Safety in Mines Research Advisory Committee

Final Project Report

Respiratory Diseases among South African Coalminers

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SIMHEALTH 607

March 2002

Executive Summary

1. Background

In many studies published in the international literature, occupational exposure to dust among coal miners has been associated with adverse respiratory health outcomes in a dose-related fashion (i.e., increasing exposure dust is associated with increasing likelihood and/or severity of the adverse outcome). These adverse outcomes have included:

- **Coalworkers' pneumoconiosis (CWP).** CWP is reflected by the presence of increased densities in lung tissue which are visible on chest radiograph as increased opacities.
- **Accelerated loss of lung function**. In some coal miners, this loss of function has been of sufficient severity to result in clinically significant chronic obstructive lung disease (COLD).
- **Emphysema** diagnosed at autopsy. This is seen as the destruction of gas exchange regions of the lung (alveoli). These autopsy findings often are correlated with loss of lung function while the person was still alive.

There are no previously published studies investigating the respiratory health of coal miners in South Africa. The current study was designed to investigate whether such dust related health problems appear present among South African coal miners.

Specific aims of the study included:

1. To estimate the prevalence of coal worker's pneumoconiosis (CWP), reduced levels of pulmonary function, and chronic obstructive lung disease (emphysema and chronic bronchitis) among living and deceased South African coal miners;
2. To investigate dose response relationships between these health endpoints and respirable coal dust while controlling for potential confounders such as cigarette smoking; and
3. To develop a set of evidence-based recommendations for the South African coal mining industry to address any risk for work-related adverse respiratory effects.

2. Study Design

Parallel assessments of living and deceased coalminers were conducted. A review was conducted of all coalminer autopsies performed by the National Centre for Occupational Health between 1975 and 1997 that were captured on a computer database system known as PATHAUT. A validation study by 3 pathologist verified the findings of interest in the PATHAUT database. Of the 5714 cases that were eligible for analysis, 3176 (40.93%) had exclusive coal exposure - most analyses were run on this subset.

The assessment of the living workers was conducted on a sample of miners (including both active miners and those who had left the industry), who had been employed for at least one year in underground mining between the years 1985 and 1998 in one of three mines in Mpumalanga owned by the participating mining corporation. A total of 896 workers participated in the study, of whom 212 were ex-miners and 684 currently employed. Associations were investigated between measures of exposure and respiratory outcomes, based on questionnaires, lung function testing (spirometry) and chest radiographs.

Exposure estimations were derived through the use of historic dust sampling data together with dust samples collected by the research team in each of the mining operations. Cumulative exposure to respirable dust was estimated for participating miners through a combination of these historical and current exposure samples, written work histories, miner interviews and other record review.

3. Results

Key findings are summarised in the box below:

- **Measured dust levels were generally within legal standards in South Africa**
- **Significant associations between dust exposure and health outcomes were seen both among the living cohort and in the autopsy study. Nevertheless, prevalences of disease were considerably lower than that those which have been seen among South African gold miners.**
- **Over a lifetime of 30 years of employment, the magnitude of the loss of lung function is of about the same size as would be expected from five years of aging.** In other words, the effect of exposure to dust would make the lung function of an exposed coal miner upon retirement looks similar to that of a never-exposed man five years older than the miner
- **Miners who left employment before normal retirement age experienced a 128ml greater exposure-related loss of lung function than those who remained employed, suggesting that there are subpopulations of miners particularly sensitive to the adverse effects of coal dust.**
- **A past history of TB was associated with a striking loss of lung function, equivalent to that from 17 years of aging.**
- **In the autopsy study, coal miners with the greatest number of years of work underground (12-55 years) had a striking 15–fold risk of emphysema compared to miners with the fewest number of years of exposure (0.1 - 3.5 years)**
- **Smokers had a three-fold increased risk of emphysema as compared to lifetime never smokers**

Although the study found an overall moderate to low prevalence of coaldust related diseases among the study population, important dust related findings in declines of lung function were observed.

The prevalence of pneumoconiosis diagnosed by chest x-rays was low at 2.59% (this is the mean prevalence of the two readers). On autopsy, amongst those exclusively exposed to coal, the prevalence of CWP and silicosis was 6.95% and 10.22% respectively, with the prevalence of moderate to marked emphysema of 6.45%. Symptoms of chronic bronchitis were reported in 11.30% of the living population, with 10% reporting with symptoms of breathlessness and wheezing. Only 2.93% of workers reported having had previous TB.

The effect of coal dust exposure on declines in lung function was equivalent to a loss of five years of breathing capacity over a lifetime of employment. This was irrespective of the age of the coalminer, his smoking status or past history of TB. As an illustration, for a 40 year old, 170cm tall man, dust exposure alone has an effect of a 1.33ml loss in FEV_1 per year per mg/m^3 dust exposure. While seemingly small, over a 30 year working life period, upon retirement, such a coalminer has the effective breathing capacity of a non exposed worker five years older.

The above estimate of exposure related decline in lung function is likely to be an underestimate of the true effect. The study data provide strong evidence that those miners with the most significant respiratory problems and the greatest sensitivity to coal dust exposure are the ones most likely to leave employment before normal retirement age and/or move from higher exposed to lower exposed jobs. An example of the evidence for this kind of "healthy worker survivor effect" is that there was an unexpected **inverse** relationship between exposure and respiratory symptoms when looking at the entire cohort. When stratified on employment status (i.e., active versus retired), this inverse relationship was no longer present, and, in fact, was now in the expected (i.e., reversed) direction for the retired miners. Another example of evidence of a healthy worker survivor effect is that current miners had, on average, a 128ml greater FEV_1 than ex-miners, while adjusting for age and other risk factors. Past history of TB had a striking effect on lung function, resulting in an average 698ml decline in FEV_1. This is almost equivalent to a 17 year loss due to age alone.

In the autopsy data, a miner in the higher exposure category (12 to 55 years of work in a coalmine) had a 15 times greater chance of developing emphysema compared to a worker in a lower exposure category (0.1 to 3.5), while adjusting for the effects of smoking. Smoking status itself (i.e., ever smoker versus never smoker) resulted in only a two times greater risk for the development of emphysema.

Smoking in this sample was generally low (mean pack years = 4.34), with over 40% of the entire sample not having smoked in their entire lifetime. Smoking is known to independently result in loss of lung function and emphysema. This result was seen in our study. Pack years was statistically significantly associated with declines in lung function. In the pathological data, smokers were three times as likely to have emphysema as never smokers, an increased risk notably lower than that related to coal dust exposure status. The prevalence of pathological outcomes were persistently higher amongst ex- and current smokers than never smokers (e.g. 17.94% of smokers had significant emphysema compared to 4.78% of non smokers).

There is a good degree of confidence in the respirable dust cumulative exposure estimates, in part because they are based on the combined usage of historical and current sampling data. Historic exposure levels (from 1991 forward) across the three the mines ranged from averages of average range of 1.30 – 2.56mg/m^3 at the coalface - the majority of these are below the statutory limits in South Africa. Results of the investigator collected dust data were quite similar.

In considering the positive findings described above, it should be kept in mind that the absolute level of work related respiratory diseases appears substantially lower than that which has been shown in South African gold miners. In autopsy studies, gold miners had a prevalence of moderate to marked emphysema of about 26% versus the 6.45% in coal miners. Similarly, in a study of ex-miners from South African goldmines, 14% of workers had radiological evidence of pneumoconiosis of ILO grade greater than 1/0, compared to 2.11% among ex-coal miners in the current study.

The current study results strongly suggest that, under currently prevailing conditions in the South African coalmining industry, dust exposures contribute to the development of respiratory disease. This conclusion is reinforced by the independent and complementary findings of exposure related to decrements in lung function in the living cohort and exposure related risk for emphysema in the autopsy study. These findings are quite similar to those reported in the international literature, providing support for the robustness of the results of this study.

4. Recommendations

Given the evidence among coal miners of dust-related adverse effects in respiratory health from this study, the following key recommendations appear warranted:

- Substantially increased engineering controls, such as improved ventilation and ventilation design and improved design of continuous mining equipment, together with work practices designed to minimise exposure.
- Statutory occupational exposure limits for exposure to respirable dust in coalmines should be enforced with a view to aid progressive reduction.
- Health and safety education campaigns for miners emphasising both the hazards of exposure to respirable coal dust but also the particular importance of cessation of smoking for those with such exposures.
- Ensuring that rigorous respiratory medical surveillance programmes, as per the Mine Health and Safety Act (MHSA), are instituted and maintained.
- Review of the dust sampling strategies employed on the mines, including review of the current CIP10 sampler, in terms of assessments being conducted by the Health and Safety Executive in the United Kingdom.
- Further research investigation of the healthy worker effect that may be influencing the data, in particular, prospective cohort studies, which are able to follow both currently employed and ex-miners, may be required to give valid estimates of true lifetime risk.

Acknowledgements

The research team recognises that this large scale project would not have been possible without the considerable support of a variety of organisations and individuals. These are:

- The Safety in Mines Research Advisory Committee, for the funding of the project;
- The Safety in Mines Project Support Services (SIMPROSS), for their ongoing advice, support and interventions at various stages;
- The National Union of Mineworkers National Health and Safety Desk, for facilitating the interactions with their structures at the participating mines;
- The Shopstewards' Committee at each of the mines, for ensuring the active participation of their members in the project and for their continuous support during the data collection phase of the project;
- The senior executives of the Ingwe Mining Corporation that accepted to become a partner in this project. Their facilitation of the proposal amongst Corporate management ensured the smooth process at the mining operations;
- The three mining operations that participated in the project: Douglas Collieries, Koornfontein and Khutala. All the individual members of staff at each of the mines that participated in the project, including the Medical Services, the Safety Managers and the Occupational Hygiene sections, Human Resources and Industrial Relations at each of the mines, for their patience in addressing our numerous demands and, at times, what must have been strange requests!
- The roles played by Dr Steve Goosen, Mr Frans Gume, Mr Reg de La Hunt and Mr Eugene Dabner;
- Drs Francis Green and Val Vallyathan for participation in the autopsy review studies; Dr Jill Murray (Head: Pathology, NCOH), for her advice and direction in the conduct of the autopsy study, her detailed review of the draft autopsy reports, and Ms Lizet Coetzee for support in the analysis of the PATHAUT database;
- Profs A. Solomon and Neil White for the reading of the chest radiographs.

The principal members of the Research Team (as mentioned on the cover page) would further like to thank the interviewers (Mr Tom Mashigo, Ms Christina Mabuza, Sr Christine Mathibela and Mr Sam Jele) for their commitment to the project; Mrs Mariette Goosen for the chest radiographs; Mr Nathi Ndlovu, for working abnormal hours collecting the dust samples and finally, Ms. Jenny Pillay and other members of the Department of Community Health, Faculty of Medicine, University of Natal, for their strong administrative support.

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Glossary

Emphysema is defined histologically as an abnormal, permanent increase in the size of the airspaces distal to the terminal bronchiole, accompanied by the destruction of their walls. In the centriacinar type, the respiratory bronchioles are predominantly involved, while in panacinar type, the whole acinus is generally uniformly involved. The radiographic definition based on postero-anterior films used in the study: an increase in the lung fields and decrease of the overall pulmonary vasculature. The two criteria that had to be met for this definition: (1) diaphragms flattened for $^2/_3$ of their diameter below the 10th intercostal space, and (2) the presence of radiolucent areas, including the presence of bullae (Kilburn, 1986). In the report, phrases such as “autopsy defined emphysema” or “emphysema diagnosed at autopsy” are meant to differentiate from emphysema diagnosed either radiographically or on clinical symptoms. The latter two methods of diagnosis lack a high degree of accuracy while, when noted at autopsy (under specified conditions), the diagnosis has a high degree of certainty.

Coal Workers’ Pneumoconiosis: Histologically this was defined by the presence of coal macules distributed primarily in the upper lobes of the lungs, surrounded by focal emphysema; and radiographically by “q” or “p” size and shape opacities in the upper and middle lobes (Merchant et al, 1986).

Silicosis was defined radiographically by the presence of small, rounded pneumoconiotic opacities in the lung fields predominantly in the upper lobes of the lung fields. Histological definition used in the study was the formation of characteristic hyaline and collagenous nodules (Weil et al, 1994).

Chronic Bronchitis: The presence of a persistent cough productive of sputum for at least three months in two sequential years (Kilburn, 1986).

Forced Expiratory Volume in one second (FEV_1): The amount of air (volume) exhaled within the first second of a forced exhalation manoeuvre, in accordance with the criteria set out by the American Thoracic Society.

Forced Vital Capacity: The total amount of air (volume) exhaled from the lungs during a forced exhalational manoeuvre, conducted according the criteria of the American Thoracic Society.

Clinically important declines in lung function: This refers to a drop in lung function that is greater than what would be expected for an individual of a specific gender, from a particular population, of a specific height and age. Abnormal lung functions are defined when an individual’s test value (FEV_1, FVC or ratio) is lower than the 5th percentile for that particular age and height, based on what would be expected from the population standards (predicted equations). Those workers with FEV_1 less than 65% of predicted are likely to have interference with normal activities of daily living. This value is also used in the report to determine the extent of effect of dust exposure. These lung function concepts are further elaborated in Section 4.10.0.

Cumulative Dust Exposure: an estimate of the total amount of dust to which a worker has been exposed for their duration of employment on the coalmines. This is calculated on the basis of best available knowledge and quantitative data. It takes into consideration the different levels of exposure that each worker is exposed to within a particular area (coalface, backbye or surface) for a specific duration in a particular mine. All of these exposure level-mine-zone-time indices are added up for the entire duration of employment to produce a “cumulative dust exposure” (CDE)

1. Introduction

Exposure to respirable dust in underground coal miners has long been recognised as a cause of pneumoconiotic disease (coal worker's pneumoconiosis). It has also been long understood that advanced pneumoconiotic disease (progressive massive fibrosis) is associated with decrements in pulmonary function. The pathogenesis of coal related lung disease is related to the development of the "coal macule", which is seen in the lung at post mortem. These coal macules arise following exposure to respirable coal dust. These macules are black lesions found mostly in the upper lobes of the lung. Macule formation is due to the attempts of the lung defence system to remove the foreign dust particles. This results in the release of enzymes which subsequently cause tissue damage to the lung tissue adjacent to the macules, resulting in emphysema and interstitial fibrosis, both of which produce the primary coal related pathology, coalworkers' pneumoconiosis and emphysema.

More recent studies conducted over the past fifteen years in a number of countries have repeatedly found a dust-related decline in respiratory function among coal miners without progressive massive fibrosis (PMF) or even simple coal workers' pneumoconiosis (CWP). These studies have usually reported changes in an obstructive pattern with the estimated slopes of a decrement in FEV_1 of 0.69ml to 3.39ml per gram hour/m^3 of cumulative lifetime exposure to respirable dust. Other researchers have contested the validity of these findings, attributing most of these changes to cigarette smoking and claiming that dust related effects are rarely, if ever, of a clinically important magnitude. Our research intended to contribute to this understanding of the relationship of coal dust and respiratory health outcomes. We hypothesised that exposure to respirable coal dust is causally related to obstructive lung disease in a dose-related fashion among South African coal miners.

The number of large studies which have been able to examine the association of dust exposure and pulmonary function with anatomical evidence of obstructive lung disease (emphysema) in autopsies is limited. No studies of the respiratory health of South African coal miners have been published in the peer-reviewed literature.

We tested these hypotheses by looking at respiratory health outcomes among both a sample of deceased coal miners, and a sample of living miners. The development of measures of cumulative lifetime exposure of coal dust by using measures such as years employed or actual environmental sampling, was intended to clarify the dose response hypothesis in both samples.

1.1 Overview

Underground coal miners have long been recognised to be at risk for developing coal workers' pneumoconiosis as reflected in opacities on chest radiographs. In addition, a growing literature from international studies indicates they may also be at risk for the development of accelerated declines in lung function and chronic obstructive lung disease. These risks have been related to the cumulative exposure to respirable coal dust. The level of risk for these outcomes among South African coal miners is unstudied.

South Africa is the second largest coal producer in the world and, at Secunda, has the world's largest underground coal mining complex. Amcoal and Ingwe are responsible, in total, for 85% of the coal mined in the country. Coal mining in South Africa dates back to the middle of the previous century with the discovery of the mineral in the midlands of the then Natal province (now renamed KwaZulu-Natal). At that early stage of the development of the industry, immigrants from Britain arrived in large numbers to work on the mines. Bringing with them the strong tradition of British craft unions, these miners advocated for, and were able to obtain, certain measures concerned with their health and safety. These measures included the passing of various laws for compensation, research into occupational related diseases and hazard controls. Indigenous black miners were not afforded the same consideration.

Notwithstanding this early attention to health and safety, research into occupational health hazards in the coal mining industry in the country has been virtually non-existent. The Leon Commission into Health and Safety in the Mining Industry stated, "...The major difficulty faced by the Commission ...is the absence of data which can be used to define occupational risk by class of mine or mineral and by location of workplace within a particular mine" (Leon Commission, 1996).

It appears that occupational disease in the South African mining sector may have been, in general, considerably underestimated historically. A recent research project identified cases of occupational diseases in ex-goldminers from a single district (Libode) in the Eastern Cape province. Of the 800 men randomly selected from the area using data from a mining employment bureau, 238 retired men were subjected to clinical and radiographic examination (446 men from the sample had died and another 116 were currently employed in mining service). Preliminary analysis of the data of 150 of the subjects revealed that 55% of the identified cases had pneumoconiosis (with or without TB) and 32% had TB (with or without pneumoconiosis). Only 32% were considered to have had no compensable disease (Trapido et al, 1996). Calculations suggested that compensation of all such individuals throughout Southern Africa (under the Occupational Diseases in the Mines and Works Act) would result in the near bankrupting of the national compensation fund (Lewis et al, 1996). A similar study of 304 ex-miners, formerly employed by South African mines from a district in Southern Botswana, revealed that 26.6% had a history of TB (a compensable disease for mineworkers), with prevalence of silicosis ranging from 26 - 31% (categorised according to the ILO Classification of Radiographs) (Steen et al, 1997). The majority of the workers in this study were from the gold mines (85.5%), with the remainder from various other mines such as platinum and chrome. These studies, though not focused on coal, suggest that the general prevalence of occupational lung disease among miners in South Africa may be quite high. However, in the face of the lack of scientifically valid data, this remains speculation which will not assist in the development of appropriate programmes to improve health and safety on the coal mines.

