, Wheeler, et al. (2009)

This seems to be a well thought-out study with sound methodology. Results support the conclusions that 1) cumulative exposure to respirable coal mine dust or coal dust retained in the lungs are good predictors of emphysema severity; and 2) coal mine dust and cigarette smoking have a somewhat equal contribution to the severity of emphysema.

However sound the analyses and methodology employed, the results are only as good as the data, which has definite limitations. We have previously discussed (*see* Chapter IV) shortcomings in the methodology and estimation of pre-1970 exposures (Attfield and Morring 1992a). These estimates overestimate low exposures and underestimate high exposures, thereby biasing upward the risk associated with cumulative CMD exposure. The total description relating to cumulative exposures found on page 258 of Kuempel, et al., in this paper is filled with much guess work where missing or incomplete data existed and should be viewed with extreme caution. We have no doubt that respirable coal mine dust is a contributing factor to the occurrence and severity of emphysema, but during these very early years the exposures of these miners were likely to have been extremely high (well above the 3 and then 2 mg/m^3 standard. Exposure estimates in this study are underestimates, and have little to no relevance to the current or proposed coal mine dust standard.

The source of work histories is not well explained. Smoking data were obtained from "medical records or questionnaire (sic) completed by next-of-kin." "Coal mining tenure records varied in detail and quality." Next-of-kin and "miners work history" are mentioned as sources for determining miner or former miner status and tenure. Inconsistencies were resolved by "checking the original records." The methods described for collecting these data need to be more specific, as their reliability is suspect. The accuracy and completeness of data from these sources are questionable as suggested by the amount of missing data. Of the 616 coal miners, 11% are unaccounted for, 11% have some missing data and 14% have "minimal" data (no work history or evidence of being a miner) and are not included in the analysis. Only 63% had "complete" information. The most reliable data for exposure would appear to be lung burden based on these considerations and bias inherent in pre-1970 exposure estimates.

Beyond the issue of exposures is the reliability of smoking history data. The time period of this study was a critical time frame when miners were applying for compensation and the issue of smoking vs. dust was quite heated Most of this smoking information was

taken from next of kin, and one is asked to believe that around half of the miners were non-smokers (see authors' Table 2). During this time both the next of kin and others were well aware of the smoking vs. dust controversy. Although the authors used available data, on balance, because of the severe limitations of the data used in this study the results are biased, and remain at least suspect to virtually non-useable.

Emphysema severity score was the measure of response, and the scale went from 0 to 1000. Severity scores were generally below 500 for cumulative exposures less than 90 mg/m^3-years (or 45 years x 2 mg/m^3) for non-white smokers, the most severely affected miners. Severity was generally less than 200 for white non-smokers (Figure 4 in Kuempel, et al., 2009).

Two measures of occupational exposure were used to assess biological gradients and were said to show linear relationships with severity. Cumulative exposures for pre-1970 employment were in mg/m^3-years with a unit risk of 1.10. A mean exposure of 90 mg/m^3-years CMD exposure was calculated to produce a predicted emphysema severity score of 99 (65-133) from the weighted regression model. Cumulative exposure was highly significant ($p<0.0001$) as was age at death (169 score at average age at death of about 65 years) and race (152 score for non-white). Smoking and the interaction of smoking x age contributed about 67 units at an average of 42.4 pack-years (authors' Figure 8).

The smoking association in this cumulative dust model appears lower than expected for several reasons. First, pack-years of smoking for smokers above the mean is very high (>2 packs/day for 20-years or >1 pack/day for 40-years). Second, the coefficient for pack-years alone is negative, suggesting an inverse (or protective) association, while the only adverse effects are based on the interaction of pack-years and age. This seems implausible, but the unlikely protective effect may be due to a small group of outliers among non-miners less than 30 years of age (who comprised 1% of the study population) and the lack of any miners in this age group. Finally, being an ever-smoker was estimated to produce a mean increase in severity score of 178 units. It seems unlikely that an ever-smoker category would have a larger effect on emphysema than heavy smokers.

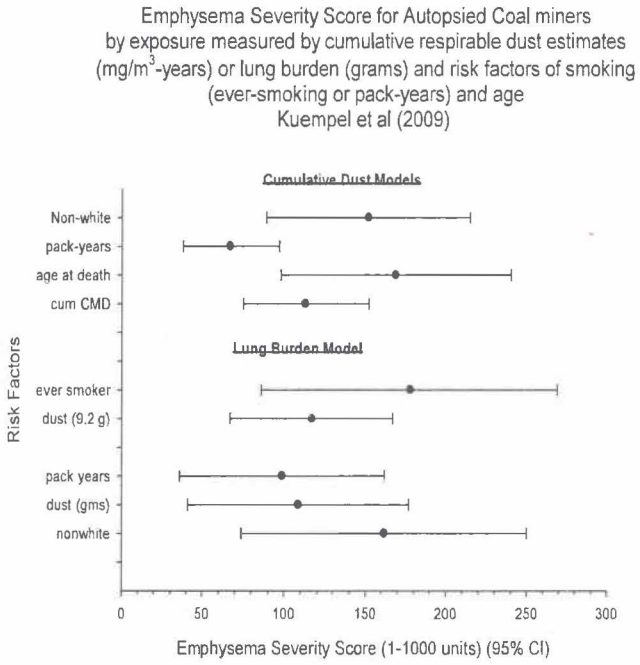
In the lung burden model there were strong associations for all included variables. Lung burden (or dose) was calculated to increase severity about 110 units depending on the model. Ever-smoker produced about 178 units and non-white genetics a score of 162 units (Figure 8 below). Age produced the largest effect in this model, producing an estimated severity score of 517 when dying at the mean age of 66 years.

The authors suggest that the strengths of this study was that collection of data occurred in 1960s and 1970s when smoking was not a contentious issue and before Federal compensation programs were introduced. It is unclear why the authors consider these models and findings relevant to current conditions given that most exposures were pre-1970 and much higher than current exposures. This study suffers from the same

exposure limitations reported in the CWP morbidity and mortality studies of NIOSH (Attfield and Morring 1992b; Attfield and Kuempel 2008).

Limitations include potential biases from misclassification of smoking and exposure, which have already been discussed. The authors mention of misclassification of smoking exposure tends to negate their claim that a strength of the study is that smoking was not a contentious issue during data collections. The r^2 values were 0.52 and 0.44 for the cumulative exposure and lung burden models respectively. Strong associations of emphysema and risk factors of smoking, race, age at death, and CMD exposures were consistently observed. It would be helpful if non-linear statistical models were presented, as it seems implausible that exposure-response and dose-response trends were all linear and the smoking-race categories all had what appear to be the same slopes (the authors' Figure 3). Based on the lung burden data, there is unlikely to be exposure misclassification. But the lung burden data cannot be reliably transformed into cumulative exposure estimates, and the exposure-response data based on cumulative exposure from these data are inadequate to determine the effect of CMD on emphysema under post-1970 or current exposure conditions.

Figure 8



Kuempel, Vallyathan, et al. (2009): "Emphysema and pulmonary impairment in coal miners: Quantitative relationship with dust exposure and cigarette smoking." Journal of Physics Conference Series 151: 1-8.

This study population is comprised of 116 individuals with spirometry drawn from the same 722 autopsied miners and non-miners just discussed (Kuempel, Wheeler, et al. 2009). Of those 116 individuals, 65 of the miners had FEV_1 tests performed within five years of death. Thus, this is an analyses of the Laqueur data base from Beckley, WV plus pulmonary function data (FEV_1) supplied by Dr. Rasmussen from Beckley. The purpose of the study was to determine if cumulative exposure to respirable coal mine dust is a significant factor for developing emphysema at a clinical level of severity.

Clinically, severity of emphysema at autopsy is estimated from two cut-points of percent predicted FEV_1 (adjusted for age and height) and a measure of COPD. Less than 80% and <65% of normal FEV_1 has been associated with exertional dyspnea in UK coal miners. Cumulative exposure was estimated by the method of Attfield and Morring (Attfield and Morring 1992a) for exposures prior to 1970. As noted previously, the work history data from past records and next of kin plus the methodology employed regarding exposures are not very reliable. Smoking histories in this article are a bit confusing because it is the same cohort as previously commented on where about half of the group were non-smokers (questionable indeed). In this article (same group), 87% were reported as smokers or ex-smokers (ever smokers).

The spirometry (FEV_1) data base is of questionable reliability. It is well known that data such as these were collected in southern WV at various clinics where miners were coached on how to perform the maneuvers to their benefit for compensation purposes. There was a significant trend between the emphysema index and FEV_1 but much of the variability was unexplained as seen in the authors' Figure 1 and in an R^2 of 0.17.

The authors' Tables 1 and 2 show results of the analysis supporting the conclusion in the abstract that "cumulative exposure to respirable coal mine dust was a statistically significant predictor of developing clinically relevant emphysema severity, among both ever and never smokers". In this study population of miners, pack-years has similar strength of association (similar ORs that are not statistically significantly different). It is not convincing that the dust effect is greater than the smoking effect. For this cohort, both of these factors remain questionable. When compensation matters are involved, smoking histories are likely to be unreliable. These autopsied miners were exposed to respirable dust far in excess of today's standard, and the estimates are biased to overestimate high exposures and underestimate low exposures. Dust can have an effect on the development of emphysema and COPD, but the general literature still considers "ordinary" levels of occupational pollution to be minor compared to cigarette smoking and aging.

Relative Risks at Average of Risk Factor

Risk Factor	RR (95% CI) FEV_1 < 80% predicted	RR (95% CI) FEV_1 <65% predicted
Cumulative exposure (87 mg/m^3-years)	2.38 (1.42-3.32)	2.38 (1.54-3.65)
Smoking (42 pack-years)	1.95 (1.40-2.71)	1.52 (1.09-2.12)
Race (non-white)	2.41 (1.39-4.17)	2.23 (1.29-3.85)
Age at death (64 years)	22.7 (3.55-76)	12.3 (1.89-41.6)

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VI. MORTALITY STUDIES

1. Summary of Mortality Studies and CMD Exposure

The earliest reliable data on coal miner mortality is from occupational statistics from the 1906 British Registrar General for the years 1890-2 and 1900-2, which suggested mortality was declining. In 1928, CWP was reported among coal trimmers unexposed to silica (Merchant et al, 1986). Early studies focused on cancer mortality where there were generally no excesses related to the respiratory system. Early on there was a hypothesis extending into the 1960s that early death from CWP could be a factor in reducing lung cancer mortality. Miller and Jacobsen (1985) found no association between lung cancer and CMD and no evidence that miners with CWP were at increased risk.