The South African recommended standard of 2mg/m^3 respirable dust is similar to the standards of the United States and Britain, who have standards of 2mg/m^3 and 4mg/m^3 (mean concentration at the coal face) respectively (Parkes, 1994). Studies done in the latter two countries have indicated considerable risk from respirable coal dust. Although this has been the recommended level on South African coal mines, the dust levels were reportedly several fold higher until the late nineties. A report commissioned by the governmental agency, SIMRAC (Safety in Mines Research Advisory Committee) in the Department of Minerals and Energy, indicated that according to the Department’s database, in 1996, from a sample of 20 179 coal miners, approximately 25% of workers were exposed to respirable dust levels greater than or equal to 2.5mg/m^3 (Kielblock et al, 1997). This suggests that the prevalence of coal dust related diseases in South Africa may be higher than suggested by anecdotal reports (personal communications with the Head, Pathology Services, National Centre for Occupational Health and various Mine Medical Officers).

Although no scientific study has been conducted in South Africa to determine adverse respiratory health outcomes in coal miners, there have been only a handful of cases submitted for compensation (personal communication, Dr. Audrey Banyini, Director, Medical Bureau for Occupational Diseases). In addition, deceased coal workers being autopsied are seldom diagnosed with occupational related respiratory pathology. There could be several reasons for this discrepancy between higher levels of exposure and lower levels of disease when compared to international studies. These findings could be real, and be due to the higher grade and therefore less toxic character of South African coal. However, other factors could result in apparently low levels of disease. These factors could include the lack of adequate medical surveillance in coal mining operations, and the absence of routine lung function tests and clinical assessments, i.e. low detection rates. In addition, miners could be selected out of the industry, and given that follow up of ex-miners is poor (and for higher exposed Black miners, essentially non-existent), underdiagnosis of ill-health could be occurring.

Recent judicial developments provide a further incentive to carry out research among South African coal workers. The British legal system had to decide in a civil suit whether exposure to coal mine dust is a cause of chronic bronchitis and a disabling loss of lung function as a result of emphysema and small airways disease, in the absence of progressive massive fibrosis. The judge, Mr Justice Tanner, ruled that coal mine dust is a cause of emphysema, which in turn may lead to a loss of lung function. The role of smoking was recognised as playing an important role in the development of these health outcomes, but could not be claimed to be the exclusive cause given exposure to coal dust (Rudd, 1998).

The current study was therefore important for several reasons:
1. The unclear role of exposure to coal dust in causing clinically important declines in lung function, independently of, or in interaction with smoking.
2. The uncertain dose response relationship between exposure to respirable dust and post-mortem outcomes such as emphysema, in coal miners.
3. The apparent low prevalence of adverse respiratory health outcomes among South African coal miners, given the apparently higher levels of measured exposure when compared to international reports.

1.2 Overall Objectives and Specific Aims

The overall objectives of this study were to:
1. estimate the prevalence of coal worker's pneumoconiosis (CWP), reduced levels of pulmonary function, and obstructive lung disease (emphysema and chronic bronchitis) among living and deceased South African coal miners;
2. investigate dose response relationships between these health endpoints and respirable coal dust while controlling for potential confounders such as cigarette smoking;
3. develop a set of evidence-based recommendations for the South African coal mining industry to address any risk of work-related adverse respiratory effects.

These objectives have been achieved by an examination of nationally-maintained autopsy data and a study of a living sample of current and ex-mineworkers.

These overall objectives have been accomplished through the following specific aims:
1. Among a sample of autopsied coal miners; to
    1.1. determine the prevalence and severity of emphysema;
    1.2. determine the prevalence of pneumoconiotic lung disease (CWP and silicosis);
    1.3. determine the prevalence of all compensable respiratory disease including tuberculosis;
    1.4. develop estimates of exposure-autopsy outcome relationships based on reconstruction of historical exposure from available written records.
2. Identify and locate a sample of living current and ex-miners from specific mines through an examination of work records and tracing of addresses of ex-miners.
3. To determine the exposure characteristics for each type of mine and mine process, duration of employment, specific job descriptions, smoking and respiratory health histories of the selected sample of living workers.
4. To obtain historical and new measures of lung function data and chest radiographs of the sample of living workers.
5. To examine confounder-adjusted cumulative dose response estimates for the development of CWP, and decrements in lung function in this sample of living workers.
6. To compare the prevalence of clinically diagnosable disease from the time of exit from the industry to several years later, in order to better characterise the natural history of the disease, not confounded by healthy worker selection effects. This would help elucidate the potential social and economic burden of the disease.

2. Literature Review

Over the last three decades numerous studies have reported adverse respiratory health effects among miners in relation to inhalation of respirable coal dust. (Cochrane and Higgins, 1961; Higgins and Oldham, 1962; McKenzie et al, 1969; Rae et al, 1970; Ryder et al, 1970). While most of the early research was conducted on the British coal mines, later studies included other European and American experience (Attfield and Seixas, 1995; Seixas et al, 1992; Soutar and Hurley, 1986, Carta et al, 1996). These have been based mostly on extensive field research in the British industry, the Pneumoconiosis Field Research (PFR) and, in the United States, the National Study of Coal Workers' Pneumoconiosis (NSCWP). The weight of this scientific evidence has been reflected in legal decisions and in mine health and safety legislation in these countries.

2.1 Coal Workers' Pneumoconiosis (CWP)

Coal worker's pneumoconiosis has been well documented historically (Morgan and Lapp, 1976). There have been various studies which have attempted to characterise the nature of the disease in terms of symptomatology, functional impairment and dust exposure-response relationships.

Progressive massive fibrosis is unequivocally associated with decrements in lung function. The relationship of lung function decrements with simple CWP is less clear. Several studies have been conducted into determining the relationship of particular categories of CWP and types of radiographic opacities with changes in pulmonary function. In a group of 223 US coal miners, no significant differences were observed in FEV_1 or FVC between the different shape and size of radiographic categories, even when stratified on smoking status (Seaton et al, 1972). Contradictory to this, a study of 895 British coal miners (controlling for age, smoking status, height, weight and dust exposure) found that statistically significant declines in FEV_1 and FVC of 192ml and 191ml respectively were associated with small irregularly shaped opacities (Collins et al, 1988). Attfield and Seixas found that the risk of CWP was positively associated with increasing cumulative dust exposure, older age and harder rank of coal. It was estimated that workers with exposure to medium or low rank coal, exposed for a period of 40 years to dust levels of $2mg/m^3$, have a 1.4% risk of having progressive massive fibrosis (PMF) on retirement (Attfield and Seixas, 1995). The reduction in concentrations of respirable dust since 1970 in British mines has reduced the incidence of pneumoconiosis since 1970 by a third (Lloyd et al, 1982).

It would appear that the studies which carefully documented exposure have concluded that there is indeed a dose response relationship between coal dust and CWP. However, whether simple CWP is actually associated with a significant decline in respiratory function is inconclusive.

2.2 Respiratory Symptoms

Symptoms of persistent cough, phlegm production, breathlessness, wheeze and previous chest illness have repeatedly been associated with coal mining. The relative contributions of exposure to respirable coal dust, the quartz content of the mixed dust or confounders such as smoking, to these symptoms are still in some dispute.

Using the British Pneumoconiosis Field Research (PFR) project data, Ashford and colleagues compared the prevalence of symptoms among 30 000 miners with different smoking habits and different categories of pneumoconiosis. The prevalence of symptoms was consistently higher in the smoking and pneumoconiotic individuals. It was shown that symptoms appeared between 17 - 22 years earlier in smokers with pneumoconiosis, than non-smokers without pneumoconiosis. This study provided evidence that coal dust contributes to the development of respiratory symptoms at an earlier than expected age (Ashford et al, 1970).

The US Coal Mine Health and Safety Act of 1969 set the legal respirable dust standard for US coal mines at 3mg/m^3 in 1970, with a reduction to 2mg/m^3 in 1973. Notwithstanding these measures, studies in the US have shown that there are statistically significant associations between cumulative exposure to respirable dust and respiratory symptoms among miners entering the industry after 1970. (Seixas et al, 1992).

Lloyd and co-researchers found 31% of coal miners from a single colliery in South Wales exhibited symptoms of chronic bronchitis, as opposed to 5% in telecommunication workers matched on age, socio-economic status and smoking (Lloyd et al, 1982). There were statistically significant differences between the groups with regard to shortness of breath. A similar trend was seen in the analysis restricted to non-smokers. A study of young coal miners in Sardinia also found an odds ratio at the 75th percentile of cumulative dust exposure for any respiratory symptom to be 2.26 (Carta et al, 1996). This study suggested the presence of symptoms is more prevalent in a younger population of coal miners exposed to moderate levels of dust.

The findings in the literature support the conclusion that a dose-response relationship is present between dust exposure and the development of respiratory symptoms among coal miners, that such symptoms are seen at an earlier age than one would expect for a similar smoking population, and that workers with recent exposures and younger populations of workers are at greater risk.

2.3 Accelerated Decrements in Lung Function

Decline of lung function among coal miners with advanced pneumoconiotic disease has been well documented in the literature (Higgins and Oldham, 1962; Morgan et al, 1972; Cochrane and Higgins, 1961). However, the decrease in lung function in workers with lower categories of CWP is not as apparent and, in the absence of pneumoconiosis, is still the subject of debate.

Among 3581 coal miners from 20 British coal fields (as part of the PFR), a loss of 0.1L in FEV$_1$ was associated with a mean cumulative exposure of 174.8 gh/m^3 to respirable dust, while controlling for smoking, age, height and weight (Rogan et al, 1973). In a longitudinal study of 909 coal miners from Sardinia, conducted over a period of 11 years (1983-1993), the decline in FEV$_1$ per unit cumulative dust exposure during follow up was 0.019L for the 7.08 years of follow up. Decline in FVC and FEV$_1$/FVC ratio was 0.0045L and 0.0788% respectively. In this study the respirable coal dust concentration ranged from 1.73 to 3.05 mg/m^3 (Carta et al, 1996).

Studies conducted in the mid eighties in the UK and the US also reported a decline in lung function. Attfield analysed medical data for miners from 31 US mines from the National Study of CWP (NSCWP) conducted over two periods, 1969-1971 and 1977-1981. Using several regression models, each with different exposure indices, they indicated that over the 11 years, the decline in FEV$_1$ ranged from 0.036 to 0.084L. These models all controlled for age, smoking and height (Attfield, 1985). In a similar study of British miners, data of 1677 coal miners from five collieries who had been subjected to serial cross-sectional epidemiological surveys as part of the Pneumoconiosis Field Research from 1957-1973, was re-analysed as a longitudinal study. Over a period of 11 years the average dust exposure levels prevalent in British mines at the time of the study would have resulted in a decline of FEV$_1$ of 0.087L, while controlling for age and smoking (Love and Miller, 1982).

A more recent study conducted by Seixas and colleagues made use of the data generated by the NSCWP in the US in round 2 (R2) (1972-5) and round 4 (R4) (1985-8). This study looked at miners starting work in a mining environment in or after 1970, the date of the new US standards. Linear regression models controlled for age, height, cigarette smoking status, race and mining state. Higher cumulative exposure at pre R2 was significantly associated with a 0.0304L per mg/m^3 years and 0.0275L per mg/m$^{3\cdot}$years decline in FVC and FEV$_1$ respectively. The fact that at R2 (1972-75), this sample was employed for no more than five years, suggested that the initial years of mining exposure were associated with a more rapid loss of lung function than those with a longer duration of employment (Seixas et al, 1993).

Apart from these findings of decline in respiratory function in the general mining population, other studies have documented more striking losses in specific sub-populations, which suggests that there is a need for the development of more appropriate standards and control measures at the coal face. These sub-populations include those miners more susceptible to the effects of dust exposure, and young miners.

A review of the data for 1867 miners and 2192 ex-miners selected from the original British PFR study was conducted. All those with PMF were excluded. Ex-miners under the age of 65 had lower levels of FEV$_1$ and FEV$_1$ /FVC ratio than active miners while controlling for factors such as age, smoking, height and weight. The difference in the effect of dust exposure in ex-miners under 65 as compared to current miners was 0.21 ml FEV$_1$ gh/m^3 (Soutar and Hurley, 1986). This seemed to imply that a healthy worker effect was present, with those workers in poorer respiratory health, but not yet at retirement age, leaving the mining industry preferentially.

The role of age as a possible effect modifier has been examined by several researchers. In the study by Seixas and co-workers. Separate regression analyses were run for workers above and below the age of 25. The latter cohort consisted only of participants with less than five years of coaldust exposure. A cumulative dust exposure related decrease of 35.8ml per mg-years/m^3 in FEV$_1$ (statistically significant) in miners over the age of 25 was seen, over and above the expected age related lung function decline (Seixas et al, 1993), as compared to those under 25 who had a statistically non significant decrease of 13ml per mg-years/m^3. This study also suggested that the dose-related decline in lung function is more pronounced in newer coal miners that those exposed for a longer period. An initial loss of about 30 ml per mg-years/m^3 in FEV$_1$ was seen in the first few years, whereas the average for 20+ years of mining was 6ml per mg-years/m^3 (Seixas et al, 1993).

While these numerous studies have shown that a probable dose response relationship exists with exposure to coal dust, there seems to be a significant variation in dose response coefficients, with variations from 0.08ml/gh/m^3 - 7.6ml/gh/m^3. These variations could be due to several factors including differences in age mean exposure and duration of employment of the populations studied. The systematic over or underestimation of the levels of exposure in the various countries in which these studies have been conducted could play a role. The regional differences in the grade of coal could be another important factor in the observed differences.

Notwithstanding these differences, there are strong implications that certain populations are at greater risk for the development of decrements in lung function. These sub-populations include younger miners and newly employed workers at the coal face. Another sub-population, irrespective of age or employment status, is those who have a particular sensitivity to exposure, and who subsequently leave the industry at a far earlier age. It is our intention in this study to further explore some of these postulates, especially reviewing data of ex-miners, and to attempt to provide a clearer understanding of the dose response relationships.

[Conversion of the cumulative exposure units from mg-years/m^3 to gram-hour/m^3 (gh/m^3) is by the factor of 1740 hours per year/1000 mg per g - based on the assumption that each miner works approximately 1740 hours per year (Attfield and Hodous, 1992), thus 1mg-years/m^3 = 2gh/m^3. As different authors make use of different units, it is necessary in some instances to use the conversion factor in order to compare the findings in the various studies].

2.4 Clinical Significance of Exposure: Impaired Function and Chronic Bronchitis

While exposure to respirable coal dust may be responsible for the decline in lung function parameters, whether this decrement results in impairment or obstructive lung disease needs to be clarified. The debate of whether chronic bronchitis among coal miners is due to respirable coal dust or primarily to smoking is well documented (Coggon and Newman Taylor, 1998).

In a study in 1970 using data obtained from the second and third surveys of the PFR (UK), 4122 coal face workers were reviewed with respect to "bronchitis" and "smoking" status. The prevalence of bronchitis increased with increasing categories of exposure ($p < 0.001$) and with the presence of pneumoconiosis ($p < 0.0001$). Although subjects were stratified according to smoking status, and prevalence of bronchitis was consistently higher in the smoking category, there was no information on whether statistically significant differences existed between the two categories (Rae et al, 1970).

These findings were contradicted by the investigation of 8 555 bituminous coal workers from the US by Kibelstis et al (1973). This study found that bronchitis was not significantly more common in the non-smoking coal face workers as opposed to non-smoking surface workers, except in the group that had between 10-39 years of face experience. The prevalence of bronchitis increased with age and smoking status as measured in pack years. The authors found that smoking was a more important factor in airways obstruction than job category.

The differences between the Rae et al study and the latter study was that bronchitis was defined with specific time periods (symptoms on most days for at least three months for at least one year) in the former, whereas the latter defined it simply as the presence of symptoms. This definition is likely to have introduced greater variability in the results. This is supported by the findings (Rae et al) that bronchitis appeared to be more related to smoking habits at the time of the assessment, rather than a cumulative smoking history. While Rae et al made use of cumulative exposure measures, Kibelstis et al used usual job as a surrogate measure of exposure.

Becklake continued this debate in her reviews of chronic bronchitis in dusty occupations. The conclusion was that certain dusty occupations such as coal mining resulted in chronic airflow limitation, which could be disabling (Becklake, 1985; Becklake, 1989). Oxman et al (1993) arrived at similar conclusions in their review of the literature, and additionally claimed that while occupational exposure was a cause of marked chronic obstructive disease in smokers, both smokers and non-smokers experienced clinically important losses in lung function. The risk among non-smoking gold miners was three times as large as that for coal miners, although the cumulative exposure of the gold miners was 21.3gh/m^3 compared to that of coal miners of 122.5 gh/m^3. This differential risk was probably due to the higher silica content in gold mine dust (Oxman et al, 1993).

2.5 Role of Smoking

The key controversy with respect to smoking is whether most important effects seen are really due to smoking and not coal dust. Love and Miller, in their study of loss of lung function in 1677 British coal mines (part of the PFR), showed that smoking over an 11 year period resulted in a mean loss of 0.51ml in FEV$_1$ for all participants. The excess decline in FEV$_1$ in current smokers compared to non smokers was 0.111L while controlling for cumulative dust exposure (Love and Miller, 1986). In a sample of British coal miners from the PFR study, followed up 22 years after the initial assessment, it was found that the effect of dust on FEV$_1$ decline in non-smokers was 0.9 ml/gh/m^3 and in smokers, 0.65 ml/gh/m^3 (Soutar and Hurley, 1986).

The data of Rogan and fellow researchers, when analysed by age, cumulative dust exposure and smoking status, showed a greater decline in FEV$_1$ with increasing age, increasing cumulative exposure and cigarette smoking. Both smoking and dust exposure were significantly related to a decline in FEV_1: Regression models indicated that smoking (cigarettes/day) resulted in a decline of 4.6ml while per cigarette/day controlling for age, height and dust exposure. Dust exposure, controlling for cigarette smoking, resulted in a decline of 0.6ml per gh/m^3 (Rogan et al, 1973). No interaction between cigarette smoking and dust exposure was seen. Marine and co-workers found, in a sample of 3 380 coal miners (PFR dataset), that the dust associated gradient for FEV_1 <80% was virtually identical for both smokers and non smokers. The odds of having an FEV_1 < 80% due to dust exposure was 1.29 times greater in smokers than non-smokers while controlling for age. The same researchers found an interaction between smoking and age - the finding of a less than predicted FEV_1 was more likely with increasing age in smokers than non smokers (Marine et al, 1988). In the study on coal miners from the United States, Attfield found that smoking was associated with an average excess reduction in FEV_1 of about 0.1 L over an 11 year period. In contrast, exposure to coal mining dust resulted in a loss of about 0.08 L over the same period (Attfield, 1985).

That the decline of lung function is caused primarily by smoking is strongly argued by other researchers. Morgan has argued that the healthy worker effect in longitudinal studies is likely to affect smokers to a greater extent than non smokers, thus affecting the findings of such studies. Morgan concludes that it is far more important to change smoking habits “than it is to lower dust levels by 20 or 25 percent” (Morgan, 1986). Other authors have challenged this view and concluded that an interactive relationship actually exists between smoking and respirable coal dust exposure in the decline of FEV_1.

Henneberger and Attfield (1996) found that a statistically significant interaction existed between current smoking status and cumulative exposure, resulting in a decline of FEV_1 /FVC of 0.030% per $mg.year/m^3$ amongst current smokers. Interactions were not seen in ex-smokers, suggesting that the effect of smoking is acute and reversible.

Although the comparisons of losses in lung function in most of the above research cohorts are dependent on the relative smoking and dust exposure profiles of the specific cohort, statistically significant losses due to coal dust exposure are evident. The effects of dust and smoking on FEV_1 appear to be additive, but this requires additional research. In more heavily exposed workers (and, especially, sensitive sub-populations) dust effect is in the same absolute range as smoking effects. Studies have repeatedly shown dust related effects among never smokers.

2.6 Autopsy Based Studies

A 1986 estimate indicated that approximately 86% of deceased white miners underwent autopsy in South Africa (Hessel, 1987). There is a centralised storage of results at the NCOH. A 1992 in-house report from the National Centre for Occupational Health (NCOH), which houses the Pathology Automation System (PATHAUT) database, indicated that 54% of white miners and 21.6% of black miners autopsied from the coal industry over a two year period (1988/9) suffered from emphysema of some grade (Mangena, 1992). Apart from this preliminary report, no other comprehensive study of this database has been undertaken among coal miners. This is in sharp contrast to the numerous studies that have been conducted on the South African gold mining industry using this database (Sluis-Cremer, 1980; Becklake et al, 1987; Hnizdo et al, 1991; Hnizdo et al, 1994; Murray et al, 1996; Hnizdo and Murray, 1998).

Early autopsy based studies of coal miners looked for relationships between emphysema and CWP. A sample of 247 Welsh coal miners who had been diagnosed with CWP during life and had an autopsy at a single hospital in Cardiff were selected by Ryder et al (1970). This population was contrasted with matched age and gender population who had autopsies conducted at the same hospital. All coal miners were excluded from this “non-exposed” group. 34.5% of those workers with category “A” pneumoconiosis and lower (n=139) (according to the ILO Classification of 1958) had emphysema scores of 15 or more (with 30 indicating maximum severity). Only 9% of the contrast population had similar scores.

Autopsy studies on British coal miners have been conducted to explore the relationship of autopsy diagnosed emphysema to coal dust exposure, controlling for age, pulmonary fibrosis and smoking. Adult men (in the catchment area of two South Wales hospitals) dying from ischaemic heart disease, on whom post-mortems were conducted, were included in the study. Subjects were categorised into coal worker (n=39) or non coal worker (n=48). An odds ratio of 10.95 for emphysema among coal workers as compared to non-coal workers (smokers and non-smokers combined) was found. The odds ratio for emphysema in coal workers without progressive massive fibrosis was 5.67 compared to non-coal workers (Cockroft et al, 1982). To determine whether any specific dose response relationships existed between the findings of emphysema on post-mortem and coal dust exposure, a subsequent study looked at the autopsied lungs of 450 coal miners, for whom reliable estimates of cumulative exposures were available. While the presence of emphysema increased with the level of fibrosis, 47% of those workers with no evidence of fibrosis had emphysema. In the groups with some degree of fibrosis, a clear dose response relationship of emphysema with coal dust exposure was seen. The authors concluded that a causal relationship was likely (Ruckley, 1984).

Leigh and co-workers reviewed the data of 886 coal worker autopsies conducted between 1949 and 1982 in New South Wales, Australia. Emphysema score was significant for years worked at the coal face; FEV_1 and age at death. Gland-wall ratio was significantly correlated with emphysema score and $FEV_{1.}$ Emphysema was more strongly correlated with pneumoconiosis in non-smokers than in heavy smokers (Leigh et al, 1983).

The studies discussed above clearly show that autopsy diagnosed emphysema is found in coal worker's pneumoconiosis; however, it has not been shown consistently in coal miners without CWP. Only a single study has been able to show any dose response relationship with emphysema and exposure to respirable coal dust. The role of smoking as a confounder in these studies is unclear.

2.7 Healthy Worker Effect (HWE)

The concept of the HWE is based on the premise that workers, especially those in occupations with specific risks, are somehow resistant to poor health effects associated with such risks, and therefore remain in their occupations for a longer period than those more susceptible to the adverse outcomes. Therefore cross sectional and case control study designs, in choosing working populations, are likely to see less of an effect due to particular exposures, as those "sensitive" workers have already selected out of these populations. In studying coal miners, this presents as a significant limitation to determining the effect of coal dust exposures.

The study of Lewis and co-researchers in the United Kingdom found that increasing age resulted in a decrease in the effect of mining exposure on FEV1 and concluded that those workers most sensitive to the effects of underground mining are more likely to leave the industry or transfer to surface jobs (Lewis et al, 1996). Similar conclusions were reached in another study using responsiveness to methacholine challenge as a marker of adverse respiratory effects. Miners with the longest duration of exposure underground had a lower prevalence of responsiveness compared with miners who never worked on the coal face ($p< 0.01$). Workers with more respiratory tract symptoms and lower lung functions responded more to methacholine than those with fewer symptoms and better lung function. They concluded that workers employed in dusty jobs are less likely than unexposed workers to show increased non-specific airway responsiveness, probably due to "health related job selection". Thus studies which do not follow changes in jobs and/or employment status of a cohort from entry into the mining industry forward may underestimate the effects of dust exposure on respiratory health (Petsonk et al, 1995).

2.8 The Role of Coal Grade and Geographic Differences

Regional differences in health outcomes among coal miners have been attributed to the grade of coal mined and the quartz content of the dust. This has been suggested as a reason for the low levels of disease in South African coal workers as silica content in SA coal mines averages less than 5% (Doug Rowe, Department of Minerals and Energy, personal communication). However, a hypothesis put forward by Seaton may contradict this. He claims that the lower ranked coal dust, such as that found in the majority of South African mines, may actually contain more quartz and silicates. He postulates that low quartz content dust may accumulate in the lung and result in emphysema and progressive massive fibrosis, while high concentrations of quartz may produce rapid fibrosis (Seaton, 1983).

In the review of data from 22 different coal mining counties in the United Kingdom, proportional mortality ratios for CWP, chronic bronchitis and emphysema varied from 135 (confidence intervals, CI: 16-488) to 3825 (CI: 1538-7881) for the different regions. There was an absence of geographic correlation for the proportional mortality ratios between emphysema and CWP. This led the authors to postulate that the mechanisms by which coal dust causes these diseases differs, depending on the features of the dust itself (Coggon et al, 1995).

2.9 Description of the Autopsy Data

The study used the PATHAUT database for the autopsy part of the project. Current legislation places an obligation on physicians attending to deceased miners to remove, with family permission, the cardiorespiratory organs and submit them to the Medical Bureau for Occupational Diseases (MBOD) in Johannesburg. The autopsies are performed for the MBOD by pathologists employed at the NCOH.

Three types of autopsies are performed: full body examinations, examinations of cardiopulmonary organs, with access to the other organs (limited autopsies) or examination of cardiopulmonary organs only. Full and limited autopsies are only performed on those bodies that come from within a 100km radius of the NCOH. Deaths further afield result in only the formalin preserved cardiopulmonary organs being sent to Johannesburg. Only full autopsies are subject to lung inflation - preferable for the accurate diagnosis of emphysema. The type and grade is assessed using a grid system of 20 radiating zones. Scores are assigned for centriacinar emphysema and panacinar emphysema in each zone, ranging from 0 - 5. The score for all zones are summed and the total score is expressed as a percentage. A four stage classification system is used: absent; insignificant (up to 33%); moderate (33%-66%) and marked (>66%).

Computerisation of all autopsies began in 1975, when the PATHAUT was instituted. PATHAUT is a single database which combines data from a variety of sources, including coded autopsy summary sheets, occupational histories and clinical files. In brief, the database provides identification data, exposure (mineral) type and years worked in mines, mine at which the worker last worked, cause of death, smoking history (this information is generally obtained from the mining operation’s medical records or the MBOD records), autopsy material description, and macroscopic and microscopic reporting. In turn, medical data and occupational histories can be traced from identification numbers back to the MBOD's data storage system.

There are several limitations with both the PATHAUT database and the MBOD records that were addressed in the study. The first is selection effects in which subjects come to autopsy. Workers who have been fully compensated while alive are less likely to have their bodies submitted for a post mortem because there is no additional compensation. Thus unbiased prevalence rates of disease outcomes cannot be directly estimated from the PATHAUT. In addition, due to the peculiarities of the mining industry in the country, determinations of the population eligible for autopsy upon death is difficult. Families of white miners, who are generally more aware of financial benefits, are more likely to submit organs for assessment than those of black miners (Hessel et al, 1987b). Black miners, upon retiring, return to their homes in rural South Africa, often with little access to health services with diagnostic facilities for occupational diseases, or with little knowledge of legal benefits from the compensation system. These miners are unlikely to have autopsies performed on them as compared to retired or ex-white miners who are better informed of their legal rights. Autopsies on black miners are more likely to be conducted on those who die in while in service or from mining accidents.

2.10 Description of the Exposure Data

The Department of Minerals and Energy (DME) is responsible for legislation which prescribes to mining companies schedules and methods of environmental monitoring. The Minerals Act and the Occupational Diseases in the Mines and Works Act (1973), require companies to determine their dust levels to calculate their contribution to the Compensation Fund (risk levies). This is done according to the following sampling strategy: mining operations are divided into an unspecified number of sampling areas based on expected similarity of dust exposures among miners within each sampling area. The group of miners in each of these sampling areas is referred to as a statistical population. A minimum of five personal samples for respirable dust per each defined statistical population must be collected in each six month period. The total number of samples per statistical population taken should be greater than, or equal to 5% of the miners in the statistical population sampled during the period. Full shift sampling must be done. Analytic methods that are used must be approved by the South African Bureau of Standards. The analysis of the samples must be forwarded on a six monthly basis to the DME, stating details of the areas and populations sampled and any abnormal operation at the time of sampling (DME, 1994). Mines differ in their approach to sampling, with some conducting in-house measurements and others contracting accredited authorities.

Personal sampling was first started around 1985, although this varies among mining operations. Prior to this only area sampling was done. Recently the French gravimetric sampler, CIP10, has been used for dust sampling at a sampling rate of 10L/minute. Prior to gravimetric sampling, thermal precipitators were used. All mines are expected to sample the respirable fraction of airborne particulates using internationally approved standards of occupational hygiene. In a study comparing the measurements of the CIP10 with the US coal mine dust personal sampler unit, the relationship was dependent on the size distribution and density of the aerosol being sampled. The conclusion was that the CIP10 failed to sample according to any of the respirable dust criteria valid at that time, namely the ACGIH and BMRC criteria (Gero and Tomb, 1988). In a UK Health and Safety Executive (HSE) funded project, a seven nation European consortium evaluated eight samplers to determine compliance with the newer sampling criteria (the ACGIH-CEN-ISO standard). These studies have included the CIP 10 (Kenny et al, 1997). While most samplers had poor but predictable efficiency at high wind speeds (>4.0ms^{-1}), the CIP 10 was not as predictable. At low speeds (0.5ms^{-1}), it was one of two samplers (out of the eight tested) which required a correction factor. It also required a correction factor at speeds of 1ms^{-1}. The report also cites other field trials comparing the CIP 10 with the Institute of Occupational Medicine's (IOM) personal sampler, which found that the CIP 10 undersamples by a ratio of 1.5. The more recent report by Görner et al (2001), indicates that the sampling efficiency characteristics of the CIP 10 differ from the conventional 50% cut off of 4.0µm, by 0.26µm, with a slope of 1.43 (convention = 1.5 geometric standard deviation).

No check sampling was done by external agencies or by the governmental department on a routine basis. A recent research report conducted by the Centre for Industrial and Scientific Research (CSIR) compared their own sampling data from four gold mines with the data submitted to the DME. The percentages of workers exposed to lower concentrations (<0.8mg/m^3) were overestimated by the company data as compared to the CSIR data, and this was marginally reversed at higher concentrations (0.8 - 2mg/m^3) (Kielblock, et al, 1997).

2.11 Description of Mining Operations

The study was based at three of four mining operations in the Mpumulanga province. A leading international producer of coal agreed to participate in the study and operations belonging to this multinational participated in the project. In general, mining technology on South African coal mines has changed over the last 15 - 20 years, especially with regard to the use of continuous mining technology, reduction in blasting etc. The actual dates of introduction of advanced technology varied from mine to mine.

2.11.1 Mine 1

This mine is situated 55 km west of Witbank in the Mpumulanga province. It has approximately 1 868 employees. The dominant methods used are underground mining using the bord and pillar method with continuous miners. Some opencast mining is also done. It is estimated that the life of this mine is 38 years. The operation plans to introduce single-pass continuous miners who cut and bolt simultaneously (Group Mining Operations Report, 1997).

2.11.2 Mine 2

This mine is situated 48 km south east of Witbank, with 2 310 employees. The mining methods are, once again, underground continuous miner bord and pillar mining, together with opencast mining. The life of this mine is expected to be 11 years. New ventilation and service shafts were sunk to improve ventilation and reduce travelling time to the sections. This latter engineering improvement is likely to have an effect on the development of cumulative dust exposures (Group Operations Report, 1997).

2.11.3 Mine 3

This mine is located some 25 kilometres south east of Witbank in the Mpumalanga Province. It has both opencast and underground sections. It produces 9.5 million tonnes of coal sales per annum and supplies its products to the export, domestic and local power station markets. The underground operation employs bord and pillar methods using continuous miners and recently introduced continuous haulages to extract coal from the number 2 and 4 seams. The mine has a 20 year life and employs 1600 people.

2.12 Geological Description of South African Coal

The coal found in the South African coal fields was deposited during a 35 million year geological time period. The coal is found in thick shallow lying coal seams, with the majority of reserves in the Witbank area, Mpumulanga province. The rank of carbon content of the coal increases eastwards in the country, but simultaneously, the number of seams and their thickness decreases. Thus Mpumulanga and Northern Province have bituminous coals with seams several meters thick, while KwaZulu-Natal coal is anthracitic and in thin seams (Chamber of Mines, Education/Reference section, 1998). As previously mentioned, the silica content of the South African coal is generally less than 5%.

3. Research Methodology

3.1 Overview of methodology

The overall plan of the research team was to conduct two linked studies:

1. an autopsy analysis which included review of all coal miner autopsies from 1975 to 1997 to determine the prevalence of emphysema and its association with measures of exposure (years worked);
2. an analysis of living miners (both active and those that have left the industry), who have been employed for at least one year in underground mining between the years 1985 and 1998 in one of three mines owned by the participating Mining Corporation. Additionally a sample of surface workers was chosen as a comparison group. Cumulative exposure to respirable dust was estimated through a combination of written work histories, miner interviews, historical and current exposure samples and review of records. Associations between measures of exposure and respiratory outcomes, based on questionnaire, spirometry and chest radiographs, were investigated.

In each of these two linked studies data was also collected on potential confounders, including age, smoking, non-occupational dust exposures, non-coal mining exposures, other respiratory diseases such as TB, family history of TB or asthma/allergies and personal history of childhood respiratory illness.

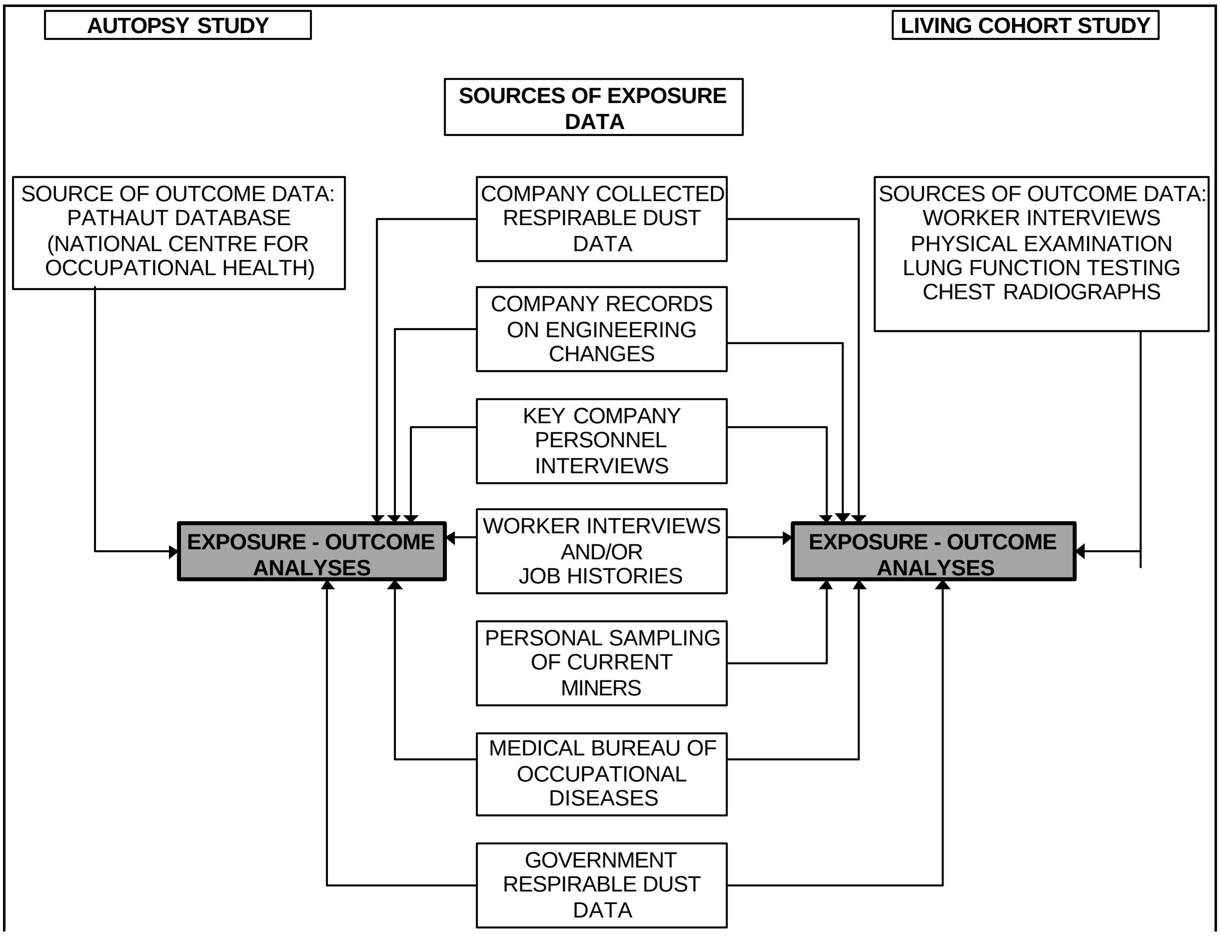

Figure 3.1.1.1 Diagrammatic representation of the methodology showing the linking of the studies

3.2 Autopsy Study: the PATHAUT Database

The objectives of the pilot study were to validate the diagnoses contained within the PATHAUT database, specifically the diagnoses of coal workers' pneumoconiosis, silicosis and emphysema, made by the conducting pathologists at the National Centre for Occupational Health. This validation study was conducted by Dr Jill Murray, NCOH, Dr Francis Green, University of Calgary, Alberta, Canada and Dr Val Vallyathan, National Institute for Occupational Safety and Health, Morgantown, West Virginia, U.S.A.