Similar studies began in the 1960s in the US. An early study by Enterline found a two-fold excess of lung cancer but a USPH mortality study found a deficit (0.67) of lung cancer, and Appalachian coal miners appeared to have lung cancer rates similar to miners in the UK. Rockette found no association with lung cancer but did find a slight increase in stomach cancer mortality that was consistent with several other studies. In 1997 the International Agency for Research on Cancer concluded there was *inadequate* evidence in humans for the carcinogenicity of CMD. Finally, in 2008, a US study found no associations of carcinogenicity and CMD exposure (Attfield and Kuempel, 2008).

The story of CWP mortality shows a pattern of consistent findings of increased risk. The first case of CWP was described in 1928 in a coal trimmer not exposed to silica. Standard mortality ratios ("SMRs") for respiratory diseases were consistently elevated, but it was not always clear that it was due to CWP. That is, there were few and inconsistent differences between categories 1, 2, 3 of simple CWP and category A complicated CWP compared to miners with no radiological abnormalities. However, these miners' pulmonary function status were somewhat impaired compared to controls, and miners with categories B and C complicated CWP had higher SMRs in both the UK and US. Neither simple CWP nor PMF have been eliminated and there have been slight reported increases in both in the last few years at concentrations below the 2.0 mg/m^3 standard.

There are only two mortality studies of coal miners with quantified estimates of CMD exposure and stratified by radiographic categories of pneumoconiosis. The British study showed no association with non-violent causes of death for radiographic categories 2 and below, and a slight trend toward increased mortality for category 3 and stronger association with PMF (Miller and Jacobsen, 1985).

The US studies showed strong associations of pneumoconiosis with CMD and radiographic categories 2, 3 and PMF and at cumulative exposures below the standard (Kuempel, et al. (1995), Attfield and Kuempel, (2008)).

Although additional analysis is required for confirmation, the associations of CWP and CMD appear to be confined to high rank coal dust. There appears to be no increased mortality risk of CWP associated with coal mined in eastern Appalachia, western Appalachia, and the Midwest. Numbers were too small for a mortality analysis of Western coal, which is the lowest ranked coal and presumably the lowest risk if the coal rank hypothesis is correct.

Section 2 reviews exposure-response studies that have evaluated mortality studies of coal miners. The autopsy studies supported the morbidity findings that quartz is a major factor contributing to respiratory mortality among coal miners.

2. Comments on Studies of Mortality Studies of CMD Exposure

Miller BG, Jacobsen M (1985). Dust exposure, pneumoconiosis, and mortality of coalminers. Br J Ind Med 42:723-733.

Summary and Comments

This is the first mortality study of coal miners with quantitative estimates of CMD exposure. The purpose of the study was to answer the questions: "Does exposure to respirable coal mine dust increase mortality risks? If so, to what diseases are the excess deaths attributed?"

The cohort comprised 26,363 British coal miners in 20 collieries who attended medical surveys between 1953-1958. Follow-up ended in 1980 with 32% mortality. Data collected at the surveys included chest radiographs and work history. The response data involved the percentage survival at 22 years of follow-up.

CMD concentrations were estimated from systematic sampling collected approximately ten years after the medical surveys for six broad categories of coal mining activity.

Generally mortality increased in severity with increasing age and the higher the category of CWP, the greater the mortality rate. Percentage survival from "non-violent causes of death are shown by radiographic category and after 22-years follow-up (from Table 4). Survival decreased with increasing CWP radiological category and with increasing age at the first survey (Figure 1). Weak trends were also present for digestive cancer and chronic bronchitis and emphysema, and there were no associations with ischemic heart disease or lung cancer).

There were strong exposure-response trends for CWP and CMD. Out of 164 CWP deaths, 159 deaths had first exposures greater than 51 mg/m^3-years (most were >103 mg/m^3-years) and only 0.3% (n=5) had initial exposures <51.3 mg/m^3-years) (Figure 2 from the Institute for Occupational Medicine). The exposure-response trends for chronic bronchitis, emphysema were not statistically significant ($p>0.1$) (Figure 2) although there appears to be an association for the 55-64 year age group.

About 6% of the cohort could not be traced. This number is unlikely to bias results. There were no dust exposures for 19% of those who were traced, and a high proportion of these were older with a higher than average proportion of CWP. These missing data may have produced an information bias that may have produced spuriously low exposure-response trends.

The authors note three findings of particular interest.

(1) The survival rates for category A PMF were substantially and significantly lower than those with no CWP initially. This is not unexpected because of increased mortality for categories B and C, but it is contradictory for earlier studies with shorter follow-up.

(2) There are reductions in survival in most subgroups with simple CWP when follow-up is not short. However in this study with 22-year follow-up there did not appear to be a tendency for mortality to increase with increasing category of simple CWP (categories 1, 2, 3).

(3) There is a "tendency for men with higher exposures to dust at the outset, particularly in the two older age groups, to have reduced survival rates from all non-violent causes." Yet this exposure-response is more obvious for non-violent deaths than CWP deaths, which "reinforces our opinion that the quantitative estimates of exposure that we have used here are more realistic reflections of the miners' actual exposures" than the radiological categories at the start of follow-up. The effects of dust exposure are considered probabilistic, which means that most "miners who are exposed even to fairly high levels of dust do not develop radiological signs." For example, in one study only 7% of coal miners exposed to 200 gh/m^3 for more than 20-years had CWP 2 (Hurley, et al. 1982). In this study at least 25% of miners had exposures greater than 103 mg/m^3-years and 64% in that exposure range had no CWP.

Additional Comments and Critique of Miller, Jacobsen et al. (1985)

Exposure estimates in this study suffer from the same limitations of the US study (Kuempel, et al. (1995), Attfield and Kuempel. (2008)) in that samples for exposure estimates were conducted about the same time or after initial follow-up and after considerable time underground, often at very high concentrations without CMD samples. The sampling covered about ten years (Dodgson, Hadden, et al. 1971) and 74% of the cohort. Work histories were collected via detailed questionnaires and are subject to recall bias.

The 6% lost to follow-up tended to be older with a higher prevalence of CWP, and, thus, their absence might have understated the true mortality. On the other hand, the comparisons are between subgroups of different ages. Those lost to follow-up spanned all the age groups and all categories of CWP. Therefore, the authors suggest their loss is unlikely to have seriously distorted the mortality contrasts within the whole population.

These are percent survival analyses rather than SMR analyses common in the US. Age is adjusted for by using different age groups, and there is no non-exposed control group

with which to compare survival rates relative to exposure. In the published version there is no exposure-response analysis for CWP, and this limits the ability to interpret the effect of mortality from CWP and dust exposure.

There are no exposure-response analyses for CWP in this paper. For non-violent causes of death there is increased mortality for miners in the older age group at lower exposures, but no association with CMD exposure above about 30 mg/m^3-years. The younger age groups show no apparent exposure-trends with increasing cumulative exposure (Figure 2).

For chronic bronchitis and emphysema ("CBE") there are no apparent exposure trends with exposure in the two younger age groups, but for the oldest age group there were marked reductions in survival at average exposures of 35 and 115 mg/m^3-years and no apparent change in survival between about 35 and 90 mg/m^3-years (Figure 2).

Figure 1

Estimated percentage survival at 22 years from non-violent causes of death
by age and radiological classification at first survey among
24,736 UK coal miners
Miller and Jacobsen (1985)

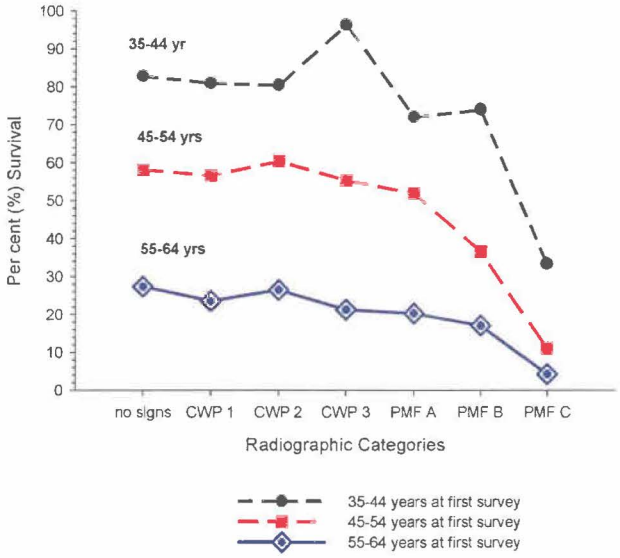
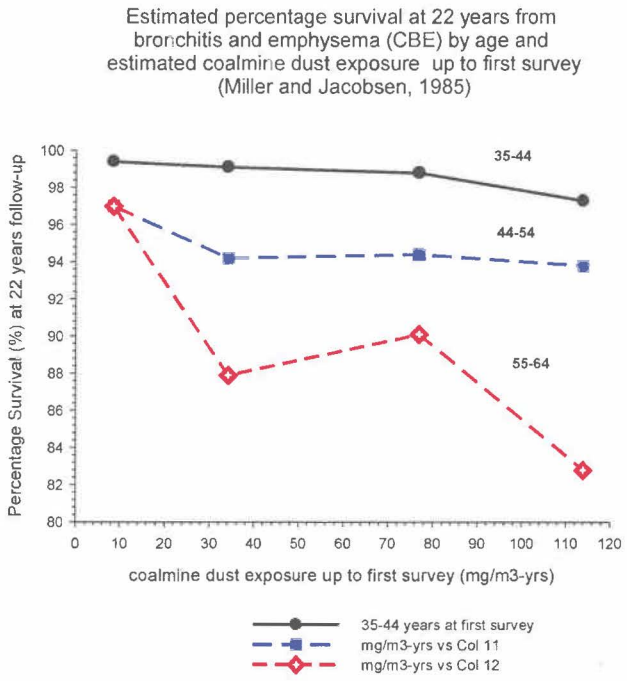


Figure 2



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Summary and Comments

The objective of this mortality study was to investigate exposure-response relationships between CMD and mortality from nonmalignant respiratory diseases ("NMRD") primarily (including CWP, chronic bronchitis, and emphysema), as well as lung and stomach cancer. The primary variables studied included intensity, duration, and coal rank.

The cohort consisted of 8,878 coal miners who participated in the first survey of the NSCWP, 1969-1971. Mortality follow-up was to 1979. The only work history considered occurred prior to the first round of the NSCWP, or before about 1970. CMD estimation was based on the methods described previously (Attfield and Morring 1992a). Work exposures during the nine-year follow-up were not included. Exposure is underestimated for high exposure jobs because of the methodology for estimating pre-1970 job exposures. It is under-estimated for the entire cohort because nine years of post-1970 exposure are not included.

Exposure-response trends were analyzed with six exposure categories using SMRs, standardized relative risks ("SRRs"), and proportional hazard models with variables of age, cumulative exposure, rank, and pack years, smoking status, race and interactions.

The overall SMR for pneumoconiosis is 3.72 (2.89-4.71), and the standardized relative risk ("SRR") is 1.57. The categorical analyses show clear exposure-response trends with a straight-line trend to a two-fold increased SRR at 120 mg/m^3-years after which the curve is flat and there is no trend. The SMR's show a similar trend with significantly elevated SMR's in all groups except the lowest exposed group below 50 mg/m^3-yrs. For the SRR analysis miners in the lowest exposure group are the reference group and the highest relative risk ("RR") is 2.0 at about 120 and 180 mg/m^3-years. There is a clear and significant ($p<0.05$) trend for risk to increase (Figure 3).

The proportional hazards model uses cumulative exposure as a continuous variable. The fit of the model was significantly improved by including variables for age, smoking and coal rank in addition to cumulative exposure. A quadratic term for cumulative exposure was added, making the exposure-response non-linear with an apparent reduced risk at about 140 mg/m^3-years. The hazard ratio ("HR") at 90 mg/m^3-years (2.0 mg/m^3 x 45-years) was 5.92 (2.18-16) for CWP. Pneumoconiosis in this model is the combined diagnosis that includes both underlying and contributing cause of death; that is CWP was considered the cause of death if it was mentioned anywhere on the death certificate, without consideration for other causes (Figure 3).

In the full model, overlapping causes (e.g. CBE) could be considered spurious causes of mortality. To test this hypothesis, the 54 cases without mention of CBE were included in the analysis (CWP was the only cause of death). With CWP as the underlying cause of death and cumulative exposure as the only variable in the model, the categorical analysis showed a clear and significant exposure-response trend. When age is included in the model as a significant confounding variable, exposure was no longer significant ($p>0.2$), RRs were markedly reduced, and lower confidence intervals were <1.0 (CI data not shown) (Figure 4).

In the proportional hazard model where CWP is defined as an underlying cause, cumulative exposure showed a significant ($p < 0.0001$) exposure-response trend. When the confounding effect of age was adjusted for in the proportional hazard model the risk of CWP mortality never increased to more than two-fold, and the exposure-response trend was not significant (Figure 4). The HR was 1.43 (0.73-2.78). Pack-years and anthracite coal rank were significant variables when added to the model but did not affect the exposure-response trend.

There were no exposure-response trends for other causes of death including all causes, emphysema, chronic bronchitis, lung cancer and stomach cancer (Figure 5).

The authors conclude there were clear exposure-response trends for CWP as an underlying cause of death and cumulative exposure in the categorical analyses is consistent with other mortality studies of coal miners with respect to high SMRs. Smoking and age were significantly associated with CWP mortality in all analyses.

Several limitations were mentioned by the authors. One is the uncertainty of the reliability of the death certificate in diagnosing the underlying cause of death compared to autopsy results.

Exposure prior to 1969 used the same methodology as for the morbidity studies (Attfield and Morring 1992a) and so exposure was under-estimated for high exposure jobs and over-estimated for low exposure job and upwardly biased risk estimates in the exposure-response curves. Several reasons were postulated to explain the downward trend in risk at high cumulative exposures. One was that exposure may have been over-estimated for miners with high cumulative exposure. Exposure misclassification may be greater in these largely older workers because of recall bias in completing the work history questionnaire, or because the extrapolation from post-1970 samples to pre-1970 exposures may be poor reflections of job exposures decades earlier. More likely reasons were considered to be that exposures were overestimated; and selective retirement out of the workforce among older miners with disability from CWP who could receive compensation via the 1969 Coal Mine Act which was enacted before the study began.

The current standard of 2.0 mg/m^3 would not be considered adequate based on these data which show a nearly six-fold increased risk (= 5.92) calculated for a 45-year working lifetime at 2.0 mg/m^3 and increased risk occurring below 2.0 mg/m^3.

Additional Comments and Critique of Kuempel, Stayner, et al. (1995)

This is a very complete mortality study, but it has several limitations, especially regarding (a) death certificates and use of contributory causes of death; (b) exposure data; and (c) other factors such as miner recall regarding the work history.

The last sentence of the abstract concludes that "Miners exposed at or below the current U.S coal dust standard of 2 mg/m^3 over a working lifetime, based on these analyses, have an elevated risk of dying from pneumoconiosis or from chronic bronchitis or emphysema".

- CWP as Underlying Cause of Death:

The authors' conclusion of an association is true when pneumoconiosis (largely CWP) is defined as "underlying and contributory causes" (Figure 3). This definition includes overlapping causes of death such as CBE, which according to the authors can affect the exposure-response relationships. CMD is a cause of CWP, but overlapping causes of death such as CBE may not be caused by CMD. This definition may include conditions unrelated to work exposure.

The more appropriate and defined underlying cause of death is when overlapping causes of death are not included in the analysis. When this is done exposure-response relationships are markedly changed and reduced as shown in Figure 3. Cumulative exposure suggests a strong exposure-response relationship with CWP mortality. Adding

age to the models produces a weak non-significant exposure-response trend with no significantly increased risks at any concentration (Figure 4).

Combining CBE and using only underlying cause leaves only nine deaths. This number is too small for analysis. Thus, no conclusions are plausible for the relationships between chronic bronchitis and emphysema in this study.

• Exposure: the evaluation of exposure estimates are based on the method reviewed previously (Attfield and Morring 1992a) and so are biased upward.

• Other factors:

The healthy worker effect has been mentioned in the article and it is noted that shortcomings exist in prior studies using mortality in the general population for control purposes. The idea that coal miners are a selected healthy group is supported by this study and others. In this study the SMR for all-cause mortality was 0.85, quite a deficit of death with no exposure-response trend. A healthy worker effect might explain the tendency for CWP mortality to be reduced at higher exposures.

The authors' Tables III, IV and V seem to be the critical tables on which most conclusions are based. This study takes into account underlying and contributing causes of death (combined) and uses them as the primary data on which conclusions are reached. As can be seen, the underlying cause (alone) is used in table III, while the RRs (table IV) with the low exposure group as reference uses both underlying and contributing cause of death. The differences caused by different definitions for CWP are seen visually in Figure 3 as the difference between the HR (underlying and contributing causes) and SRR (underlying causes only). As discussed in a) conclusions should be based on underlying death only as shown with SRR's (Figure 3) and age adjusted hazard ratios (Figure 4.)

In Table III, the number of deaths by exposure category is about the same (around 132 each). The authors' note that exposure categories were chosen before analyses based on equal numbers of deaths in each group. The good thing is exposure categories were chosen *a priori* before seeing the data and thus avoiding selection bias.

In Table III and Figure 3, SMRs and SRRs are defined by underlying cause alone, and show a trend (with slight exception) with increasing estimated exposure. Age and exposure might be hopelessly tangled -- they are clearly collinear but the correlation is not reported.

The addition of 14 miner deaths (ICD codes 510-519, obviously excluding code 515) to the 54 (ICD code 515) is questionable and could affect the SMRs and SRRs. How these 14 additional cases are distributed across the exposure categories is unknown. Diseases of these additional 14 cases include emphysema, pleurisy, spontaneous pneumothorax, abscess of the lung, pulmonary congestion and hypostasis, other pneumoconioses and related diseases, other chronic interstitial pneumonia, bronchiectasis, and other diseases

of the respiratory system. These conditions might well be caused by factors other than CMD exposure.

Nothing much is mentioned about bronchitis and emphysema deaths shown in Table III – the numbers are small and most are from emphysema, likely age and smoking taking their toll. The relative risks (Table IV) show an expected similar pattern as in Table III, here using the low exposure category as the reference or control group for comparison within the cohort. It is interesting that in order to obtain some indication of an exposure-response trend for bronchitis and emphysema, both the underlying and contributing cause of death were combined. When only underlying cause is used the numbers are too small to analyze exposure-response trends (Figure 5).

Figure 3

SMRs and SRRs (Standardized rate ratios) and Hazard Ratios for 68 Pneumoconiosis and other respiratory deaths by cumulative respirable coalmine dust exposure (mg/m3-years)
Hazard ratios accounting for age, smoking, and coal rank.
Kuempel et al (1995)

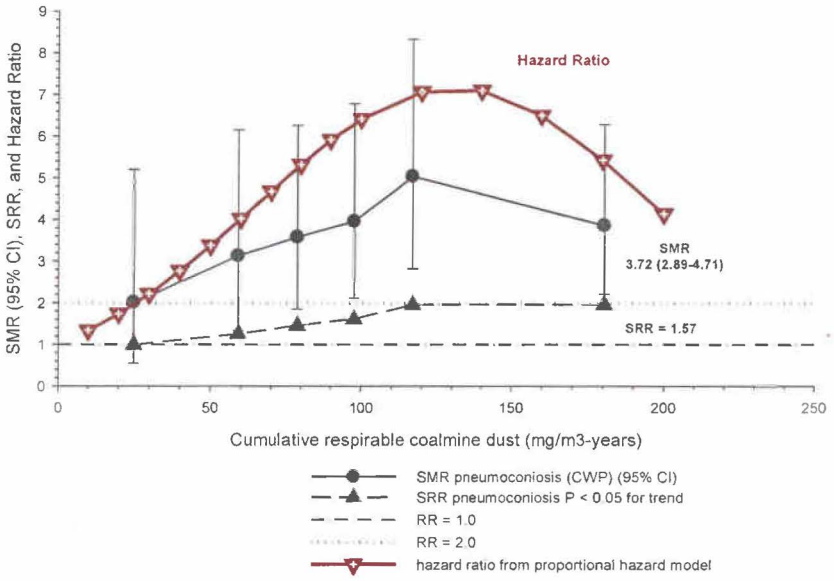


Figure 4

Categorical and Proportional Hazard E-R results from National Study of Coal Workers' Pneumoconiosis when CWP is underlying or contributing cause of death (n = 157) (CWP anywhere on death certificate) and CWP is only underlying cause of death (n = 54)
Kuempel et al 1995)