The process of validation occurred at two levels: histological review and whole lung section review. The assessors independently reviewed histological slides from 30 randomly selected cases of miners on a blind basis without any knowledge of occupational exposure or other demographic information. The purpose of this was to determine agreement between reviewers and PATHAUT diagnoses. Kappa statistics were used to determine agreement. The first review of the histological slides revealed that the majority of slides were from miners with mixed exposure (coal + other mine). A second review was done on the same basis, using slides from 31 miners that worked only in coal mines.

The second step was to independently grade 31 whole lung sections for emphysema, taken from the files of the miner cases in the second review mentioned previously. When available, the Gough Wentworth technique of classifying emphysema using whole lung sections, is highly preferable to microscopic recognition and grading.

Data on all autopsies that were done on coal workers and recorded on the computerised database from 1975 to 1997 was evaluated for prevalence of emphysema, chronic bronchitis, chronic bronchiolitis, CWP and silicosis. The association between the prevalence of emphysema and measures of exposure (years worked was the only measure that was usefully collected on the database) was examined, including multivariable regressions controlling for smoking, age and race.

3.3 Living Sample Study

3.3.1 Selection of a sample of living workers

Based on expected variability in key exposure and outcome measures from previous studies conducted by members of the research team, and by the levels of exposure experienced by the proposed sample, a recommended number of 750 miners was chosen. The original sample size was calculated based on the data from the Seixas et al study (American Journal of Industrial Medicine, 1993; 21:715-734).

- Exposure effect = 0.0055ml/mg/m^3
- Std error = 0.0025
- Power = 0.8
- α (type 1 error) = 0.05

This produced a sample size of 1900. The mean levels of exposure in this population was 1.46 mg/m^3. In our preliminary enquiries, our population had been exposed to levels considerably higher in the past, and lowest levels currently are at least twice as high. Calculations done on 1.5x exposure effect, using the same type 1 error and power data, provided a sample size of 680 and, taking into consideration confounding and other issues, a figure of 750 was decided upon.

The definition of the sample had to consider different categories of exposure. Three groups were decided upon:

- More than 10 years exposure at the coal face
- Between 2 and 10 years exposure at the coal face

- Those currently employed in non-face jobs with less than two years face exposure or an appropriate category of surface workers.

The reason for choosing this stratified population was because of the difficulty in comparing lung function parameters with an external population – the intention was to do internal comparisons. This stratification allowed for a broad range of exposure in the sample, while maintaining comparability on socio-economic status and other environmental factors.

On the basis of this plan, using the following calculation:

- Effect size (mean effect/std deviation) = 0.25 (0.0055/0.025) between low and medium; medium and high exposure groups
- Power = 0.8
- α (type 1 error) = 0.05

resulted in a sample size of 200 per category. Taking into consideration confounding factors etc, this was increased to 250 per category, giving a total of 750. At least 80 – 85 workers per category per participating mine was set as the target figure. With regard to current and former employees, at least 200 of the above 750 miners were to be ex-miners, from the various categories in the three mines, however, because of the high participation rate in the mines, it was decided that having 700 currently employed and 200 former employees increased the power to detect any differences between the employment groups.

Selection of workers using this rationale required considerable data collection. While company databases keep track of current job descriptions, no tracking of previous jobs or exposures is readily available. Unfortunately, even the existing databases was not satisfactory, as one or the other important variable was absent from any one particular database (for example, absent data on dates of engagement in one, or lack of job descriptions in another). This necessitated careful merging of databases, created in different formats. Following this task, all employees graded as category 13 and above were excluded in order to ensure participants remained within a narrow socio-economic grouping. Detailed exposure information on remaining workers was obtained from the employee records. Each worker was then ranked according to their years of exposure at the face and years of no coal dust exposure (surface workers). A random stratified sample of workers based on years of exposure at the face and non exposure was then selected.

In order to effectively characterise the exposure grouping as indicated above, delving into each worker’s employment record was necessary. This meant obtaining detailed information on years worked in different areas in the mine in different job descriptions for as many sub grade 13 workers. Once again, the research team was faced with the task of trying to track down files in the company’s archive, which were not maintained in any strict alphanumeric order. In order to capture this information, the research team had to familiarise themselves with all the job descriptions used at the mine, recorded on their databases and in employee files. Job descriptions follow a specific salary grading and once again, all descriptions graded 13 (i.e. job titles such as supervisory, surface management, human resources or administrative related) or above were ignored. Subsequently, the remaining descriptions were classified into face job, nonface job, surface or a combination of these. This classification was done after consultation with the Human Resources Manager and the Occupational Hygiene Manager at the collieries.

The original strategy for sampling ex-miners was to use the company records or trade union membership data of last known address. Those living within a 100km radius of the mine were to be asked to participate by means of a letter. Transportation costs of these workers was provided.

However, because of the inadequate mining company records, this strategy had to be considerably revised. Our review of the ex-employee records at each of the mines failed to provide an adequate number of employees who met the criteria (primarily residence and duration of employment criteria). Information contained in the company records was generally outdated, hence people had moved from their recorded addresses. Additionally, ex-employees who, according to company records, lived in distant areas (Lesotho, Eastern Cape, etc.) were actually found to be still living in and around the townships of Witbank. During the course of the study, two of the participating mines began conducting retrenchment programmes. Workers retrenched during these programmes were excluded from this group of ex-employees, as their exposure profile would not have been dissimilar to that of the current workers.

Ex-employees were identified in the townships by the fieldworkers. This was not a volunteer sample in the traditional sense (ex-workers were not asked to submit themselves to the project staff, but were solicited after information was obtained about their whereabouts from external sources). Upon identification, the ex-employees were visited by the field worker, informed about the study and requested to volunteer. The study questionnaire was then completed at the individual's home. The worker was then given a notification form informing them of the time and place of the medical assessment. These assessments took place at the Mpungwe Hospital (formerly the Ingwe Hospital). Transport was arranged with the local community taxi association to ferry workers to the assessment venue.

A total of 212 ex-employees were assessed. These ex-workers were analysed combined with the currently employed (n=684) (often in the same regression models, as dummy variables) and also separately to determine whether any significant differences existed between them and the currently employed workers.

3.3.2 Evaluation of exposure data

When using retrospective hygiene data in epidemiological studies (especially where the collection of such data was not intended for such use) there is substantial potential for exposure misclassification. Various strategies have been proposed to minimise such misclassification. In instances where a large set of past measurements are available, the use of regression models to predict the missing information has been successful. In situations where there are a variety of non-random factors such as changes to the production process, product changes and use of protective equipment, these must be accounted for in the modelling approach. One method to do this is to first identify the sources of exposure and factors which are likely to influence exposure levels such as historical changes of the workplace, in production processes and dust control methods such as ventilation. Using this collated information, the concentration of the substance can be estimated through mathematical modelling, using current concentrations as a starting point, together with a multiplicative matrix of factors (Cherrie et al, 1994).

In our study, cumulative exposure variables for each worker were constructed based on job descriptions, occupational histories, which included job titles, and worker interviews. The information available from the DME database was reviewed; however, its utility was limited because of the inability to identify individual workers, or to trace individual workers to a specific statistical population at the mining operation. Exposure data was obtained from two sources: company collected historic data and research team collected data.

Given that the company data is self collected, analysed and reported data, used for regulatory purposes (a system of risk levies are based on exposure data from individual mines), there may have been inherent biases in the information collected. This issue has been investigated by Boden and Gold (1984) in the case of US coal mines. Two methods were used: regression analyses to compare dust concentrations from sampling devices collected by companies with those collected by Mine Health and Safety Administration inspectors and standard coal dust concentration distribution curves for detecting biased sampling. They concluded that company collected samples showed a systematic bias toward lower concentrations.

The sampling by the research team followed standardised occupational sampling strategies for personal monitoring of respirable coal dust. A subset of the selected workers that were previously assessed, working in a representative sample of job descriptions and mine sections, were asked to wear personal dust samplers for a full 8 hour shift. Approximately fifty workers were tested at each mine over three time periods, each period separated by a few weeks. Thus approximately 150 workers were sampled for a total of 450 dust samples. Among the 50 miners sampled in each session, 30 were taken from high exposure areas (coal face), 15 from the backbye and the remainder from surface areas. All of these personal samples were taken from individuals that had participated in the health assessment phase of the study. The analysis was done by the Colliery Environmental Control Services (CECS). Analysis also included assessment for silica content.

3.3.2.1. Sampling methodology

Each worker on whom gravimetric sampling was conducted was briefed about the process. Membrane filter appropriate for respirable dust sampling was used. This filter paper was weighed before use. A sampling train was set up for each worker by a trained occupational hygienist, with the flow rates of each pump calibrated according to the specific needs of that pump. A flowrate check was conducted after each sampling, and if flow rates varied by more than 5%, the samples were discarded. All filters were subsequently analysed by specialist laboratories.

Additional sources of information to be used to characterise exposure included:

1. interviewing knowledgeable company people for information on changes in production methods, production levels, ventilation, etc;
2. reviewing any records of production, engineering, ventilation changes ;
3. interviewing participating miners about work history using a copy of their actual work records to jog their memories.

3.3.3 Description of the occupational history and job descriptions

Occupational histories of the sample of workers employed in the participating mines were extracted from the employment records maintained by the participating mining operations. This involved determining the specific job descriptions of each participant over the entire period of employment at the mine, the specific seam and section worked, and the duration of work in that job description on the seam and section. This was done to enable us to allocate an exposure index to a worker with a specific job description within a specific time period. Details on each worker’s job history at the mine were obtained from personnel files in the preliminary data collection. The completeness of this information was variable across the company records.

3.3.4 Questionnaire and worker interviews

Standardised questionnaires were administered by trained interviewers to each participant. Items covered included demographics, respiratory symptoms, chest illnesses, detailed work histories (past and current employment details), tobacco use and family history. The NIOSH Occupational History Questionnaire used in the US Coal Workers’ X-ray Surveillance Program was modified for obtaining details on lifetime occupational histories. Information extracted from written work histories in company records was available at the time of interview to help jog participant recall. The use of worker interviews to reconstruct a comprehensive lifetime/company work history of individual workers has been validated against company records in a number of studies. Agreement levels typically above 80% have been obtained (Bourbonnais et al, 1988; Baumgarten et al, 1983). Our use of interviews with work histories available to jog the memory of the worker helped to improve validity.

Respiratory symptoms and smoking histories were obtained by using a modified version of the questionnaire used in the Round 4 of the US National Study of Coal Workers' Pneumoconiosis.

There was approximately 5% re-interviewing to test intra- and inter- interviewer variability. The questionnaires were administered in the language of the worker’s choice and were available in English, Zulu and Sotho/Tswana. The English version of the questionnaire was translated and back translated by independent linguists. The interviewers were fluent in the chosen language of the worker. In a study of a working population in the Witwatersrand, Becklake et al found that the mother tongue of the population consisted of Zulu (20%); Tswana/Sotho (31%) and the remainder being a range of other ethnic languages including Tsonga, North Sotho and Xhosa (49%). In this study of language effects on responses to respiratory questionnaires, it was found that a high agreement (using the Kappa statistic) existed for wheeze, shortness of breath, and historical questions (measles as a child and past chest illness) when interviewers conducted the interview in their mother tongue. An improvement in the kappa score was seen when the interview was conducted in the mother tongue of the interviewee (Becklake et al, 1987).

3.3.5 Radiological assessments

New chest radiographs were obtained for all the participants in the living sample study. All radiographs were taken in accordance with the criteria set out by the International Labour Organisation (ILO, 1980). The mining operations routinely conduct their own radiographic assessments. These facilities were used to perform the chest radiographs on the workers. The quality of the radiographs conducted at these facilities were reviewed by the research team and the quality found to be acceptable.

These radiographs were assessed according to the ILO standard plates on pneumoconiosis, each read independently by two experienced readers, one of whom was a NIOSH accredited “B” reader, blinded to exposure status. Evidence of pneumoconiosis was defined as ILO category 1/0 or greater.

3.3.6 Pulmonary function assessments

Lung function assessments were performed on the sample of living workers (current and ex) according to the American Thoracic Society criteria (American Thoracic Society, 1995). Testing was done by appropriately trained technicians. The same make of equipment was used at all sites. Equipment was volume calibrated every four hours on the days of testing with a 3 litre calibrated syringe. Systems were checked for leaks as well. A minimum of three acceptable forced vital capacity (FVC) manoeuvres were performed up to a maximum of eight, when reproducibility criteria were not met. An end of test criterion of at least two seconds of no change in volume with an exhalation time of at least six seconds was used. Start of test criterion was taken as an extrapolated volume reading of less than 5% of the FVC or 0.1 litres, whichever was greater. The largest FVC and FEV_1 obtained from any acceptable curves was used for recording purposes. Reproducibility criteria was taken to be a less than 5% variation or 0.1L difference of the largest FVC and FEV_1 and the next largest of these parameters among all acceptable curves. The prediction equations developed by Louw et al (1996) were used to calculate FEV_1 and FVC percent predicted. These prediction equations have recently been proposed as the standard for work entry and in-service screening of black South African miners by Ehrlich et al (2000) on the basis of being drawn from a black, healthy, non smoking sample not exposed to dusty environments,.

Failure to meet reproducibility criteria was not a basis for exclusion of the subject from the data analysis, as prior studies indicate that this can introduce a substantial selection bias. “Test failure” may be an indication of ill-health, as was shown in the study by Eisen et al (1984), where subjects with persistent test failure had a greater longitudinal decline in FEV_1 than those without test failure (Eisen et al, 1984).

The administration of the questionnaire, radiography and lung function testing was done during official working hours for those on day shift. For members of the sample on night shifts, this was done either before or at the end of the shift, depending on the convenience of the worker and the availability of facilities.

3.4 Statistical Analysis

3.4.1 Data capture and management

All data was captured on computer. Questionnaire data were double entered, with the validation procedures SAS being used to ensure that data entry was accurate. Similarly, data from the radiographic readings was also read into a computer based form. All analysis was done using the SAS statistical analysis package. Independent checks of range, consistency and missing data were performed in SAS. No personal identifiers were present in the database.

3.4.2 Outcome variables

For the autopsy study the following were the outcome variables of interest:

a) emphysema
b) chronic bronchitis
c) coal workers' pneumoconiosis
d) silicosis

See the METHODOLOGY section for the definitions of each of these variables.

For the living sample study:

a) symptoms of shortness of breath, sputum production, cough and wheeze, symptoms of chronic bronchitis (the presence of a persistent cough productive of sputum for at least three months in two sequential years), symptoms of airflow obstruction (shortness of breath with wheezing)
b) abnormalities in lung function parameters: FEV_1; FVC and FEV_1 /FVC as measured by spirometry
c) radiographic changes of emphysema, pneumoconiotic disease and tuberculosis.

3.4.3 Exposure variables

3.4.3.1 Autopsy study

a) duration of employment in the coal industry

3.4.3.2 Living sample study

a) cumulative dust exposure in the coal mining industry

3.4.4 Covariates

The following covariates were considered for potential confounding and effect modification:

- Age
  Increasing age is related to a decrease in pulmonary function. Confounding may be present since older workers are likely to have been employed for a longer period and thus have greater cumulative exposures.
- Smoking status
  Cigarette smoking is a risk factor for obstructive lung disease and was controlled for in the analysis. All participants were asked for details of their smoking history in order to determine the number of pack years smoked. Smoking status, defined as current, ex or never, was also evaluated.
- Other dusty occupational exposures
  Coal miners are likely to have worked in other dusty environments, especially in other mining occupations, and this could confound the relationship between coal dust exposure and health

outcomes. The variable, “years of employment in other mining or dusty manufacturing occupations” was obtained by means of questionnaire and was evaluated in the analysis.

- Tuberculosis
  Coal miners are at an increased risk of contracting TB, especially due to the exposure to silica. This could confound the relationship between coal dust exposure and decline in lung function. History of TB was obtained during the worker interviews. In addition, TB was considered in the radiographic assessments.

Table 3.4.4.1: Summary of the variables of interest for the autopsy and living sample studies

OUTCOME VARIABLES	EXPOSURE VARIABLES	COVARIATES
AUTOPSY STUDY		
• Emphysema • chronic bronchitis • coal workers' pneumoconiosis • silicosis	• duration of employment in coal mining industry	• age • smoking • tuberculosis • other occupational exposure
LIVING SAMPLE STUDY		
• respiratory symptoms • lung function changes • radiographic changes	• duration of employment • current exposure measure • cumulative exposure measure	• age • smoking • tuberculosis • other occupational exposure • non occupational exposure

3.4.5 Analytic approach

Descriptive, bivariate and multivariate analytic techniques were used to describe the data. Before conducting formal statistical analyses, preliminary analysis was performed. Frequency distributions of categorical variables and means, standard deviations, and ranges of continuous variables collected were examined. This was followed by bivariate analysis of outcome and exposure variables.

Statistical analyses proceeded from univariate analyses, which were used to describe the characteristics of the study population and to examine the crude associations between variables of interests. For categorical dependent variables, odds ratios were calculated. For continuous dependent variables, correlation coefficients were calculated. In order to consider the role of confounding or effect modification in the data, a stratified analysis was done for potential confounder/modifiers and their role on the outcome and exposure variables was examined. Multivariate analyses using multiple regression models for cross-sectional data and retrospective data were performed to study the effects of the dependent variables on disease outcomes, while adjusting for potential confounding variables. These models were modified to study possible effect modifications.

Decrements in pulmonary function, especially of FEV1, are the outcome variables of primary interest in the sample of living workers, along with chest radiographic findings and respiratory symptoms. Emphysema is the outcome variable of primary interest in the autopsy study. In the living sample, the main exposure variable of interest was cumulative lifetime exposure to respirable dust in coal mines, although years worked at coal face and total years worked underground were also examined. For the autopsy study, years worked was the exposure variable of interest. In this dataset, information was not available on where in the mines the individual worked. Potential confounding variables examined were age, smoking, other non-occupational dusty exposures and other occupational exposures, and past TB.

For continuous outcomes such as pulmonary function measures, means in each quartile of cumulative lifetime exposure were examined to help determine whether a linear model was appropriate and tests for trend – (Cochrane Armitage), were conducted. The standard tests for assessing the linear model were conducted. Transformations and interaction terms were considered. Logistic regression models for dichotomous outcomes and continuous exposure variables were developed. Dichotomous outcomes included emphysema and respiratory symptoms.

The prevalence of emphysema, pneumoconiotic lung disease and tuberculosis among the sample of autopsied miners was calculated and stratified by age, smoking habits, respiratory symptoms, and duration of employment. Chi-squared tests, Mantel-Haenszel methods and logistic regression using the SAS procedures PROC FREQ and PROC LOGISTIC were used to study the differences of prevalence by these factors.

A similar process was adopted in describing the prevalence of disease among the sample of living miners. Comparisons were made between current and ex-miners. This latter assessment was intended to determine of the role of the healthy worker survivor effect in the data. The relationships between outcome variables and exposure variables were examined using the analytic techniques described above in each of the categories.

3.5 Human Subjects

3.5.1 Institutional ethical clearance

The research proposal has been approved by the Health Sciences Institutional Review Board of the University of Michigan and the Ethics Committee of the University of Natal Medical School.

3.5.2 Individual informed consent

No individual consent was necessary for the autopsy study, as the next of kin consented to the use of the data for research purposes at the time of submitting the miner for autopsy. Institutional consent is sufficient for accessing this data. Individual informed consent was necessary for the living sample study. In this instance, each participant was given a comprehensive explanation in the language of choice. The content of this discussion included the aims of the research, the purpose of the interview, the tests that were to be conducted on them, use of their data and confidentiality of all results. It was emphasised that participation was voluntary and withdrawal at any time was permitted. Each participant was asked to sign a consent form. No financial incentives were provided for participation in the study.

3.5.3 Participants' confidentiality

All participants were given a copy of their results, together with interpretations of the data and, if indicated, referral to an appropriate centre of their choice for further medical management. Those workers with features of compensable occupational disease were directed to assessment centres for compensation purposes. Individual results were strictly confidential and only accessible to the research team. These results were released to any clinician/guardian/agency, if so desired by the individual worker.

3.6 Research Limitations

This research project was subject to several limitations, not unusual in most occupational health research. Each limitation has been examined in depth to determine its possible impact on the study. These limitations relate to subject selection, exposure characterisation, historical data and workplace organisational changes.

3.6.1 Subject selection

Obtaining the appropriate sample size in this study presented no problems because of the large working population at each of the mines. The selection of this sample resulted in a strong, healthy worker effect. Inclusion of 220 ex-employees allowed for the study of this effect, but only to a limited extent. It is likely that having a far bigger number of ex-employees would have allowed better characterisation of this effect. Furthermore, although it is unlikely that selective factors played a huge role in those ex-workers who presented for assessments, this cannot be discounted totally. Preferred methods of selecting ex-employees, such as using a random process from records of ex-employees maintained at the mines, was not possible because of the inadequacy of these records.

3.6.2 Job histories

Characterisation of the exposure profiles of each of the participants was dependent on the accuracy of the historical job description information. These were collected from the company records of each worker and used during the interview to jog the memories of the participants. However, the recorded information was, at times, unavailable, inaccurate, or not updated. Its usefulness during the interview process was therefore restricted. There was no systematic pattern in the quality or lack thereof of the recorded information. In the instances when this was available, it corroborated with the information provided by the worker. As indicated, non differential misclassification of exposure was likely to be small.

3.6.3 Historical exposure data

Occupational health research which attempts to develop cumulative exposure indices is dependent on historical exposure information, which was generally not collected for the purposes of scientific research. The primary reasons for the collection of this data affect its quality and usefulness for research. The historical dust sampling data that was available to the investigators was limited to the period post-1991. The previous period had to be characterised on best available anecdotal information or other records. Although in this study, sensitivity analysis using different factors across the time periods did not reveal any major differences in the data, these are nevertheless untested assumptions. Standardised techniques used in similar occupational health research were employed to describe the missing data.

3.6.4 Workplace organisational changes

The use of currently employed workers in occupational health research implies that projects are subject to the vagaries of the workplace. These include retrenchments, shutdowns, strikes, personnel changes, section or shaft closures, etc. In this particular study, data collection was only affected in one instance by retrenchments at one of the mines and the subsequent closure of a shaft. By carefully assessing the retrenchment programme and ensuring that the majority of those workers originally selected by a random selection process were assessed, and that after the retrenchments, a repeat random selection process was conducted, the impact on the study, or the introduction of bias, was minimised.

4. Results

4.1 Introduction

This detailed presentation of the results of the research is presented in the following manner:

1. A listing of the exposure and outcome variables of interest together with the covariates
2. Discussion on the exposure variables and covariates and, where relevant, how these were calculated
3. Descriptive data presentation
4. Presentation of bivariate and multivariate results in the following order:
    4.1. Questionnaire based outcomes
    4.2. Lung function based outcomes
    4.3. Radiological outcomes
    Each of the above are presented in subsections depending on the specific exposure variables or covariates used (years of exposure, cumulative exposure, smoking)
    4.4. Pathology study results

KEY FINDINGS TEXT BOXES:
In sections with detailed statistical information and results, a text box is presented at the beginning of the section, containing a summary of the key findings for that section. Details are then contained in the appropriate subsections.

4.2 Variables of Interest

For the purposes of analysis, the following variables were used:

Exposure variables

- Cumulative dust exposure (CDE) (estimates in mg-years/m^3, i.e., a summation of the number of years worked on each job held multiplied by the concentration estimate in mg/m^3 on that job)

Covariates

- Smoking status (current, ex and never)
- Pack years smoked (continuous)
- Age
- Employment status

Outcome variables

- Usual chronic cough (dichotomous)
- Cough for most days at least three months per year (dichotomous)
- Chronic wheeze (dichotomous)
- Chronic phlegm (dichotomous)
- Moderate breathlessness (breathless when walking) (dichotomous)
- Severe breathlessness (breathless when dressing) (dichotomous)
- History of TB (from questionnaire) (dichotomous)
- Percent predicted Forced Expiratory Volume in 1s (continuous)
- Percent predicted Forced Vital Capacity (continuous)
- Pneumoconiosis on x-ray (all scores equal and greater than 1/1 were considered to be positive for pneumoconiosis) (dichotomous)
- Profusion score (continuous)
- Radiological emphysema (dichotomous)
- Radiological diagnosis of TB (dichotomous)

4.3 Exposure Variables

Several calculated exposure variables were developed for the purposes of analysis, including years worked at the coalface and cumulative dust exposure, the latter being calculations based on historical and current dust sampling data.

4.3.1 Years worked on the coalface

All participants in the study were interviewed in depth about their job histories, including job title, location of job (coal face, backbye and surface), year started in particular job title and year ended. The surface activities generally included workers from support services (kitchen workers, hostel guards, security and human resources. The activities of the backbye included underground support services: electricians, bricklayers, transport operators, etc. The coal face consisted of the actual drilling, shuttle car loading, roof bolting and other high dust exposure activities. This series of questions was asked about each job ever held in a coal mine, whether with current or previous employers in the coal industry. For those jobs held at the current mine, the information provided by the participant was done in consultation with the worker's job history extracted from the company files.

Using the above information, workers were grouped into three categories based on the number of years worked on the face, backbye or surface respectively. Figure 4.3.1.1. shows the mean number of years ever worked in the different general zones of the mine: surface, coal face and backbye. Statistically significant differences in mean years worked in the coal face and backbye zones existed between the current and ex-miners (p <0.005).

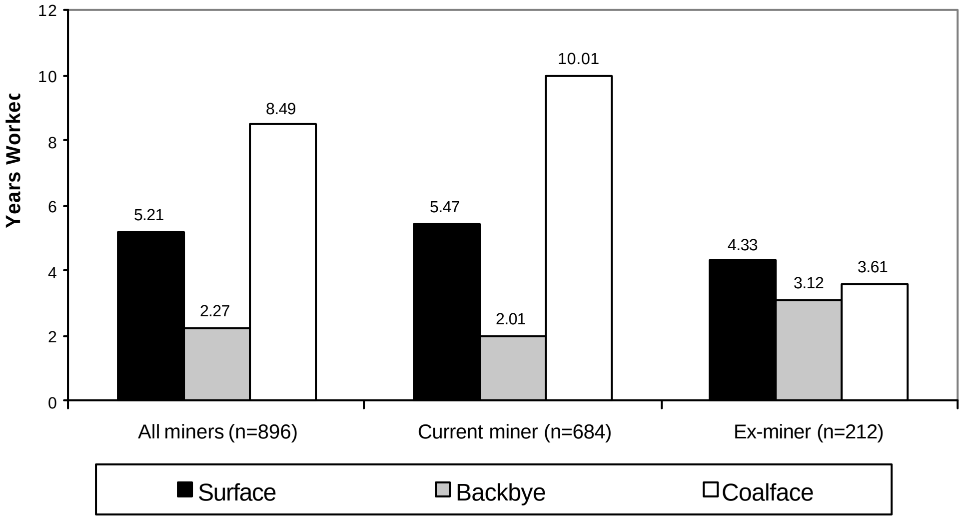

Figure 4.3.1.1 Respiratory Health of South African coalminers: mean number of years worked in defined exposure category

4.3.2 Underground exposure vs Surface only exposure

Of the entire sample that was assessed, a subset of workers had had no underground exposure (n=222 (24.78%)). This subset was analysed separately for appropriate outcomes and compared to the exposed grouping.

4.4. Current Dust Sampling Data

KEY FINDINGS (SECTION 4.4):

- Current dust levels at all mines were below 2mg/m^3 as measured at face, backbye or surface. Thus all mines were below international standards.
- Silica content for all mines was less than 3%. This level is low enough that the overall effect of “coal dust” is expected to predominate over the specific effect of silica, thus no correction to allowable levels of coal dust exposure is required for silica content. This is also below international standards.

Three rounds of sampling were conducted on each mine. Commercially available Mine Services Appliance (MSA) pumps and nylon cyclones were used. The latter sampling equipment is considered as an international standard and is recommended, for example, as part of the NIOSH dust sampling techniques. In each mine, for each cycle, there were approximately 50 sampling points – the face was more heavily sampled than the backbye, with only about 2-4 samples being taken on the surface. The reason for this strategy was to ensure that proper representivity and variability of the exposures in the high exposure areas were achieved, thus oversampling was done in the higher dust exposure zones. Because of the log normal data, the results shown in Table 4.4.1.1 (in appendix 8.6) and in the figures 4.4.1.1 – 4.4.1.3 below are the geometric means. The results show substantial variability of measures obtained in the same mine/zone/sampling cycle and also distinct differences between each zone for each cycle. With the exception of mine 3 round 1, the results from the surface were expectedly low. Significant differences in the mean dust levels between mines 2 and 3 (95% CI = 0.01 – 1.01) were found.

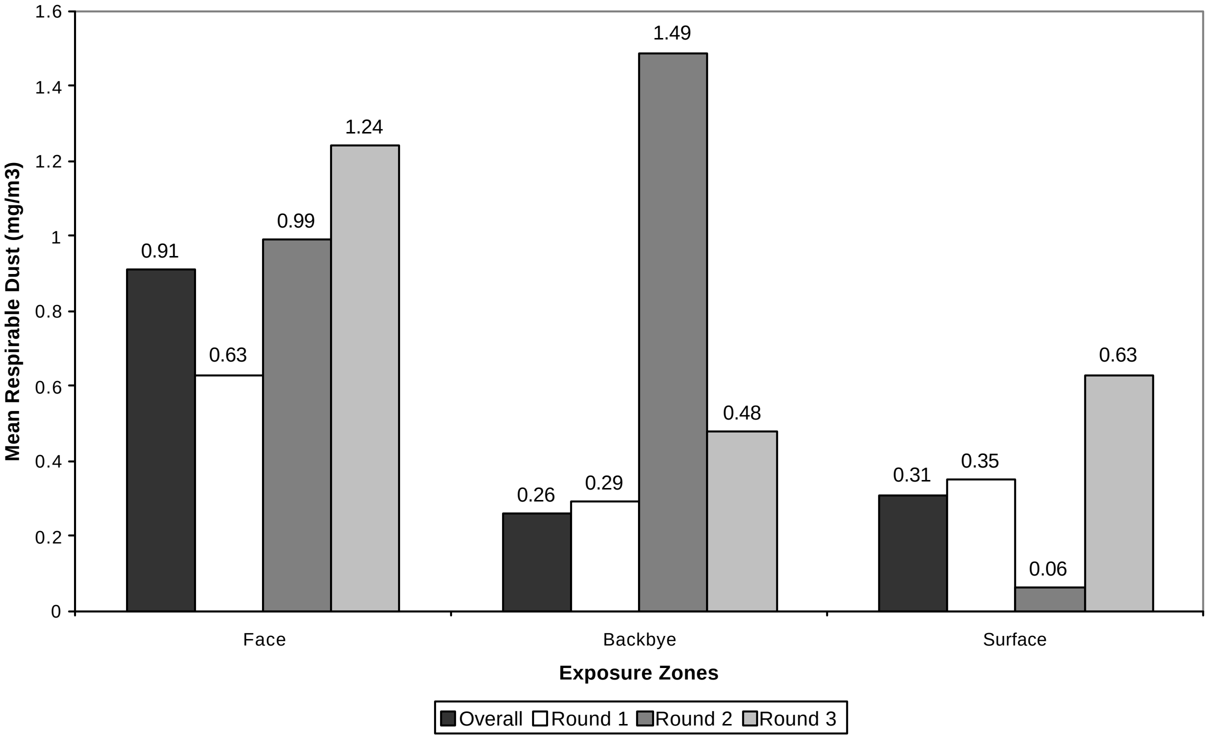

Figure 4.4.1.1 Respiratory health of South African Coalminers: geometric mean time weighted averages of respirable coal dust for the different sampling cycles in the different exposure zones in Mine 1

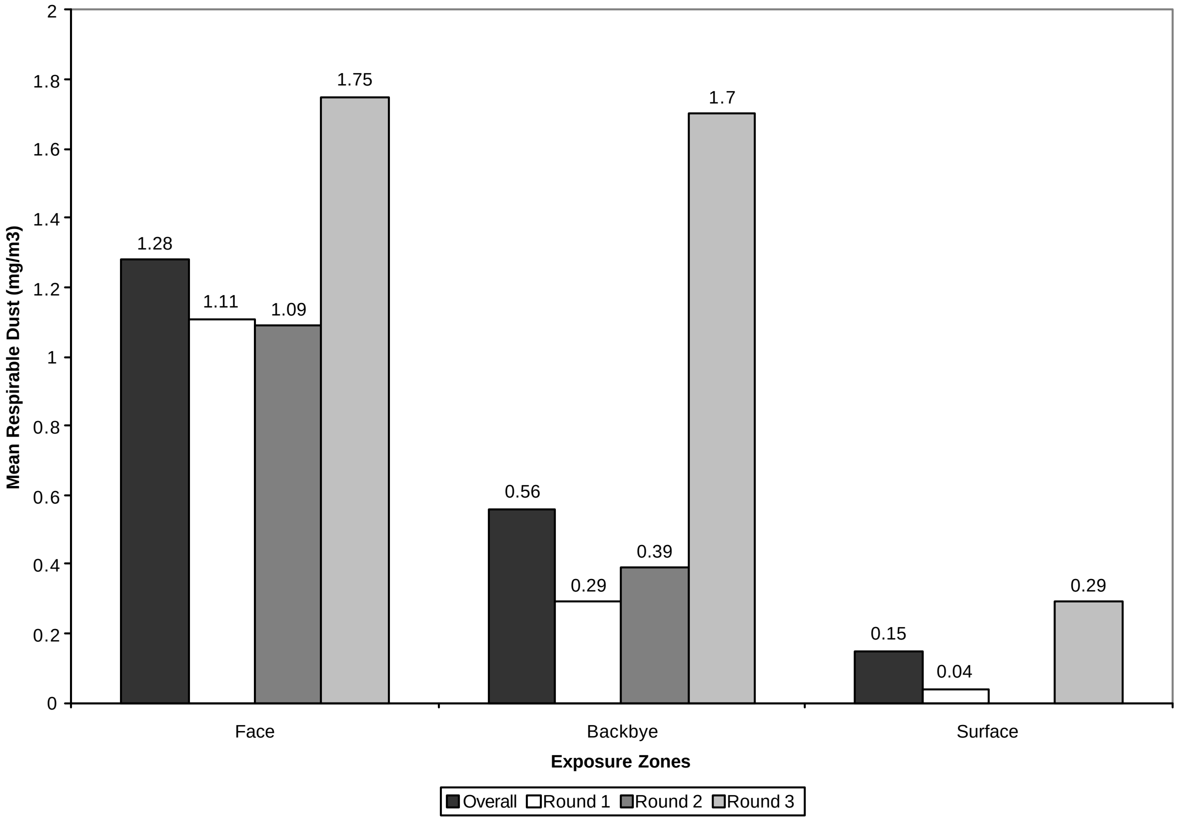

Figure 4.4.1.2 Respiratory health of South African Coalminers: geometric mean time weighted averages of respirable coal dust for the different sampling cycles in the different exposure zones in Mine 2

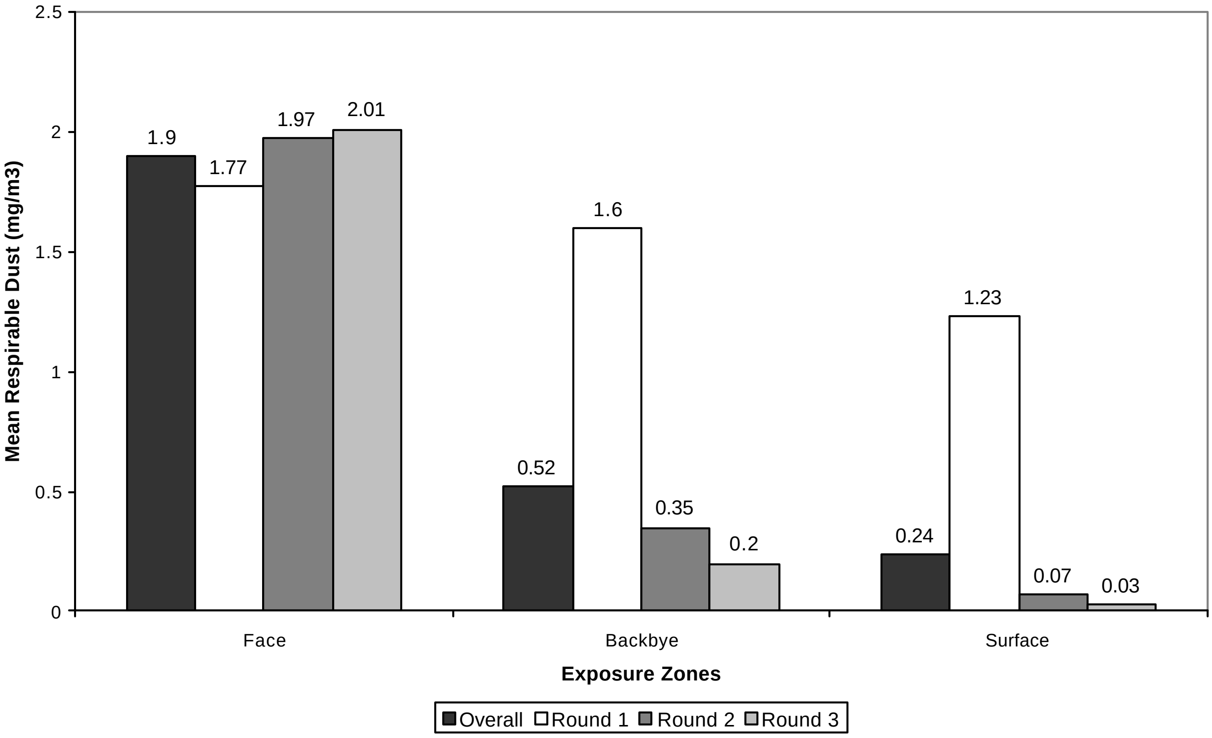

Figure 4.4.1.3 Respiratory health of South African Coalminers: geometric mean time weighted averages of respirable coal dust for the different sampling cycles in the different exposure zones in Mine 3

In addition to sampling for respirable dust, measurements were also taken for silica content. This data is reflected in Table 4.4.1.4. Only a subset of the filters was examined for SiO_2 and, in some instances, only a single sample from the surface or backbye was analysed.