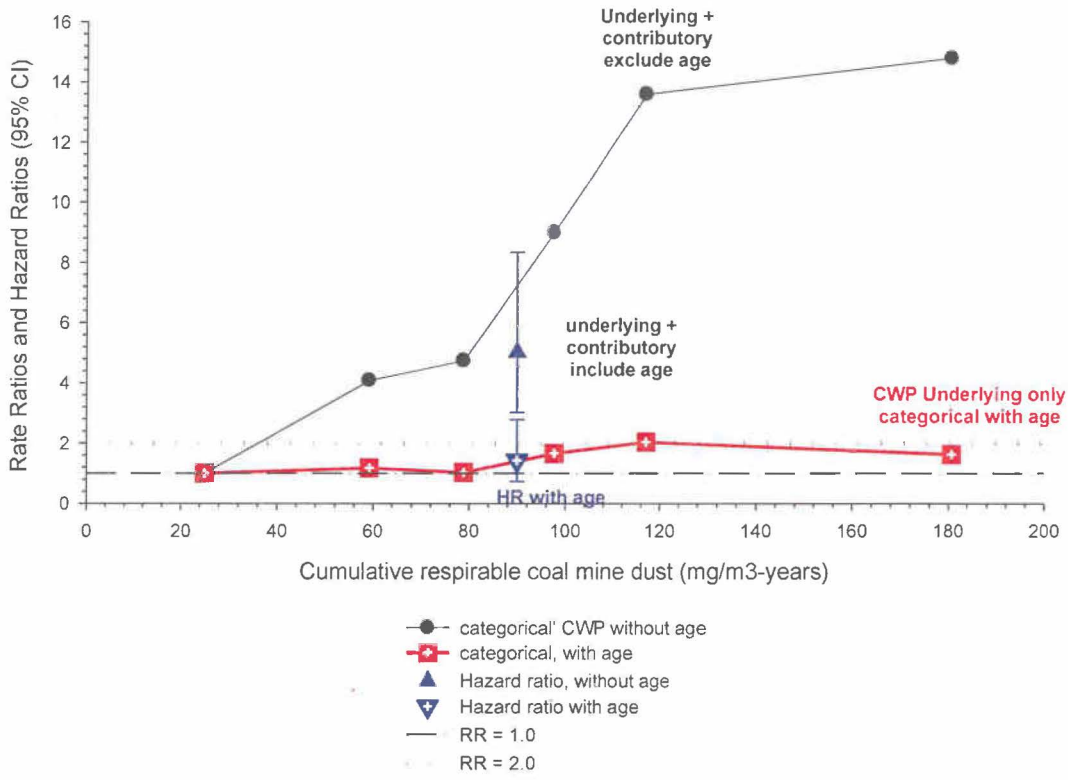
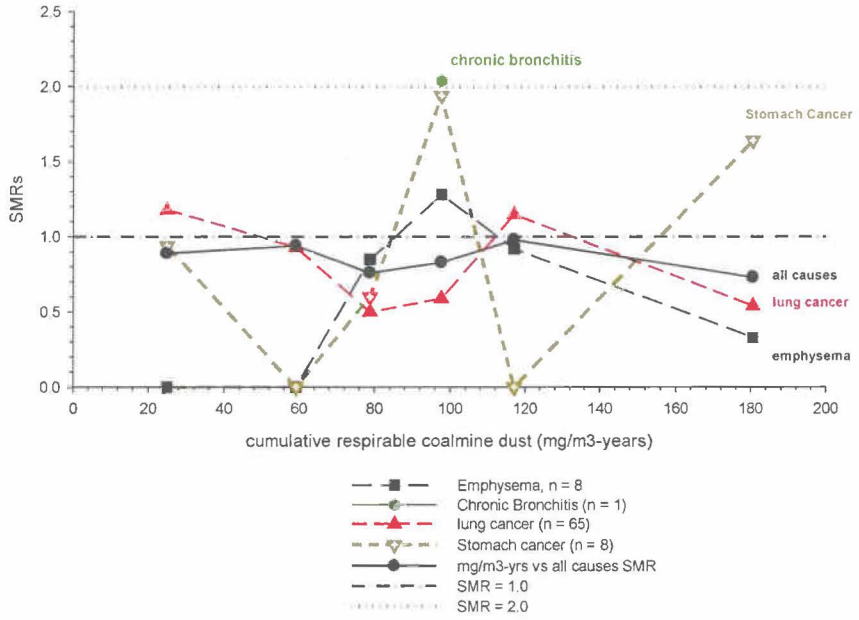


Figure 5

SMRs by Exposure Group for mortality from emphysema (n = 8; SMR=0.62), chronic bronchitis (n = 1; SMR=0.37), lung cancer (n = 65; SMR=0.77), and stomach cancer (n = 8; SMR = 0.91)
Kuempel et al (1995)



Attfield M, Kuempel E (2008). Mortality among U.S. underground coal miners: A 23-year follow-up. Am J Ind Med *51*:231-245.

Summary and Comments

This is a study of the same cohort of 9,078 miners in 31 coal mines followed for nine-years until 1979 by Kuempel, et al. (1995). The new study is essentially the same data and analysis but with 22-24 years follow-up of vital status until the end of 1993, which increased the number of deaths from 793 to 3,213 thereby increasing the power of the study. The total cohort was reduced to 8,899 because of 1.5% with missing data, 0.52% lost to follow-up or no death certificate located. Working miners >65 years of age were not excluded. There were no updates on smoking or on work history, so any changes after 1969-71 were not recorded. The updated study used underlying causes of death primarily, whereas the original study used underlying causes of death plus contributory causes of mortality in the proportional hazard exposure-response models on which conclusions tended to be based.

It is of interest to compare SMRs and number of deaths in the two studies.

Table 1

SMRs of Selected Underlying causes of mortality in same coal mine cohorts of Kuempel, et al (1995) and Attfield, et al. (2008) with 9 and 23-years follow-up

	All Causes N SMR (95%CI)	**Pneumoconiosis N SMR (95%CI)**	**CBE* N SMR (95%CI)**	**Lung cancer N SMR (95%CI)**	**Stomach cancer N SMR (95%CI)**
Kuempel et al (1995)	793 0.85	68 3.72 (2.89-4.71)	9 0.58	65 0.77	8 0.91
Attfield et al (2008)	3213 1.03 (0.99-1.06)	383 3.08 (2.78-3.41) NMRD n=474 1.95(1.78-2.14)	38 0.86	331 1.07 (0.95-1.19)	21 0.75 (0.46-1.14)

* CBE = Chronic bronchitis and emphysema

There are no major differences between SMRs for any of the selected causes of death. NMRD and pneumoconiosis are the only disease with significantly elevated SMRs.

In the life-table analysis using SMRs, CWP shows strong exposure-response associations with cumulative CMD exposure and are very similar in both cohort studies. There is a downward trend in the high exposure of the first study (Kuempel, Stayner, et al. 1995), but not in the update (Attfield and Kuempel 2008) (Figure 6).

Table V in this paper shows SMRs for NMRD and Pneumoconiosis (and other respiratory diseases) by category of CWP at the start of the survey. On the surface these data are a significant concern with a clear trend across categories of CWP (Figure 7). Mean cumulative exposure increases with each increasing radiological category going from 59 mg/m^3-years at category 0 to 116.4 mg/m^3-years for PMF. As one would expect, cumulative exposure is clearly co-linear with CWP category.

Categories 1, 2, 3 and PMF are a result of exposures prior to 1970 and these exposure estimates are biased. All of the radiological categories were due to exposures before 1970, since the data on each individual was collected 1969-71 in both studies and the only thing updated since then has been vital status. Work histories, and, therefore, exposure as well, beyond 1970 are unknown so a maximum of 22 years of exposure are potentially excluded. Thus some portion of all cohorts' work history and exposure are underestimated.

Table VII and Figure 7 show associations for selected underlying causes of death by cumulative exposure. There are no exposure-response trends for lung and stomach cancer, but the exposure-response trends for NMRD and CWP are clear.

These data provide evidence that NMRD and CWP, but not lung and stomach cancer, are caused by CMD with the risk increasing as exposure increases. These data are less useful for establishing a threshold level because the reference group is an external population, and it is not feasible to adjust for potential confounding factors such as smoking and rank

of coal. To do this requires a relative risk, a risk relative to a non-exposed or low-exposed group of similar workers. In the proportional hazard analyses, that referent group is comprised of miners with <49 mg/m^3-years cumulative exposure.

The appropriate analysis for estimating safe exposure levels is developed from the proportional hazard models beginning in Table IX. The HR is similar to the RR where the referent group is the lowest exposure category with cumulative dust exposure category of 0-48.9 mg/m^3-years in a categorical analysis. The HRs are adjusted for rank, smoking, and age, which is not feasible in the life table analysis of SMRs. The results in Table IX, and shown in the authors' Figure 3, tend to confirm the NMRD effects seen in Table VII.

In the Cox proportional hazards model, CWP shows strong exposure-response associations for both underlying CWP (n = 381) and underlying + contributory CWP (n=791). Unlike Kuempel, et al., the weakest association is in the linear Cox model of underlying + contributory CWP showing a two-fold increased risk at 110 mg/m^3-year. For underlying linear CWP, the HR is two-fold at 80 mg/m^3-years, and with the (exposure)^2 term in the model the risk is two-fold at 30 mg/m^3-years.

Figure 7 displays the life-table exposure-response analysis with SMRs for lung cancer, non-violent causes, and pneumoconiosis and other respiratory diseases. There were exposure-response associations with NMRD and even more so for CWP. There were no associations with lung and stomach cancer. Data were not shown for the combined category of chronic bronchitis and emphysema and as an underlying cause it was not associated with CMD exposure (RRs 1-2). With chronic bronchitis, emphysema and CWP on the death certificate (n = 226) the RRs were 4-8 across exposure categories.