Table 4.4.1.4 Respiratory health of South African Coalminers: mean silica content (% of respirable dust) for the different sampling periods in the different exposure zones in each mine.

Cycle	**Mine 1** **Mean (%)** **SD** **N**			**Mine 2** **Mean (%)** **SD** **n**			**Mine 3** **Mean (%)** **SD** **N**		
	Face	**B/bye**	**Surface**	**Face**	**B/bye**	**Surface**	**Face**	**B/bye**	**Surface**
Round 1	2.02 1.05 8	1.04 0.39 3	1.51 1	1.08 0.83 5	2.32 1	-	3.87 3.78 6	0.67 1	0.40 1
Round 2	3.16 2.41 10	3.15 1	0 1	1.68 1.23 7	0.69 1	-	2.97 3.08 10	1.30 1	1.52 1
Round 3	1.72 1.08 11	1.36 0.66 3	1.15 1.31 2	1.39 1.71 8	1.04 1		1.80 1.39 11	0.73 1	0 1
Overall	2.30 1.73 29	1.48 0.88 7	0.95 1.00 4	1.41 0.93 20	1.35 0.86 3	-	2.70 2.73 27	0.90 0.35 3	0.64 0.79 3

4.5 Historical Dust Sampling Data

KEY FINDINGS (SECTION 4.5):

- Historical dust levels were available for the mines from 1991 onwards.
- Average dust levels over this period was less than 1.5 mg/m^3 for all mines, ranging from 0.23 – 1.7 mg/m^3.
- No time specific trends were noted.
- A clear gradient was seen from surface to backbye to face. The range at surface was 0.08–0.74 mg/m^3, backbye range: 0.2–2.07 mg/m^3 and face: 0.67 – 3.06 mg/m^3.
- This data also indicates that the historical dust levels seen at these mines were generally within international norms.

In addition to collecting new dust sampling data, the research team also reviewed available dust data from each of the mines. The following tables provide a summary of the data that was available. The historical dust data appeared log normally distributed. For this reason the tables below show the geometric means of the data. The table 4.5.1.1 is a summary of the amount of data points (each dust sample representing a single data point), the range of years for which data was available, and a grouped mean for all sections and zones in the mine.

Table 4.5.1.1 Respiratory health of South African Coalminers: geometric means of dust levels in mg/m^3 in each mine

MINE	**NUMBER OF DATA POINTS**	**YEAR RANGE OF DATA**	**DUST LEVEL (mg/m^3) (sd)**
1	1485	1993 – 1999	0.94 (4.88)
2	701	1996 – 2000	1.33 (3.25)
3	1459	1991 – 1998	0.51 (5.62)

Of interest to the research team was how the dust levels in each mine varied over the years. The following figure 4.5.1.2 captures this information. No obvious trend is seen in the data over time, although mine 3 seems to have persistently low levels and mine 2 persistently higher levels when compared to the other mines.

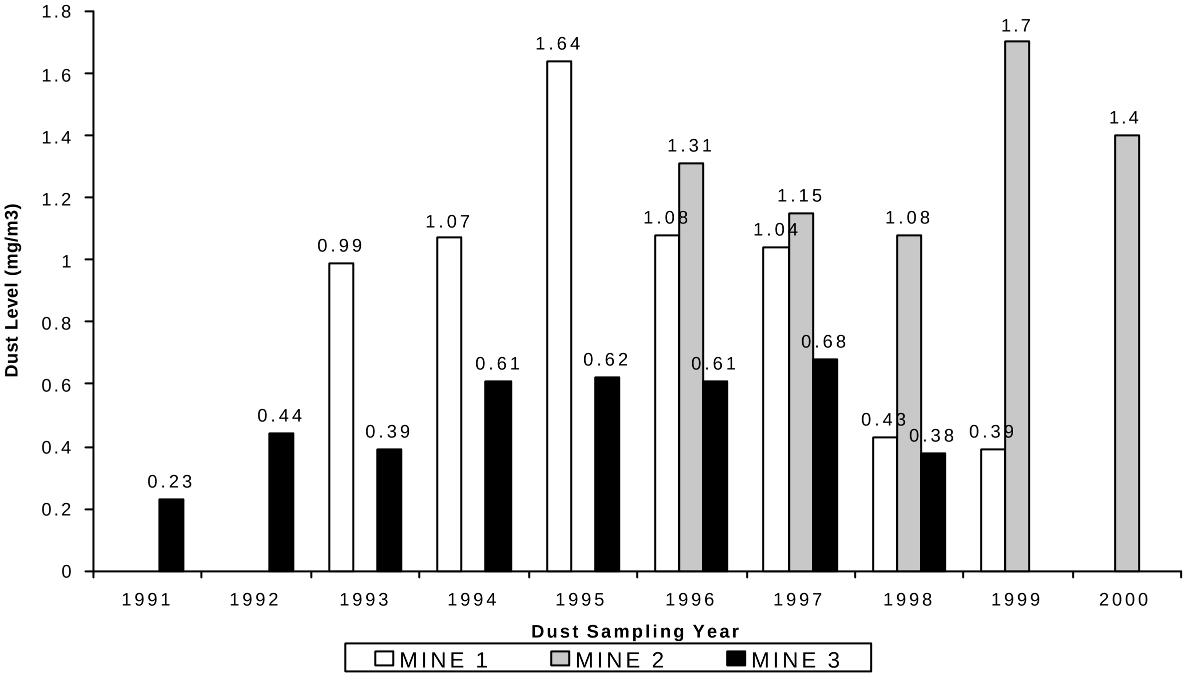

Figure 4.5.1.2 Respiratory health of South African Coalminers: geometric means of dust levels in mg/m^3 by mine and year

(Table 4.5.1.2 corresponding to the above figure is found in the Appendix 8.6, detailing the number of samples, together with the standard deviations of the means of dust levels)

Of further interest was the variability of the data across the different zones (face, backbye and surface) in each of the mines for the different time periods. The table 4.5.1.3 shows these findings. In all the results a clear increasing trend in mean dust level is seen from the surface to backbye to face working areas. Once again, no trend across time is seen.

Table 4.5.1.3 Respiratory health of South African Coalminers: geometric means of dust levels by mine, year and zone (face, backbye and surface) (n = number of data points for that category of mine, zone and year)

YEAR	SURFACE		BACKBYE		FACE	
	n	(mg/m^3) (SD)	n	(mg/m^3) (SD)	n	(mg/m^3) (SD)
MINE 1						
1993	17	0.31 (3.18)	39	0.52 (4.25)	84	1.69 (4.29)
1994	27	0.16 (3.74)	83	0.72 (3.85)	110	2.28 (3.05)
1995	33	0.38 (3.74)	105	1.38 (3.58)	130	2.75 (2.73)
1996	37	0.22 (4.42)	129	0.89 (4.51)	99	2.60 (3.96)
1997	42	0.15 (4.62)	141	1.01 (3.36)	89	2.72 (3.01)
1998	37	0.08 (2.87)	145	0.34 (3.63)	80	1.40 (3.70)
1999	9	0.18 (1.67)	29	0.25 (2.34)	20	1.02 (5.38)
MINE 2						
1996	25	0.5 (2.76)	37	1.23 (3.53)	46	2.32 (3.08)
1997	27	0.26 (1.99)	55	1.48 (2.22)	46	2.06 (2.34)
1998	59	0.44 (3.51)	55	1.38 (2.96)	49	2.42 (2.41)
1999	68	0.93 (2.43)	57	2.07 (2.17)	46	3.06 (1.57)
2000	43	0.74 (3.52)	43	1.37 (3.32)	38	2.96 (2.36)

YEAR	SURFACE		BACKBYE		FACE	
	n	(mg/m^3) (SD)	n	(mg/m^3) (SD)	n	(mg/m^3) (SD)
MINE 3						
1991	34	0.12 (4.95)	51	0.20 (4.79)	46	0.43 (3.98)
1992	55	0.25 (5.12)	57	0.39 (3.93)	45	1.03 (3.76)
1993	84	0.23 (5.74)	85	0.50 (3.82)	41	0.67 (5.74)
1994	58	0.32 (7.46)	77	0.66 (4.32)	31	1.79 (6.09)
1995	51	0.33 (5.10)	86	0.51 (4.88)	36	2.33 (5.11)
1996	81	0.26 (6.20)	110	0.58 (5.28)	74	1.69 (4.85)
1997	68	0.40 (5.09)	149	0.54 (4.23)	76	1.67 (5.21)
1998	12	0.11 (5.53)	32	0.42 (5.21)	16	0.81 (4.10)

The following table captures grouped exposure information of specific high exposure job titles across all mines and across all years. The jobs at the face clearly show a much higher level of exposure than those at the backbye.

Table 4.5.1.4. Respiratory health of South African Coalminers: geometric means of dust levels for job descriptions across all mines, across all years

JOB DESCRIPTION	Zone	N (% of total samples = 3640)	DUST LEVEL (mg/m^3) (SD)
Continuous Miner Operator	Face	180 (4.95)	3.20 (4.06)
Ventilation Attendant	Face	87 (2.39)	2.04 (3.54)
Shuttle Car Driver	Face	196 (5.38)	2.03 (3.29)
Roofbolter	Face	162 (4.45)	1.68 (3.85)
Miner	Face	168 (4.62)	1.50 (3.45)
Belt Attendant	Backbye	178 (4.89)	0.89 (4.19)
Electrical Aide	Backbye	127 (3.49)	0.83 (3.52)
General Worker	Backbye	96 (2.64)	0.77 (4.49)
Electrician	Backbye	102 (2.80)	0.66 (5.00)
Fitter Aide	Backbye	127 (3.49)	0.64 (4.12)
Shiftboss	Backbye	98 (2.69)	0.63 (4.50)
Fitter	Backbye	95 (2.61)	0.62 (4.18)
Pump Attendant	Backbye	92 (2.53)	0.61 (3.65)
Laboratory Worker	Surface	87 (2.39)	0.43 (5.77)
Boilermaker	Surface/Backbye	77 (2.12)	0.30 (3.56)
Artisan Aide	Surface/Backbye	59 (1.59)	0.28 (4.39)

4.6 Development of Cumulative Mine/Zone Exposure Matrix

KEY FINDINGS (SECTION 4.6):

- Investigator collected dust data and historical data were used to determine cumulative dust estimates using statistical modelling.
- Statistical modelling for cumulative dust estimates used mine, zone, time period and sampler variables.
- This modelling provided a cumulative dust level for each mine in the three zones (surface, backbye and face).
- Cumulative Dust Exposure years (CDE) provides a measure of the levels of dust each participant in the study was exposed to during their employment. It sums the product of mean cumulative dust level in a particular mine and zone x years in that mine and zone.
- The mean CDE was 56.83 mg-years/m^3. For purposes of analysis this was divided into three categories of low, medium and high exposure.

4.6.1 Historic and current dust data analysis

A key objective of the study was to determine the effect of coal dust exposure over the lifetime of employment (cumulative exposure) of the worker on his health. To achieve this, it was necessary to develop methods to estimate lifetime dust exposure (cumulative exposure) with the available data (investigator collected and historical data). In order to take into consideration the fluctuations in dust levels for the mines in question, specific statistical methods had to be used, separately for the current dust levels and then for the historical data. Finally similar statistical methods had to be used to combine the past and current data to allow for the calculation of a set of values for estimating lifetime exposure in each individual worker. (The statistical methods are discussed in detail in Appendix 8.2)

For the development of models to determine cumulative dust estimates for each mine with each exposure zone (face, backbye and surface) a two phase statistical modelling was done. The first involved analysing the investigator collected dust data, followed by analysis of the historically collected dust data. These statistical models made use of the variables exposure zones (face and backbye compared with surface) and mine (mine 1, 2 or 3). Job description and section worked were included in the analysis initially but were subsequently dropped because this information was not generally available for all workers over their entire lifetime of employment.

The information generated from the above analyses allowed for the development of a cumulative exposure model. This analytic step provided cumulative mean respirable dust estimates for each exposure zone (face, backbye and surface) in each of the three mines. This is shown in the table 4.6.1.1, below. The statistical methods used in this analysis are described in Appendix 8.2.

Table 4.6.1.1 Respiratory health of South African Coalminers: cumulative dust exposure estimate mine/zone matrix (mg/m^3)

	MINE 1	**MINE 2**	**MINE 3**
SURFACE	0.788	1.329	0.619
BACKBYE	1.796	3.166	1.474
FACE	4.870	8.202	3.830

4.6.2 Cumulative dust exposure years (CDE)

The aim of the exposure estimation was to develop a cumulative measure of lifetime exposure for all the participants in the study, making best possible use of the data available. For purposes of clarification, this report refers to this exposure variable as Cumulative Dust Exposure (CDE), measured in mg-years/m^3. Cumulative dust exposure was calculated based on the product of number of years each participant spent in a particular mine within a particular zone and the dust estimate of the corresponding cell from the matrix 4.6.1.1, as shown in the following equation

$$CDE = \sum c_{ij}\, years_{ij}$$

where x_{ij} = arithmetic mean calculated for particular mine within a specific zone (surface, backbye or face) as shown in matrix above, and $years_{ij}$ = years spent in a particular mine within a specific zone.

The mean CDE was 56.83 mg-years/m^3 (SD=51.94 mg-years/m$^{3.}$). Using the cumulative dust exposure model, three categories of exposure were calculated for use in the analysis. The categories are: low exposure (0.62 - 20.10 mg-years/m^3; n=298); medium exposure (20.11 - 72.77 mg-years/m^3; n=298) and high exposure (72.78 - 258.70 mg-years/m^3; n=300). The numbers of current and ex-miners in these groupings were as follows: low exposure: current = 179, ex = 119; medium exposure: current = 218, ex = 80; high exposure: current = 287, ex = 13 [Three categories, based on terciles were chosen as this allows for comparison between intuitive exposure groupings, as opposed to having an arbitrary grouping of 5 or 10 mg-years/m^3. The following figure indicates the mean differences in cumulative exposure experienced by all miners, and by current and ex-miners respectively.

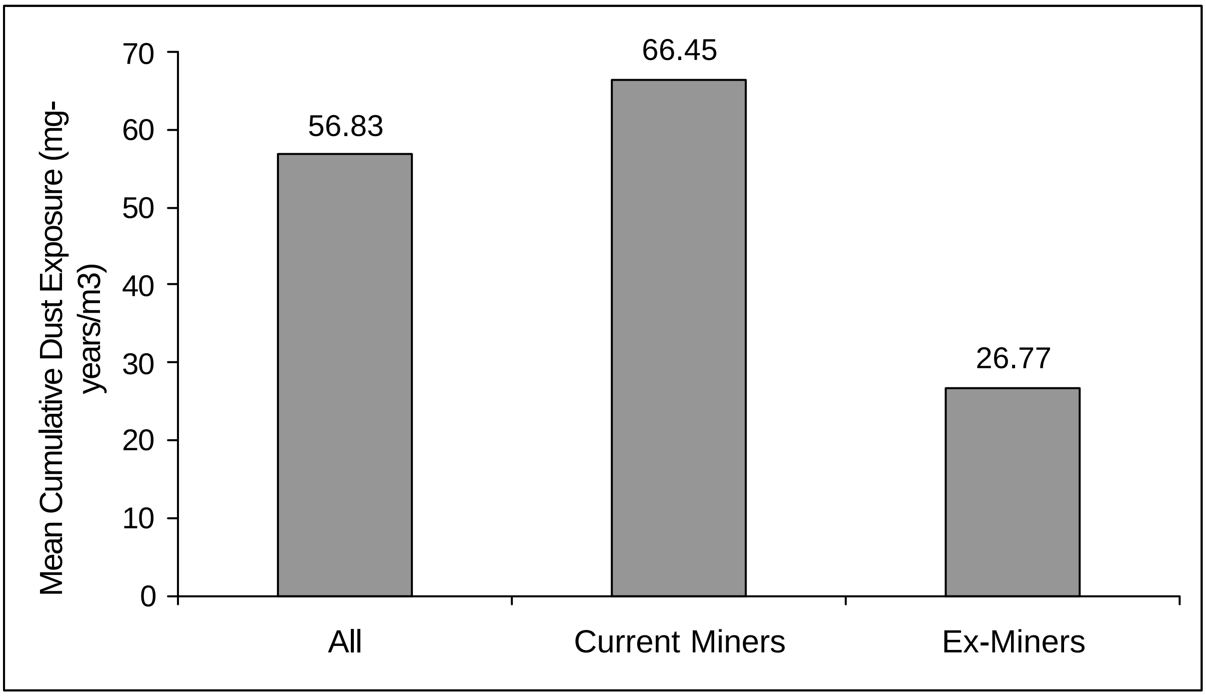

Figure 4.6.4.1 Respiratory health of South African Coalminers: mean cumulative dust exposure (mg-years/m^3) for all, current and ex-miners

4.7 Demographic Data

A total of 896 participants were interviewed, of whom 684 were currently employed on one of the three participating mines. Among the 212 ex-miners 188 presented for the medical assessments at the Mpungwe Hospital. Height and weight were not available for the twenty five miners not reporting for the assessments. Within the sample there were 246 (26.68%) participants who had never worked underground.