Proportional hazards models were used to assess exposure-response association of NMRD with CMD. The HRs approximate a RR. There is a strong exposure-response trend and significant linear trend with a unit risk = 1.0071 (1.0046-1.0096) per mg/m^3-year (Figure 8).

Risks of NMRD were also evaluated by four coal ranks in the proportional hazards model from high rank to low rank: anthracite (rank 1), East Appalachia (rank 2), West Appalachia (rank 3), and Mid-West (rank 4). These data show that the risk of NMRD is from the four-fold increased risk of anthracite, and no increased risk is associated with the lower ranks of coal (Figure 9).

Additional Comments and Critique of Attfield and Kuempel (2008)

This study has a number of points that make it an improved version of the original study by Kuempel, et al. (1995). Extending the follow-up period substantially increased the time for disease to develop, thereby eliminating inadequate latency as a reason for no increased risk for CBE. The number of deaths is quite large (33% mortality) and generally adequate for more extensive analysis.

An important limitation involves the estimates of cumulative dust exposure. At least two of these are discussed: (a) cumulative dust exposure estimates are incomplete and do not include CMD exposure occurring between 1970-1993; and (b) the accuracy and reliability of the absolute concentrations for different jobs.

(a) Work histories are incomplete as tenure and job histories post-1970 are unknown, and, therefore, not included in work history. As a result, up to 23 years may be excluded from work histories in the study, thus potentially biasing exposure-response associations by under-estimating exposure and over-estimating risk.

(b) Cumulative dust exposure is based on back extrapolations from mine operator sampling data collected in 1970-72 and adjusted using BOM data from 1968-69. The protocol and assumptions used in making these retrospective estimates are biased low for high exposure jobs (leading to overestimated risk), which means the fibrogenicity of CMD is biased high. In low exposure jobs, exposure is over-estimated and risk is under-estimated so the slope of the exposure-response should be less steep.

Cumulative exposure = Σ (intensity for each job) x (time working in that job), where tenure is before 1970. Computation of cumulative exposure is described by Attfield and Morring (1992a). The actual sampling data came from about 4,300 gravimetric samples collected by the BOM in 1968-69 in 29 underground mines, 17 of which are in this study combined with the mine operator compliance data from 1970-72.

Comments have been made that data available (or not available) prior to 1970 yield less reliable exposure estimates than estimates made from actual samples that began to be collected after development of a standard in 1969 (Seixas, Moulton et al. 1991).

Additional biases are also troublesome. One is recall bias from the 1970 work history questionnaires. They have not been validated and their completeness and accuracy are unknown. Another potential bias is the use of mine operator samples. Submitted mine operator samples were collected for compliance rather than representative values. The data indicate that, in general, mine operator samples are lower than federal mine inspector samples and the latter were excluded from analysis. When this occurs it may result in spuriously low levels of exposure associated with disease outcomes. It is the nature of business to be in compliance and not to be cited for overexposure. Thus, the possibility exists that mine operator samples may be submitted that justify this end. The magnitude of this potential bias is not known. Without detailed information from the involved mine operators, this remains a largely unanswered concern.

Many adjustments and estimates went into the development of the matrix of environmental values. One such questionable adjustment occurs when no data exist for a particular mine/occupation/year category. Data exist for the same occupation/year across several mines and these are used to estimate the stratum in question. The authors have confidence in their estimates and say they are unusually accurate and precise compared to estimates in other studies. On the other hand, others have indicated that even when large amounts of exposure data are available, estimates are subject to error (Seixas, Moulton, et al. 1991) Seixas, et al. have organized and evaluated a great deal of data in a very systematic fashion and have accounted for numerous potential biases. Some factors, however, are beyond the ability to ascertain accuracy or control in this and other studies.

In conclusion, there is clearly sufficient concern with many unknowns, especially with estimates of exposure including a multitude of adjustments to the data, to make one extremely cautious. For one reason (alone), the pre-1970 estimates are quite likely underestimated, and maybe grossly so.

Most of the data clearly indicate an association between CMD exposure and CWP mortality with a threshold at about 80 mg/m^3-years for NMRD (Figure 8). These thresholds are probably higher because of the underestimation of exposure.

Figure 7 indicates a 14-fold increased SMR for pneumoconiosis for coal miners with CWP 3 and PMF and about a seven-fold increased SMR for CWP 2. There clearly is excess mortality for CWP 2+. Whether there is an excess for CWP 1 is less clear as the SMR for category 1 already shows a two-fold increase when one would expect an SMR around the null. If this were an SRR, the value for category 1 would be approximately 1.03, for category 2 about 3.2.

The most interesting finding is in Figure 9 where all the excess mortality from NMRD, and probably CWP as well, occurs only when mining high rank coal. NMRD SMRs are at the null for lower ranking coals in eastern Appalachia, western Appalachia, and the Midwest. It would be interesting to do an exposure-response analysis by rank of coal and including quartz exposure as well. It is possible the association between CWP and CMD exposure is largely confined to high rank coal and/or quartz exposures as it was in the morbidity studies based on radiographic CWP.

Figure 6

Standardized Mortality Ratios (SMRs) for underlying CWP and mean cumulative coal mine dust exposure category from among U.S. Underground coal mine cohort from Kuempel et al (1995) and Attfield and Kuempel (2008)

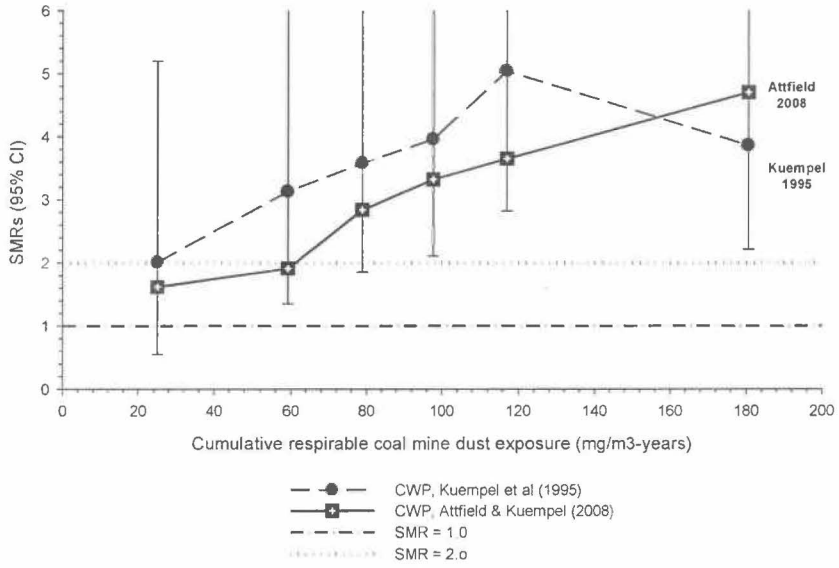


Figure 7

Exposure-response SMRs for NMRD, pneumoconiosis and other respiratory diseases, lung and stomach cancer for underlying causes and mean cumulative coal mine dust exposure
Attfield and Keumpel (2008)

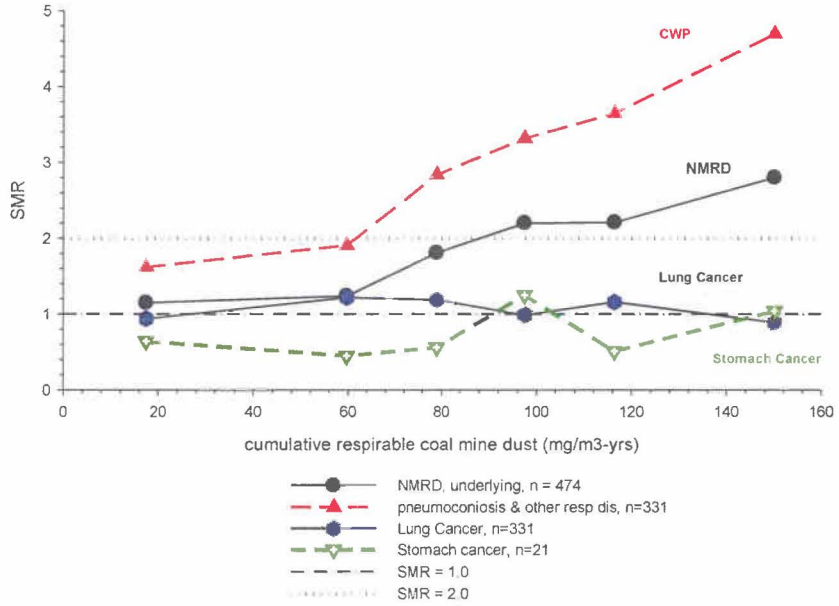


Figure 8

Hazard Ratios (HRs) for mortality due to nonmalignant respiratofy diseases (NMRD) as underlying cause of death
Attfield and Kuempel (2008)

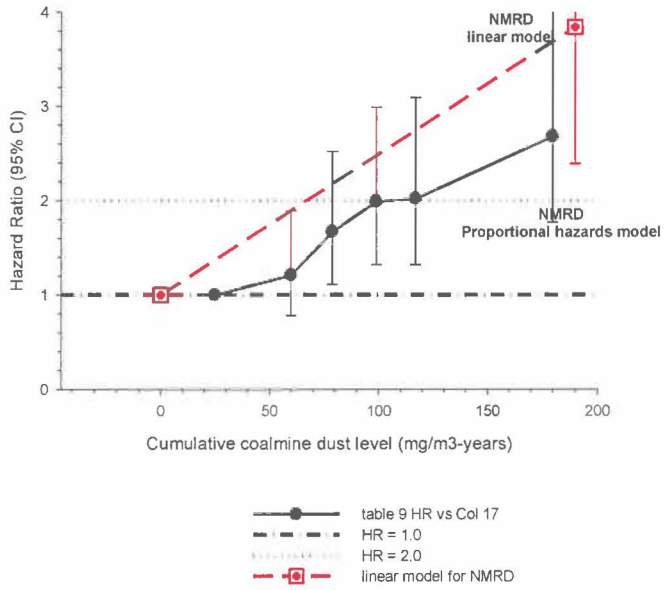
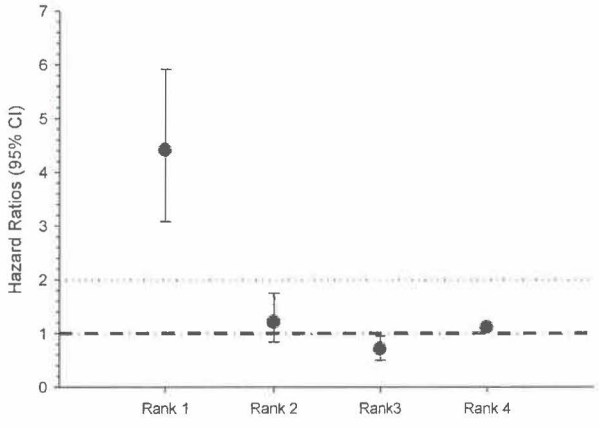


Figure 9

Hazard Ratios (HRs) for mortality due to NMRD
as an underlying cause of death
Attfield and Kuempel (2008)



Kuempel, E, et al. (1997). "Relationships between Lung Dust Burden, Pathology, and Lifetime Exposure in an Autopsy Study of U.S. Coal Miners." Ann Occup Hyg 41(Suppl 1): 384-389.