Table 4.7.1.1 Respiratory health of South African Coalminers: demographic data for all study participants

Variable	N	Mean (SD)	Minimum	Maximum
Age (years)	896	42.45 (8.44)	21.00	76.00
Height (cm)	872	168.90 (6.77)	148.00	195.00
Weight (kg)	872	70.12 (12.35)	43.00	122.00
School standard	896	4.35 (3.25)	0.00	10.00
Years in coalmining (years)	896	15.89 (7.96)	1.00	43.00

Table 4.7.1.2 Respiratory health of South African Coalminers: demographic data stratified according to employment and exposure status

EMPLOYMENT STATUS					EXPOSURE STATUS			
	CURRENT		EX-MINER		UNDERGROUND		SURFACE	
Variable	n	Mean (SD)	n	Mean (SD)	N	Mean (SD)	N	Mean (SD)
Age (years)	684	42.46 (7.71)	212	42.42 (10.41)	674	42.03 (8.27)	226	43.59 (8.79)
Height (cm)	684	168.99 (6.91)	188	168.60 (6.27)	658	169.29 (6.30)	214	167.79 (7.84)
Weight (kg)	684	71.52 (12.42)	188	65.20 (10.72)	658	69.23 (11.30)	214	72.57 (14.61)

The distribution in the mean ages and heights amongst current and ex-miners was almost equal across the strata. The fact that a statistical significant ($p < 0.0001$) difference existed for the means of weights may be important from a public health point of view and may imply a greater disease burden in the group of ex-miners. The lower weight may indicate either the existence of current undiagnosed disease or the lack of adequate nutrition.

Further analysis was done to determine whether differences existed amongst the different mines. A miner was classified as belonging to one of the three mines that participated in the study or to a category of “other”. This classification was based on the highest number of years worked in mines 1, 2, 3 (participating mines) or other mines, rather than where the worker was currently employed. On this basis, 298 (33.67%) workers worked in mine 1; 263 (29.72%) in mine 2; 268 (30.28%) in mine 3 and 56 (6.33%) in other mines. Because of the tendency of miners to move regularly between mines, this classification, based on the highest number of years worked in any particular mine is of limited value (e.g. a worker with two years on mine 1 and five years on mine 2 was classified as belonging to mine 2, while another worker with 12 years in mine 1 and eight years in mine 2 was classified as mine 1, despite having greater exposure to mine 2 than worker 1). Similarly, using a classification based on the mine of current employment ignores the duration a person may have been currently employed, which could range from a few months to several years. For these reasons, analysis to determine specific “mine effects” on outcomes have not been considered further.

4.8 Smoking Data

A detailed smoking history was obtained from each participant. This included the year of starting, number of cigarettes smoked previously, years smoking this number, number smoked currently, current status (ex smoker was defined as having stopped smoking more than a month ago); if habit was stopped for any period of time greater than one year, for how long. Information was also obtained on pipe and cigar smoking, but as this was rare, this information was not used in further analysis.

Smoking was used in two ways for analytic purposes: smoking status (current, ex, never) and as pack years. The latter was calculated as:

> Pack years = $^{1}/_{20}$ [(no. of cigarettes smoking currently per day x years smoking this number) + no. of cigarettes smoked in past per day x (years smoked this number – years stopped in between)].

Of the 544 smokers, the mean pack years smoked was 7.34 (sd=7.36). For the total population, this averaged 4.34 (sd = 6.91). Amongst current smokers (n= 398), the mean pack year was 8.71 (sd=8.25), and ex-smokers (n=146) mean pack year = 3.56 (sd = 3.71) Pack years was divided into four categories for analysis: Category 0: pack years = 0; Category 1.6: pack years = 0.1 – 3.25; Category 5.3: pack years > 3.25 – 7.65; Category 12: > 7.65. Categories were labelled using the midpoints of the pack years in each category.

Table 4.8.1.1 shows the differences in reported smoking habits amongst current and ex-miners. As can be seen, whilst smoking is a reasonably common habit amongst both groups, there is a low level of smoking as measured by pack years. The data shows statistically significant findings between the different categories of employment, with ex-miners more likely to be current smokers, while they are less likely to be never smokers. There were no significant differences seen between workers with some underground exposure or surface workers (no underground exposure).

Table 4.8.1.1 Respiratory health of South African Coalminers: smoking habits as reported by current vs ex-miners and underground vs surface

		Employment Status		**Exposure Status**	
Variable	**All miners (n=896)**	**Current miner (n=684)**	**Ex-miner (n=212)**	**Ever underground (n=674)**	**Surface Only (n=222)**
Number of current smokers	397 (44.31%)	254 (37.13%)	143 (67.45%)*	299 (44.36%)	98 (44.14%)
Number of Ex smokers	147 (16.41%)	122 (17.84%)	25 (11.79%)*	100 (14.84%)	47 (21.17%)
Number of never smokers	352 (39.29%)	308 (45.03%)	44 (20.75%)*	275 (40.80%)	77 (34.65%)
Mean packyears of smoking	4.45 (SD: 6.96)	4.04 (SD: 6.77)	5.80 (SD: 7.40)*	4.26 (SD: 6.52)	5.04 (SD: 8.15)

* = $p < 0.01$ (p value comparing current to ex-miners and ever underground to surface only)

4.9 Questionnaire based outcomes

KEY FINDINGS (SECTION 4.9):

- Ex-miners reported significantly more symptoms than current miners, with ex-miners having greater prevalence of doctor diagnosed bronchitis and asthma.
- Significant differences in symptoms prevalence between underground and surface workers was seen only in the reporting of phlegm.
- For all miners combined, statistically significant associations were seen between symptoms and categories of cumulative dust exposure (CDE). Significant trends were also seen, however, in an unexpected direction: decreasing prevalence of symptoms with increasing exposure.
- These trends and associations were generally absent when only current miners were analysed. An increase in prevalence was noted when only ex-miners were assessed, and a significantly increasing trend was seen for breathlessness.
- The prevalence of symptoms was significantly higher amongst current smokers, and least amongst never smokers. Positive trends in increasing prevalence were seen with increasing pack years.
- These reverse trend findings for (all miners combined) are generally not in keeping with findings of most other studies. The loss or reversal of these trends when stratifying on current employment status strongly implies that a particularly marked “healthy worker effect” is present, i.e healthier workers stay employed longer, and work in the dustier jobs, while less healthy workers leave the mine or dusty areas earlier in their lifetimes. This effect has been noted in one study amongst South African goldminers, where cumulative exposure was not associated with symptoms.

4.9.1 Descriptive questionnaire data

Figure 4.9.1.1 shows marked differences (reported as percentages) in symptoms amongst current and ex-miners (The corresponding table (Table 4.9.1.1) is in Appendix 8.6).

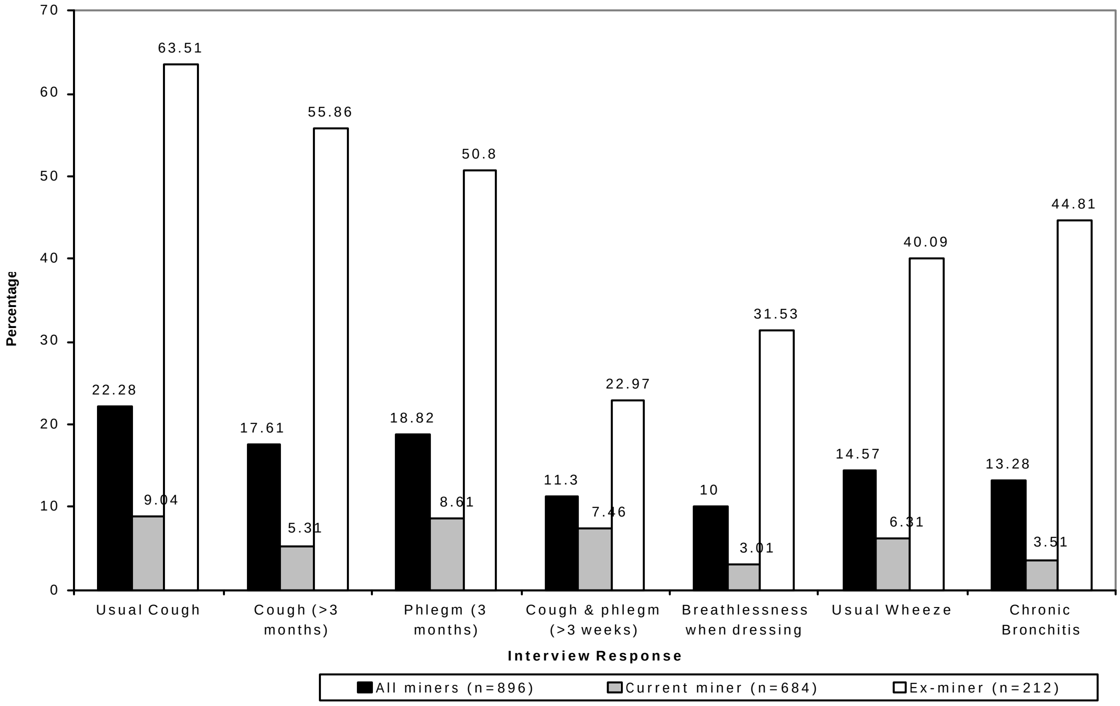

Figure 4.9.1.1 Respiratory health of South African Coalminers: respiratory symptoms as reported positive by all, current and ex-miners.

Statistically significant findings were found between the two employment status categories. These results could be due to a reporting bias, or it could be as a result of poorer health amongst this grouping of workers. No significant differences were seen in the doctor diagnosed illnesses (Table 4.9.1.2) – this could support the reporting bias or could indicate a lack of access to professional medical care by the ex-miners, most of whom were still unemployed. Most questionnaire outcomes were not statistically significantly different between underground and surface miners, with the exception of phlegm production (table 4.9.1.2 in Appendix 8.6).

Table 4.9.1.2 Respiratory health of South African Coalminers: respiratory diseases as diagnosed by a doctor

		Employment Status	
Disease	All miners (n (%)) (n=896)	Current miner (n (%)) n=684	Ex-miner (n (%)) n=212
Acute bronchitis	17 (1.90)	8 (1.17)	9 (4.25)*
Chronic bronchitis	2 (0.22)	1 (0.15)	1 (0.47)
Emphysema	0 (0)	0 (0)	0 (0)
Asthma	17 (1.90)	5 (0.73)	12 (5.66)*
TB	27 (3.01)	18 (2.63)	9 (4.25)

Percentages shown are of employment status, and not total study participants
* = significant difference, $p < 0.0001$

4.9.2. Questionnaire data vs Cumulative Dust Exposure (CDE)

The Chi Square test was used to determine whether any associations existed between categories of years of exposure and the various outcomes determined by questionnaire. The Cochran Armitage test for trend was used to determine whether a trend relationship existed between cumulative dust exposure years categories and these outcomes. To examine whether any associations existed between outcome and exposure, the exposure measure was divided into three categories (see section 4.6.2): The categories are: low exposure (0.62 - 20.10 mg-years/m^3; n=298); medium exposure (20.11 - 72.77 mg-years/m^3; n=298) and high exposure (72.78 - 258.70 mg-years/m^3; n=300).

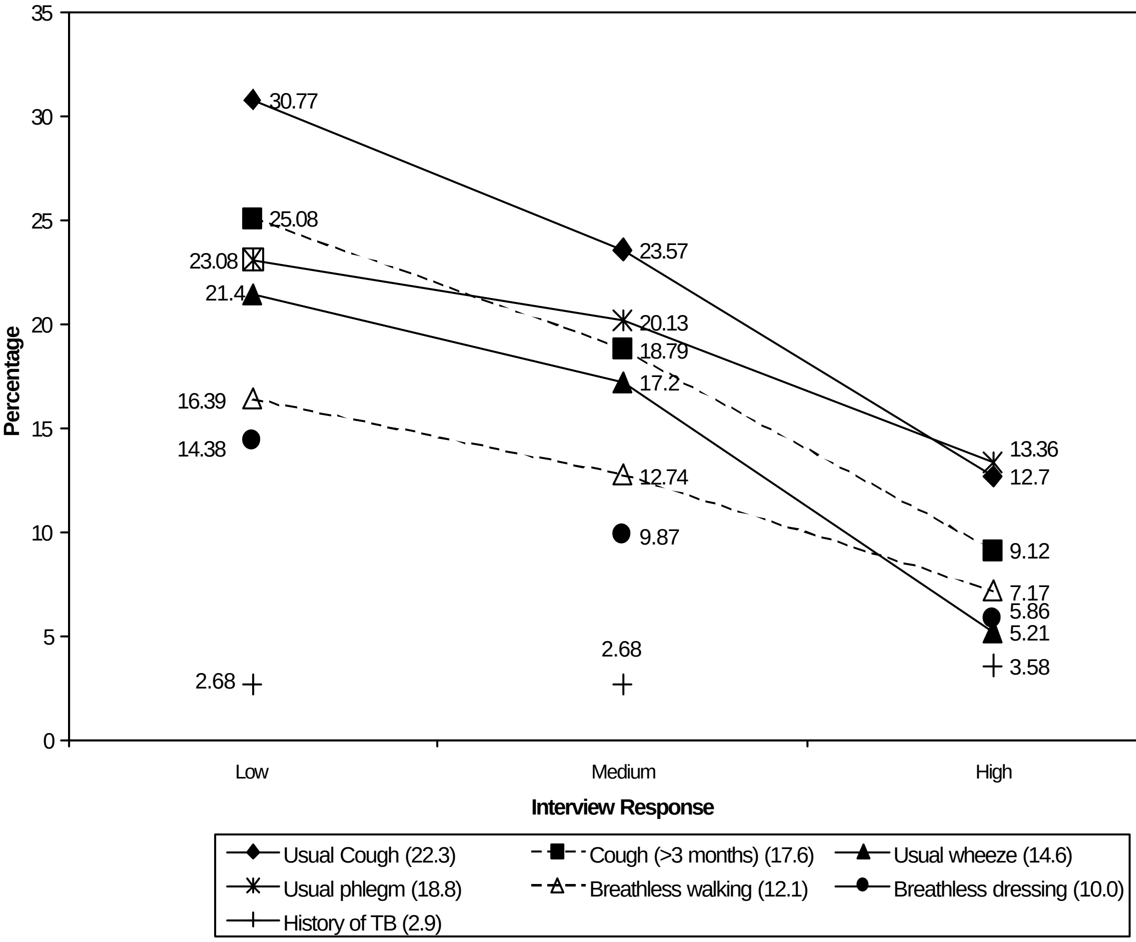

Figure 4.9.2.1 Respiratory health of South African Coalminers: trends for categorical outcomes vs categories of cumulative dust exposure

The figure 4.9.2.1 shows the percentages for the various responses in the three exposure categories. The legend contains the percent response of the entire sample. (The corresponding table in Appendix 8.6 contains the actual numbers, together with the specific chi square and trend tests p values). All the outcomes show a negative association for exposure ($p < 0.005$) with the exception of TB. Similarly, a strongly significant trend ($p < 0.001$) is seen; however this is all in a negative direction – increasing exposure results in a lower prevalence of respiratory symptoms. To further analyse the data, stratification on the basis of current employment status was done. These are shown in the following figures.

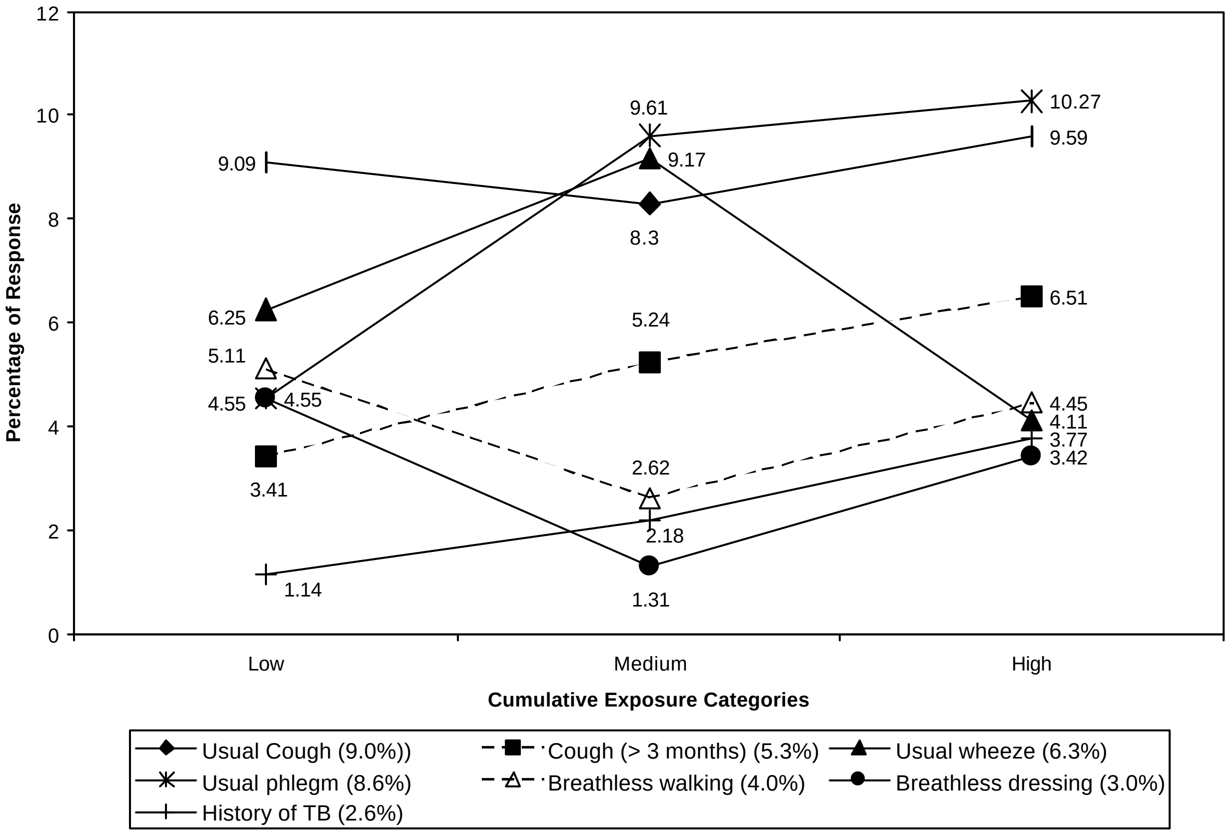

Figure 4.9.2.2 Respiratory health of South African Coalminers: trends for categorical outcomes vs categories of cumulative dust exposure – excluding ex-miners