Summary and Comments

This is an autopsy study investigating relationships between cumulative exposure (measured as coal, noncoal dust, quartz and total dust), lung dust burden, and pathological responses of macules, micronodules, and PMF.

There were a total of 131 cases with 91 smokers and 24 nonsmokers analyzed separately. Mean cumulative exposure was 108 mg/m^3-yrs and was derived from tenure x job-specific mean concentration of CMD. Mean duration of exposure was 36 years, and mean intensity was 3.0 mg/m^3.

Lung burden increased with increased tenure ($r = 0.08$) and cumulative exposure ($r = 0.17$) that may not have been linear for cumulative exposure. Lung dust burden (dose) was a better predictor of pathological response than either duration or cumulative exposure; and the statistical models fit better for smokers than non-smokers.

CMD burden was the best predictor of macules, but quartz lung dust burden was the best predictor of nodules and PMF; smoking status was not a significant predictor for either. Smoking tended to reduce lung burden, suggesting to the authors there was less deposition in the alveolar region (deep lung) because of mucous hypersecretion and dust trapping in the proximal airways combined with enhanced cough clearance.

A 10% probability of PMF was associated with about 70 mg/m^3-yrs respirable coal dust in coal miners who smoked; the probability was 0% below 30 mg/m^3-yrs. The probability of macronodules was about 15% at 30 mg/m^3-yrs.

Additional Comments and Critique of Kuempel, O'Flaherty, et al. (1997)

This cohort of coal miners was from the Beckley, West Virginia area where primarily high volatile bituminous coal is found. It is interesting that the quartz dose showed a greater association with nodules and PMF than the CMD dose. The proportion of CMD and quartz dust lung burdens were 23 for smokers and 28 for non-smokers with mass quartz lung burdens of 1.8 and 2.2 mg/g dry lung weight respectively.

These results support the hypothesis that recently observed progressing CWP observed in this area is related to silicosis (Antao, Petsonk et al. 2005).

Again, these data tend to support the importance of quartz exposure in coal mining, e.g. the best predictor of PMF was the quartz lung dust burden. In total, this is an interesting study but small and not too powerful. For example, the linear fits in the authors Figures 1 and 2 are poor with very little explained variation (8% and 17% is explained). However, the study is, nonetheless, interesting and may implicate quartz exposure and silicosis.

References

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VII. OVERALL SUMMARY AND CONCLUSIONS

A large body of literature on CWP and other coal-related diseases has been reviewed, with major emphasis on US studies and their relationship to the now existing MSHA dust standard of 2 mg/m^3, and the current MSHA proposal to lower the standard to 1 mg/m^3. The evaluation of other studies (largely from the UK) has been used to supplement and/or corroborate a point.

There is a natural progression of thought based in the epidemiological literature that leads to the current situation. Since the 1970s, when an X-ray surveillance program for coal workers in the US began, and CMD standards were initiated, there was a rapid decline in the reported prevalence of CWP from around 30% to 3%, and this decline was coupled with decreasing CMD levels. However, from around 1970 to the 1990s, CMD appeared to stabilize at around 1 mg/m^3 and then decrease slightly. In the 1990s or later, there were reports that CWP prevalence was increasing slightly without concomitant increases in CMD exposure.

In the 2000s, NIOSH reported cases of rapidly progressive CWP. Some miners were described as developing dust-induced disease of high severity over short time periods, and some cases were among relatively young men. While the frequency of these sentinel events was low in absolute numbers, they were nonetheless a serious health concern calling for a determination of their cause and how to prevent their occurrence.

No studies have been conducted to identify specific etiological agents or factors associated with rapidly progressing cases such as a case-control study. The evidence that this reported outbreak of CWP is indeed CWP, and not silicosis, has not been adequately examined.

Aside from the issue of rapidly progressing cases, the current US dust standard is based on data from the UK coal fields; and in 1970, the US standard of 3.0 mg/m^3 became operative, as a transition to 2 mg/m^3 with less than 5% quartz in 1972.

The use of British coal mine data to set a US standard raised concern about the relevance of that data for US mines. The UK has a similar range of quartz and coal rank as in US coal mines. However, both the reported and estimated CWP prevalence appears to be higher at similar exposure levels in the US than in the UK. Thus, the US exposure-response and other studies of CWP provide a further basis for a possible revised MSHA coal mine dust standard.

Two NIOSH data bases exist but for entirely different purposes; one primarily for research purposes and the other primarily for surveillance of CWP.

The first is the NSCWP which is a major research program of NIOSH to assess the relationship of CMD with CWP and lung function in US coal miners. This research program has produced a variety of studies, including two exposure-response morbidity

studies of CMD and radiographic CWP, and one exposure-response mortality study that includes NMRD as a surrogate for CWP.

The NSCWP has two important limitations which make the interpretation of results difficult and questionable. One is the low participation rates which were less than 50% in rounds 2-4. The first round had a 90% participation rate, which is quite acceptable. Like the NCWXSP, the magnitude and direction of this bias is not known, and so the effect on risk estimates is not known.

A second limitation is the potential exposure bias produced by limited environmental sampling information available before 1970. Prior to the 1969 Mine Act, CMD levels were quite high as indicated by BOM sampling and 30% or greater prevalence of CWP. Despite these limitations, exposure estimates in critical epidemiological studies were based on back extrapolations from post-1970 sampling results. The methodology employed seriously under-estimates exposure for the high exposure jobs and provides over-estimates for the lower exposure jobs. As a result the exposure-response curves are biased upward and risk is over-estimated.

Two of the NIOSH studies are based entirely on pre-1970 exposure data, and miners evaluated in these studies were working in dust levels considerably above the current standard. A proportion of miners in a third NIOSH study worked prior to 1970, and some miners were lost to follow-up because of low participation rates in the later rounds of the NSCWP.

The second NIOSH data base is the NCWXSP which began in 1969 and is considered a secondary disease prevention program that involves periodic medical screening. In addition to benefiting the miner, the radiographic interpretations of x-ray films from this program are used in assessing CWP prevalence in the US and often used in various research efforts. A severe limitation of this program is the very low participation rate of the coal miner work force. As a result, there exists a potential participation bias that could produce misleading research results. There has been no investigation of non-participants to determine why participation is low and how those that choose to participate might differ from those that do not. Thus, adjustments cannot be made that would allow the results of these studies to be used for inferences regarding CWP to the entire coal miner workforce. In the main, this program is totally inadequate as a prevention tool, and the data from it are plainly unreliable for estimating prevalence of CWP and for most uses in research studies.

Our review of this very large body of scientific studies has summarized methods, results, and critiques of both morbidity and mortality exposure-response studies regarding CWP and CMD. Issues relating to "sentinel events" and likely quartz exposure have also been evaluated, as has consideration of rank of coal. Our main objective has been to assess the weight of the evidence regarding the proposed change of the CMD standard to 1.0 mg/m^3. Overall, this review has led to several overall conclusions regarding CWP and CMD. These are:

Conclusion 1:

Prevalence (%) data from the NCWXSP are likely biased by low participation. The direction and magnitude of the bias is not known. These data may be useful for assessing trends, but the actual prevalence of CWP in the US is unknown and data from this program remain questionable for use in research studies.

Conclusion 2:

Estimates of pre-1970 CMD exposures are imprecise and biased. The use of an average adjustment factor applied to post-1970 compliance data to estimate pre-1970 data produced biased under-estimates of exposure and over-estimates of risk in high exposure jobs and the reverse in low exposure jobs. The effect is to bias exposure-response trends upward so the curves are inaccurate and produce spuriously low threshold levels of effect.

When adjustments are made for this bias, the associations of excess prevalence at exposures below the standard appear to disappear.

NIOSH should conduct a properly designed analysis of pre-1970 exposures using (to the extent possible) available pre-1970 samples directly. Such an analysis will aid in overcoming the problems that the indirect back extrapolations make the exposure estimates and the exposure-response trends too inaccurate and unreliable for use in setting a new standard base on these results.

Conclusion 3:

"Sentinel health" events such as cases of rapidly progressing disease are unaffected by limitations in participation rates or unreliable exposure estimates. They are events indicating a problem requiring investigation to determine causes and how such events can be prevented.

Our examination of these reports indicates the rapidly progressing cases of pneumoconiosis are more likely to be silicosis being misidentified as CWP. This conclusion is based largely on a number of factors in the SAR region which include: extremely high quartz exposures (two to three times the quartz standard on average); increased mining of low coal seams with high percentages of quartz admixed in the coal; a substantial number of small mines in the region which have demonstrated historically high dust exposures; and longer shifts resulting in higher cumulative exposures of CMD and quartz.

NIOSH should conduct a properly designed case-control study to produce more definitive conclusions as to the etiologic agent and exposure-response relationships,

Conclusion 4:

The prevalence of X-ray readings of category 1 or higher CWP among workers not exposed to dust is considered background prevalence. For there to be excess CWP among coal miners, the prevalence of CWP should be greater than the background prevalence. A background prevalence rate of 5% for category 1 and greater has been suggested by authors of NIOSH studies we evaluated, and this is the background rate we have adopted to assess excess risk. NIOSH and MSHA need to be cognizant of this fact in evaluating studies as it relates to whether percentage prevalence observed is a true finding.

Conclusion 5:

The NIOSH exposure-response studies show a strong association between CMD and CWP 2+ with higher exposures producing excess pneumoconiosis. Excess CWP 2+ was above background prevalence for coal miners exposed to high rank coal at concentrations below the current standard of 2 mg/m^3, or 80 mg/m^3-years. Exposure to low rank coal below the current standard was not associated with an increased risk of CWP 2+. At exposures above the current standards there was some increased risk of CWP 2+ above background prevalence, but not for all coal cohorts.

Note that this conclusion is based on a 5% background prevalence and 80 mg/m^3-year as the standard and does not take into account exposure misclassification bias. Adjustments to the biased exposure-response models are suggestive there may be **no** increased risk of CWP at exposures below the current standard.

Conclusion 6:

The cross-sectional and longitudinal studies of COPD related to CMD exposure show mostly weak and clinically non-significant mean reductions in FEV_1. In the main, these studies are suggestive that CMD exposure at the current standard is unlikely to be an important cause of COPD or clinically reduced FEV_1 in current coal miners. Increased incidence of COPD potentially attributable to CMD is relatively small and only slightly above measurement error or bias. Background prevalence of COPD in the US is needed for more reliable interpretation of US studies. We conclude that CMD does not appear to cause appreciable reductions in FEV_1 in coal miners at current exposures and less than 45-years tenure underground.

Conclusion 7:

While coal miners have an overall less than expected mortality ratio for death from all causes, CMD exposure is strongly associated with significant excess NMRD mortality among anthracite coal miners. However, this association of increased NMRD mortality is not found among miners of lower rank coals (bituminous and sub-bituminous).

This conclusion is based on only one mortality study and NIOSH should test this observation by analyzing exposure-response trends by coal rank. There are no associations with other diseases including CBE, lung cancer and stomach cancer mortality.

Conclusion 8:

Based on the data reviewed in this report, there is inadequate evidence supporting a reduction in the current standard because of increased risk of CWP; and COPD morbidity or mortality from CMD exposure is not scientifically compelling. The NIOSH exposure data are inaccurate and biased so the risks are over-estimated. Work is required to reduce this bias.

NIOSH should conduct, or fund, further research to provide improved data for more accurately determining safe exposure levels. This research could include such things as the following:

- Reanalyze estimates of pre-1970 exposures of studies where the biased estimates were used for relationships with CWP;

- Case-control studies of post-1970 CWP cases to avoid potential biases from low participation and exposure misclassification; and

- Case-control studies of rapidly progressive pneumoconiosis to determine etiology (or test the quartz hypothesis) and exposure-response so needed prevention controls can be instituted where necessary.

APPENDIX A: BIASES AND RELIABILITY OF EXPOSURE ESTIMATES

This appendix discusses limitations and biases inherent in the development of methods used for estimating exposures before and after 1970. The methodology discussed enumerates a host of biases, some of which are not and cannot be controlled in epidemiological studies, especially those involving exposure-response estimates. Moreover, this brief review describes some inherent limitations that exist with the mine operator-based environmental samples contained in the MSHA data base. These biases and limitations are especially important relating to any and all retrospective as well as prospective exposure-response studies. If significant imprecision exists with these exposure estimates, the spurious results that ensue could affect a standard based on health effects.

Seixas, N., T. Robins, et al. (1990). "Assessment of potential bias in the application of MSHA respirable coal mine dust data to an epidemiologic study." Am Ind Hyg Assoc J 51(10): 534-540.

This study utilized both inspector and mine operator samples from 1970-1987. These were full shift personal samples using the coal mine dust personal sampler unit (the "CMDPSU"). Of 314,118 samples, the vast majority was from mine operators (97.2%) and the remainder was from MSHA inspectors (2.8%). The inspector samples were most generally done at the face and due to the likelihood of the mine operator and/or inspectors adjusting certain factors (e.g., ventilation) during sampling, it was reasoned that the inspector samples would not be representative of true worker exposure over time and were thus discarded.

Three biases were noted regarding the use of the MSHA data base which are ungovernable. They include: (1) adjustment to MRE equivalents; (2) calibration concerns; and (3) voiding of samples.

(1) Data recorded in the MSHA data base have been adjusted to be comparable to the MRE instrument (*i.e.*, the CMPDSU) and are adjusted by a factor of 1.6 for face workers and 1.38 for non-face workers. These adjustments to MRE equivalents may not be very accurate in that much depends on the particle size distribution in the dust cloud.

(2) Calibration concerns involve the infrequency of pump calibration. If the sampling pump is not calibrated when the shift is over, exposure estimates may be underestimated.

(3) Voiding of samples with a large number of particles > 10 micrometers. For this bias, it is unclear what "large" means and the voiding of these samples could produce either a positive or negative bias.

At the present time, there is no resolution regarding the possible effect of these three uncontrolled biases.

On the other hand, there appear to be several potential biases which can be remedied. One is the adjustment (noted above) made on either mine operator and/or inspector controls during MSHA inspector visits to keep dust levels down. As result, inspector samples (mostly at the face) are discarded and not utilized. As far as can be determined, NIOSH appropriately accounts for this potential bias and discards the inspector samples.

Another potential bias is concentration-dependent sampling. This can be resolved by obtaining the mean for each occupation within each mine section and the mean of the section means can then be calculated. This calculation provides the mean of section means by occupation, which should be unbiased. Again, it appears that NIOSH utilizes this (or a modified version) in deriving exposure estimates.

Another controllable bias is truncation error which occurs because MSHA uses a truncation procedure on the sampling data. This is a very small bias and Sexias, et al., in subsequent work appears to correct for this bias. Very likely, NIOSH does too.

There is a potential bias dealing with filter cassette weight loss. This is a small error and Seixas, et al., in subsequent work, accounts for this bias and one must assume that NIOSH also considers it.

The last bias noted by these authors is from unexpected low mine operator values. In an evaluation of very low mine operator samples at the face, a comparison was made with inspector samples obtained at the same time. For these very low mine operator samples, *viz*. 0.1, 0.2, and 0.3 mg/m^3, the discrepancy between them and the inspector samples were 13%. In dose-response articles by NIOSH, it is unclear if an adjustment is made for this bias. However, one must assume adjustments are being made as researchers doing dose-response studies often refer back to the procedures outlined in this and other similar articles. However, this 13% bias is significant and was determined on the basis of very low mine operator samples. Apparently an assumption exists that the magnitude of this bias remains somewhat constant over all values of mine operator samples taken at the face. If so, this assumption has not been tested. Since most samples taken at the face are higher than what was used to derive this 13% adjustment factor, discrepancies involving higher mine operator samples at the face could change the magnitude of the 13% adjustment factor by an unknown amount.

On balance, this 13% adjustment seems appropriate as long as it is utilized by researchers using the MSHA data base. However, it is clear that mine operator samples used for compliance purposes must be viewed with extreme caution.

The authors provide anecdotal information regarding why there are so many low mine operator samples. In part, their information coincides with similar anecdotal information obtained elsewhere. On this issue, it is only the mine operators and the individual miners involved with this study that can provide enlightening information.

The authors conclude that if the adjustments noted in this paper are made, then exposure estimates will be as unbiased as possible using MSHA mine operator data. Overall, it seems that of all the biases considered, there are only two of major significance; *viz.* the ungovernable MSHA conversion factor used to gain MRE equivalents, and the adjustment for low mine operator values.

This article describes a well thought out study with good benefit for those using the MSHA mine operator data base to perform dose-response studies. The estimates that are derived with adjustments noted are then applied to mine worker history information where another potential and invalidated bias can occur, *i.e.* their work history.

Seixas, N., L. Moulton, et al. (1991). "Estimation of cumulative exposures for the National Study of Coal Workers' Pneumoconiosis." Applied Occupational & Environmental Hygiene 6(12): 1032-1041.

This study uses the same environmental data base as noted in the previous study (above), i.e. 300,000+ MSHA mine operator samples. The authors note that pre-1970 environmental data are sparse and do not yield reliable data. Few would disagree with this. However, pre-1970 environmental estimates are relevant to this study because post-1970 estimates are the basis for extrapolating backwards to the former.

The purpose of this study was to derive cumulative exposure estimates for a subset of workers from the 4th round of the NSCWP who had been working in mines during rounds 1 and 2, regardless of whether they were still working in the same mines (Attfield and Seixas 1995) . The subset of miners totaled 1,270 men whose first job began in 1970 or later. The issues about obtaining work histories from memory and the lack of validation to estimate recall bias were noted. Without verification the magnitude of this potential bias remains unknown.

All of the biases mentioned in the 1990 Seixas, et al. article are reiterated here. There is a clear discussion of "what exactly" was done (p. 1036) to derive the exposure estimates. It becomes clear that the 13% upward adjustment for face occupations is done (or at least it is in this study). However, there are concerns as to whether this is only a partial adjustment and whether some bias remains.

The correlation between the cumulative exposure estimates and tenure underground is fairly good (r=0.71) and is encouraging.

Unadjusted mean values (mg/m^3) by strata level and broad occupational groups are detailed in the authors' Table II. Considerable variation exists as can be seen by the large means of the standard errors. The authors report that others have estimated the sampling and analytic error of MSHA samples may be about 20-30%, assuming good technique. Using improper technique could make these errors even greater. That amount of error in technique (if existing) could be significant relating to any exposure-response estimates.

Again, the authors comment on the very low MSHA mine operator sample results. While they adjust for an apparent discrepancy due to low sample values, they note that they may have controlled (in part) for this bias. The data and methods used in this study were apparently not meant to derive actual exposure-response estimates for a specific purpose, but were more an example of how to use the methods.

The authors' note that estimates of exposure for epidemiological studies is difficult and subject to error even where large bodies of exposure data are available.

It is very important to be cautious about using compliance data for worker exposure as they may not be representative of actual exposures. Seixas, et al. realized this overall issue is highly crucial and they have done a "yeoman's" job of considering the many factors affecting estimates. They have organized and evaluated a great deal of data in a systematic fashion and have accounted for numerous potential biases. However, factors remain that are beyond their (and possibly MSHA's) ability to ascertain accurately or control.

Attfield, M. and K. Morring (1992a). "The derivation of estimated dust exposures for U.S. coal miners working before 1970." AIHAJ 53(4): 248-255.

The data used in this article are from the 1st round of NIOSH's NSCWP (1969-71), the BOM (1968-69), and MSHA (1970-72).

A major concern with the NIOSH data is the recall ability of miners on the work history. No validation of recall ability has been made.

The BOM data in 1968-69 were perhaps the very first gravimetric sampling done in US mines and 17 of the mines where sampling was done were part of the NIOSH NSCWP. For comparative purposes with MSHA data, the BOM data were converted to MRE equivalents by utilizing a factor of 1.6. Limitations with this factor have been noted previously. Job-specific ratios were obtained via comparison of the BOM (68-69) and MSHA (70-72) data. The job-specific ratios can be obtained from Table 1 in the article. An overall mean ratio of 2.3 was calculated and applied to the MSHA job-specific categories, and then back-extrapolated to the pre-1970 work experience of the miners. Or stated in a slightly different manner, this would be multiplying the 1970-72 MSHA job-specific mean dust levels by a factor of 2.3 and back-extrapolating the values to the pre-1970 experience.

The MSHA data set involved mine operator samples collected from 1970-72. Post-1970 environmental estimates were taken directly from MSHA mine operator data. Estimates for 1970 (alone) were derived in a manner like that for pre-1970 data and the factor derived was 1.26. Calculations of exposure were rather straightforward. For the years 1968-69, all BOM job-specific means were higher than existed for MSHA data in 1970-72. It is unknown and cannot be calculated what the various ratios (outlined above) would be if gravimetric sampling data existed prior to 1968.

The actual BOM sample results from 1968-9 were not used by NIOSH in a direct manner to estimate pre-1970 coal mine exposures. They were replaced by estimated exposures calculated in the manner noted above and a universal adjustment factor of 2.3 was derived.

For example, an exposure to a continuous miner operator using the NIOSH method versus direct use of the BOM data would derive different results.

- The BOM data for a continuous miner operator indicated a mean concentration of 6.8 mg/m^3.
- The MSHA data for the 1970-72 period for a mean continuous miner operator indicated a mean concentration of 2.4 mg/m^3.
- The actual conversion factor for a continuous miner operator would be 6.8 ÷ 2.4 = 2.8.
- Using this conversion factor, the estimated exposure concentration would be 2.8 X 2.4 = 6.7 mg/m^3.
- Rather than using job-specific conversion factors, NIOSH calculated a universal factor of 2.3.
- Using the NIOSH universal conversion factor, the estimated exposure concentration used in NIOSH studies would be 2.3 X 2.4 = 5.5 mg/m^3.
- Thus, for the continuous miner operator job category, the NIOSH approach would underestimate the exposure by 22%.

These extrapolations are biased because they are based on an average ratio, which appear to over-estimate risks in high exposed jobs and under-estimates risk in low exposed jobs, (see Figures 1 and 2).

The effect of this bias is to make the exposure-response curve spuriously steeper. This bias is applicable to the first morbidity study of CWP (Attfield and Morring 1992b) and the last mortality study (Attfield and Kuempel 2008) where only pre-1970 data are used. The other morbidity study used both pre- and post-1970 exposure (Attfield and Seixas 1995). The latter authors noted the potential under-estimation bias in exposure via "probable systematic underestimation of higher dust levels brought about by certain mine operator sampling practices over the years" and special sampling exercises that showed "operator sampled dust levels were indeed systematically lower than those collected by inspectors" (Attfield and Seixas 1995).

How much steeper the slopes are made by this bias cannot be estimated without more data. The bias effect could be calculated by NIOSH. Using the actual BOM pre-1970 sample data appears to be a more direct way than back extrapolation based on ratios of two incomparable data sets. The data sets are incomparable with regard to time (1968-69 vs. 1970-72) and sample source (BOM-collected samples vs. operator-collected samples).

Another method might relate to the non-use of the 2.3 and 1.26 factors that are calculated as averages across jobs. Actual job-specific means were available for both BOM and

MSHA data. Their use could possibly have been applied directly and the bias issue would have been ameliorated to some degree.

Figure 1

Mean dust concentrations (mg/m3) by job, year (pre-1970 to 1977), and data source: Attfield and Morring (1992) = BOM samples, 1968-69; NIOSH adjusted estimates = (Mean Operator samples 1970-1971) x 2.3; Parobeck and Jankowski (1979) Operator samples 1974 and 1977

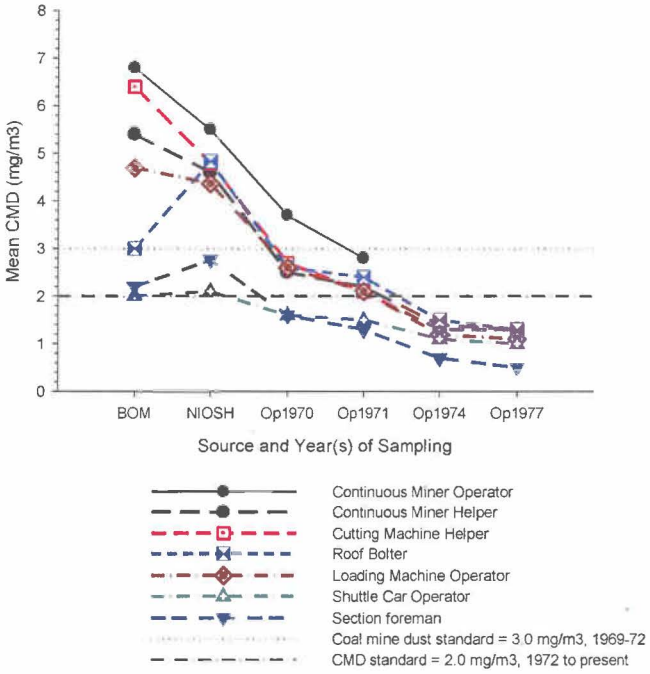


Figure 2

Effect of NIOSH using average adjustment factor for estimating pre-1970 exposure from 1971-2 Coal mine operator data
Attfield and Morring (1992)

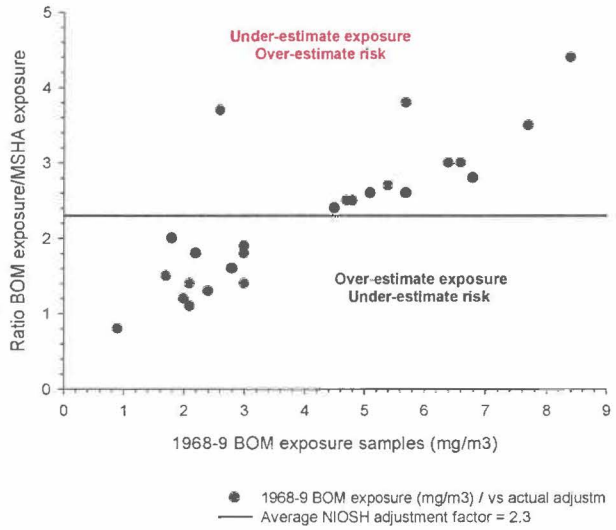
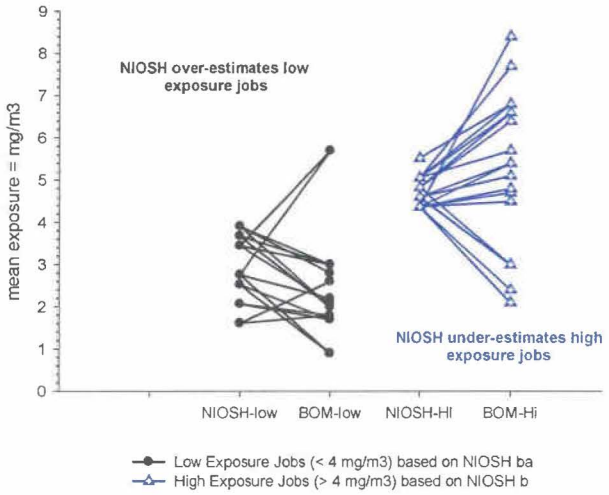


Figure 3

Effect of NIOSH using average conversion factor of 2.3 for estimating BOM pre-1970 job exposures using MSHA compliance data
Attfield and Morring (1992a)



The issue of stability of exposures has been recognized and a consensus was reached that dust levels increased in the 1950s with mechanization and remained stationary until passage of the 1969 Mine Act. This is little more than educated guess work and it is plainly unknown (but important). An attempt was made to explain temporal changes in exposure by using particle count data from 1961 (14 Pennsylvania mines), converted to gravimetric units, and comparing the means for nine jobs with 1968-69 BOM data. The authors found somewhat close correspondence; i.e. 3.7 mg/m^3 and 4.4 mg/m^3 respectively. This approach is an indirect and novel way to evaluate temporal changes in dust levels prior to 1970, but the fact remains that this issue is unresolved.

The estimates derived in this article are more of an example of methods utilization than straight-out application of the estimates. However, these methods for deriving pre-1970 estimates were used in later studies. Nowhere is it stated whether the adjustments (for various biases) to MSHA data suggested by Seixas, et al. were performed on the 1970-72 MSHA data used in this report. One would expect these adjustments were made as the lead author on this report was a co-author to Seixas, et al. in the 1991 report.

This is a rather complex study that is well done, but does have more than a few limitations.

Attfield, M. and K. Morring (1992b). "An investigation into the relationship between coal workers' pneumoconiosis and dust exposure in U.S. coal miners." AIHAJ 53(8): 486-492.

and

Attfield, M. and N. Seixas (1995). "Prevalence of pneumoconiosis and its relationship to dust exposure in a cohort of U.S. bituminous coal miners and ex-miners." Am J Ind Med 27: 137-151.

Both of these articles have either been commented on or considered in a different context. The purpose for listing them here is that both have utilized the methodology outlined in the previous three papers. On balance, the derivations of dose in these papers seem consistent with the procedures previously outlined, along with the attendant limitations and biases involved. The exposure-response estimates in these papers are markedly higher than previously estimated from the early British data. However, it is clear that a number of concerns exist with the MSHA compliance data used in exposure derivations that have yet to be clarified.

References

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Attfield, M. and N. Seixas (1995). "Prevalence of pneumoconiosis and its relationship to dust exposure in a cohort of U.S. bituminous coal miners and ex-miners." Am J Ind Med **27**: 137-151.

Seixas, N., L. Moulton, et al. (1991). "Estimation of cumulative exposures for the National Study of Coal Workers' Pneumoconiosis." Applied Occupational & Environmental Hygiene **6**(12): 1032-1041.

Seixas, N., T. Robins, et al. (1990). "Assessment of potential bias in the application of MSHA respirable coal mine dust data to an epidemiologic study." Am Ind Hyg Assoc J **51**(10): 534-540.