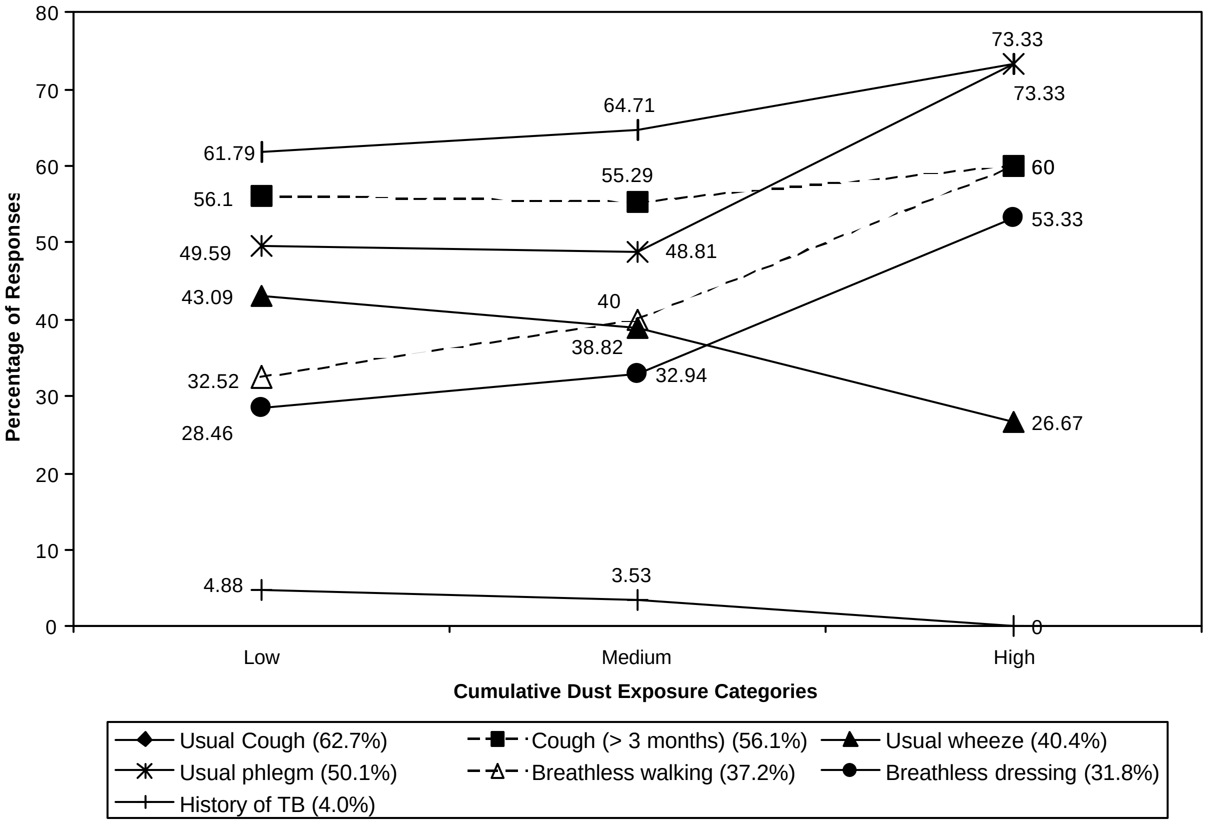

Figure 4.9.2.3 Respiratory health of South African Coalminers: trends for categorical outcomes vs categories of cumulative dust exposure – ex-miners only

The negative associations seen in the full dataset are not apparent when only current employees (Figure 4.9.2.2) are analysed. A positive association is seen with persistent phlegm (p = 0.04), and marginally with persistent wheeze (p = 0.06). History of TB, which failed to show any trend in the full dataset, shows a significant positive trend with exposure in the current miner analysis (p = 0.04).

When analysing the ex-miners exclusively, the various exposure groups have small cell sizes. For all outcomes, symptom prevalences are higher in this group than among current miners. The previously noted negative trend in the whole group is reversed among ex-miners, with an increase in rates with increasing exposure, reaching statistical significance for breathlessness (p <0.03). None of the other symptoms were statistically significantly associated with exposure, probably due to the small sample sizes. Within the ex-miner group only a small percentage of workers is seen in the high exposure grouping, suggesting that these workers leave the mining industry prior to accumulating high exposure. The effects seen are likely to be due to the fact that those most severely affected by the exposure are most likely to leave employment, and therefore be ex-miners at the time of cross sectional studies such as this. This is the basis of the "healthy worker survivor effect".

4.9.3 Questionnaire data vs smoking history

Of the 896 study participants, 544 (59.13%) had smoked in their lifetimes. Of the latter, 398 were current smokers.

As shown in figure 4.9.3.1 (corresponding table in Appendix 8.6), respiratory symptoms were strongly associated (chi square p value <0.0001) with a history of cigarette smoking, with current smokers having the highest prevalence of symptoms, ex smokers an intermediate prevalence, and never smokers the lowest prevalence. A history of TB was not associated with smoking status.

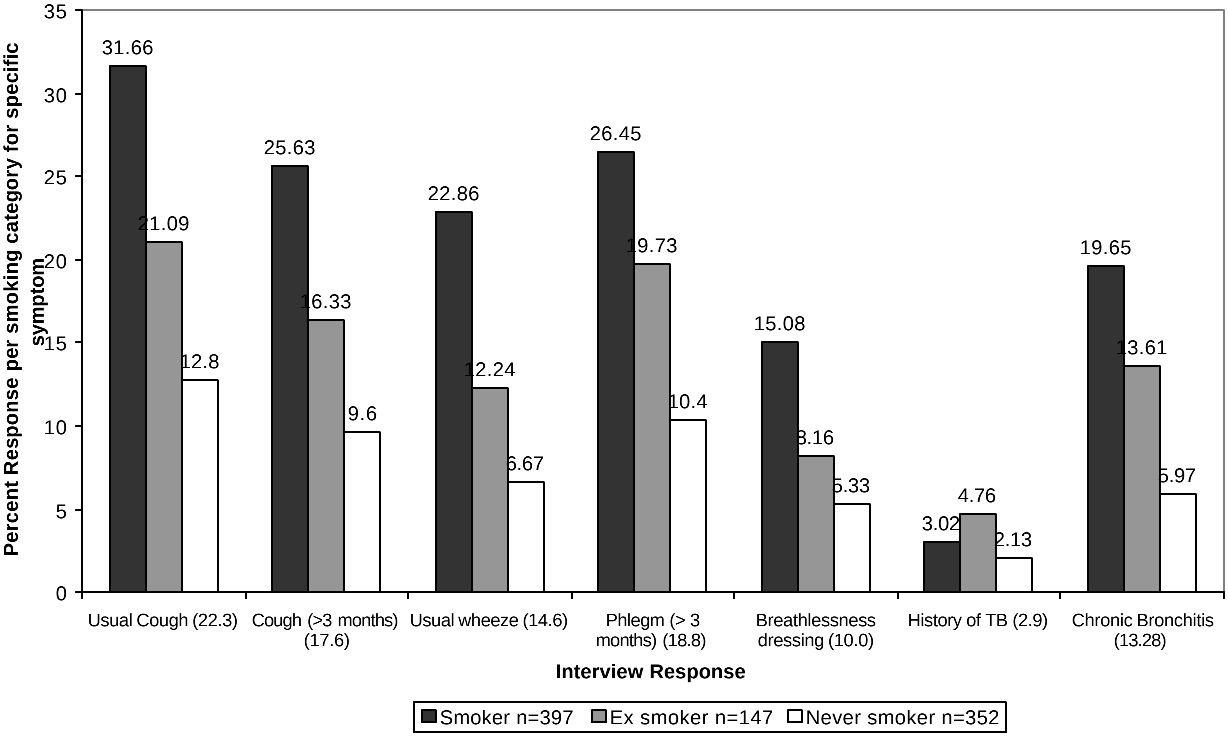

Figure 4.9.3.1 Respiratory health of South African Coalminers: association of categorical outcomes vs categories of smoking status (%)

4.9.4 Questionnaire data vs pack years

Of the 544 smokers, the mean pack years smoked was 7.34 (sd=7.36). The variable was divided into four categories as described above. With the exception of TB, all other outcomes show a strong association ($0.0001 < p < 0.0008$) and strong increasing trend ($0.0001\ p < 0.001$) with increasing pack years. These data are shown graphically in figure 4.9.4.1 below (the detailed table is shown in Appendix 8.6).

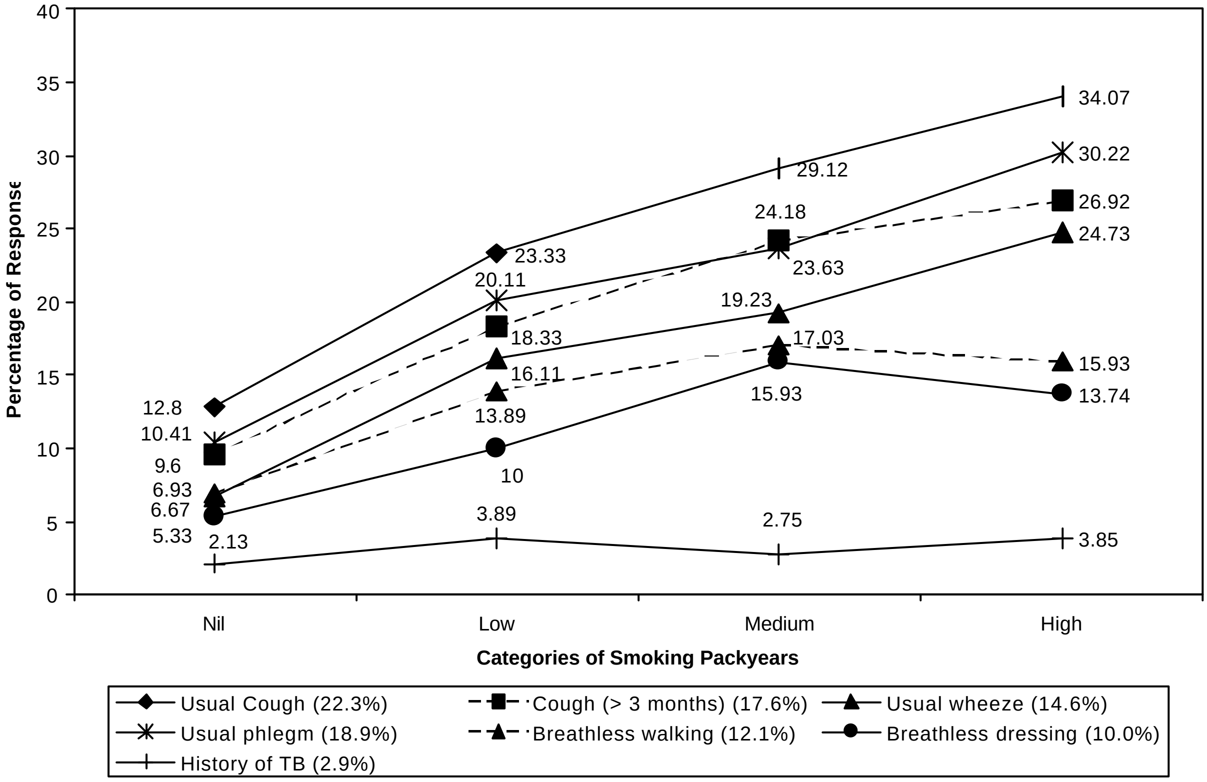

Figure 4.9.4.1 Respiratory health of South African Coalminers: association and trends for categories of packyears (entire dataset)

4.10 Lung function outcomes

KEY FINDINGS (SECTION 4.10):

- The predictor equations developed by Louw et al (1996) were used to establish the expected values for this population. Percentage of predicted lung function outcomes were calculated and used in subsequent analysis. This allows for the standardisation of age and height during comparative analysis.
- This section reports the findings as seen in the study (reported as percent of predicted). In section 5, these findings are translated into actual losses in millilitres (ml) of FEV_1 and FVC for an “average” worker.
- Bivariate analyses showed significant differences in mean percent predicted FEV_1 (107.5% vs 102.16%) and FVC (106.53% vs 100.76%) between the medium and high cumulative exposure groupings respectively. Significantly higher values of FEV_1 were seen in the current miners when compared against the ex-miners in the medium (109.19% vs 102.51%) and high (102.44% vs 95.42%) cumulative exposure categories.
- Statistically significant differences in mean percent predicted FEV_1 (102.21%, 105.14%) and FVC (100.09%, 102.21%) were seen between surface and underground workers respectively, with surface workers having a lower outcome.
- The percent predicted FEV_1 (104.92%, 101.05%) and FVC (105%, 100.44%) were significantly higher amongst current smokers than ex-smokers. No significant differences were seen amongst current and never smokers.
- Multivariate linear regression models were developed for outcomes of percent predicted lung function, controlling for cumulative exposure, smoking status, employment status, pack years and doctor diagnosed TB.
- Regression models showed that for percent predicted FEV_1, a 0.03% (i.e. percentage point) decline was associated with each year of exposure and each mg/m^3 dust level, while controlling for the other variables. A 0.30% decline in percent predicted FEV_1 was seen with each pack year of smoking, together with an 21.02% decline in the presence of previously diagnosed TB. A 3.92% increase in FEV_1 was associated with current miner status.
- A 0.03% decline in FVC was associated with each year of exposure and each mg/m^3 dust level. Declines of 0.21% for each pack year and 13.61% for previously diagnosed TB were seen. A 3.68% increase was associated with current mining status.
- At least 6% of workers were below the 5th percentile for predicted FEV_1, and 5% for predicted FVC. 2.82% of workers had lung function less than 65% of predicted – this implies these workers have interference with normal daily life.
- This data indicates that a lifetime of dust exposure in coal mines results in a decline in lung function more than that would be seen with normal declines with age. This is seen irrespective of the influence of cigarette smoking.
- Previous diagnosis of TB was a very important influencing factor of the lung function outcomes.

- The data also showed that those who were still employed had better lung functions than those who left the mining employment. This could be explained by the “healthy worker effect”.
- The effects in loss of lung function are similar to those seen in other international coalmining studies, while the loss due to TB is within the range described by other South African studies amongst goldminers. The “healthy worker effect” has also been described in the latter population.
- The study shows that dust exposure is an important predictor for loss of lung function, independent of TB and smoking.

4.10.0 Lung function estimation

Lung function testing is an objective method to test the degree of functioning of the respiratory system. It is capable of detecting abnormalities in the absence of symptoms or negative findings on chest radiographs. It can provide a quantitative index of impairment. It is important however, that these tests are conducted with the appropriate equipment, by trained technicians, in a standardised manner. The equipment and testing method standards are conducted based on the criteria established by the American Thoracic Society.

Various factors, apart from poor respiratory health, influence the results of lung function tests. It is therefore important that these tests are correctly interpreted. Key factors that influence lung function are gender, age and height. Lung function declines gradually with increasing age and reduced height in normal people. In addition, other factors, such as racial or socio-economic or some unexplained population characteristics may also influence changes in lung function in healthy people. Because of this variation in normal, it is very important that when tests are being evaluated for normality all these factors are taken into account.

These factors are taken into consideration in the development of normal values or **“predicted values”** (i.e. the value that one predicts will be seen in a healthy individual with a particular gender, height and age from a specific population group). The latter data is derived through the process of large scale research projects in various parts of the world. These projects develop **“prediction equations”** which allow for the calculation of the predicted values for specific individuals. The debate as to the most useful set of prediction equations applicable to the African working population in South Africa has been a long standing one. This is because of deciding what values will take into consideration the “racial” or “unexplained” population characteristics. Recent studies and evaluation of South African studies have established a reasonable consensus of the debate in this country, and this is explained further in the appropriate sections of the report.

Once having decided on the set of “prediction equations”, the predicted value (assume this predicted value = *Y*) for a healthy individual of the same gender, age, height and population characteristic as the tested individual is calculated (generally done automatically by the testing equipment). The tested individual’s result (assume = *X*) is then compared against this newly calculated “predicted value”. This is calculated as a percentage:

$$X/Y \text{ x } 100\%,$$

and the tested individual’s result is expressed as **“percent of predicted”**. The latter phrase is used extensively during the Results and Discussion sections of this report. This “percent of predicted” is used because to report on **absolute values** (the actual value that the tested person produces when the test is conducted) cannot be compared against his/her peers, because of the different height, age, gender and other factors as explained above.

The text of the report also makes reference to “**clinically important declines”** in lung function (this concept is explained in the Glossary). This refers to a drop in lung function that is greater than what would be expected for an individual of a specific gender, from a particular population of a specific height and age. Abnormal lung functions are usually defined when the FEV_1, FVC or the ratio of the two is below that of 5^{th} percentile (i.e. the lowest 5% of the population from which the predicted equation is derived). It must be emphasised that this is an arbitrary statistical calculation, and is subject to various factors. The lower limit of normal makes use of the prediction equation and the standard deviation (spread of the data around the average) of the equation. The 5^{th} percentile (assuming that the lowest 5% of the population is "abnormal"), is calculated in the following manner:

Predicted value for age and height – (1.645 x standard deviation)

where the predicted value is obtained from a defined prediction equation, and the standard deviation is derived from the spread of the data of that equation. Workers with levels lower than 65% of predicted are likely to suffer from disabling respiratory disease.

In the current study, approximately 15 lung function tests were rejected for not meeting American Thoracic Society criteria for either start or end of test. A standardised set of predictor equations needs to meet certain criteria, including originating from populations of non-smoking healthy individuals, not involved in activities involving exposure to respiratory hazards. The equations were derived from a study conducted by Louw et al (1996) based on a South African black population that met the above criteria. They have been recommended as a reference standard for black South African mining populations, and have been applied previously to black in-service mining populations and shown to have good statistical fit (Hnizdo et al 2000). For these reasons, the Louw equations have been applied in this study. Ehrlich et al (2000) recently reviewed this data and re-run models for standing height. These equations for FEV_1 and FVC are:

$$FEV_1\,(L) = -0.535 + 0.029\,(height\,(cm)) – 0.027\,(age\,(years))$$
$$FVC\,(L) = -3.08 + 0.048\,(height\,(cm)) – 0.024\,(age\,(years))$$

Using the above prediction equations, predicted values were determined for each case. Percentage predicted values were then calculated and used in subsequent analyses. The lower limits of normal (5^{th} percentile) were also calculated using this formula and the standard deviation as calculated by Erhlich et al (2000) as 4.6 for FEV_1 and 0.54 for FVC.

4.10.1. Lung function outcomes vs Cumulative Dust Exposure (CDE)

Employing the CDE variable, as calculated previously, further examination of the lung function outcomes was conducted. Cumulative dust exposure was grouped into the previously described categories. Stratified analysis on employment status was also conducted. The predicted values were calculated using the Louw equations.

Statistically significant differences were seen between middle and high exposure groupings for predicted values of FEV_1 and FVC. The mean percent predicted values of both FEV_1 and FVC were lower in the higher exposure category. There were no significant differences between the low and high exposure categories. Similar non significant findings were seen between the middle and low exposure groupings. Table 4.10.1.1 (Appendix 8.6) contains the details of this analysis, while the figures 4.10.1.1 and 4.10.1.2 demonstrate the findings and the trends with increasing exposure for both FEV_1 and FVC amongst all, current and ex-miners.

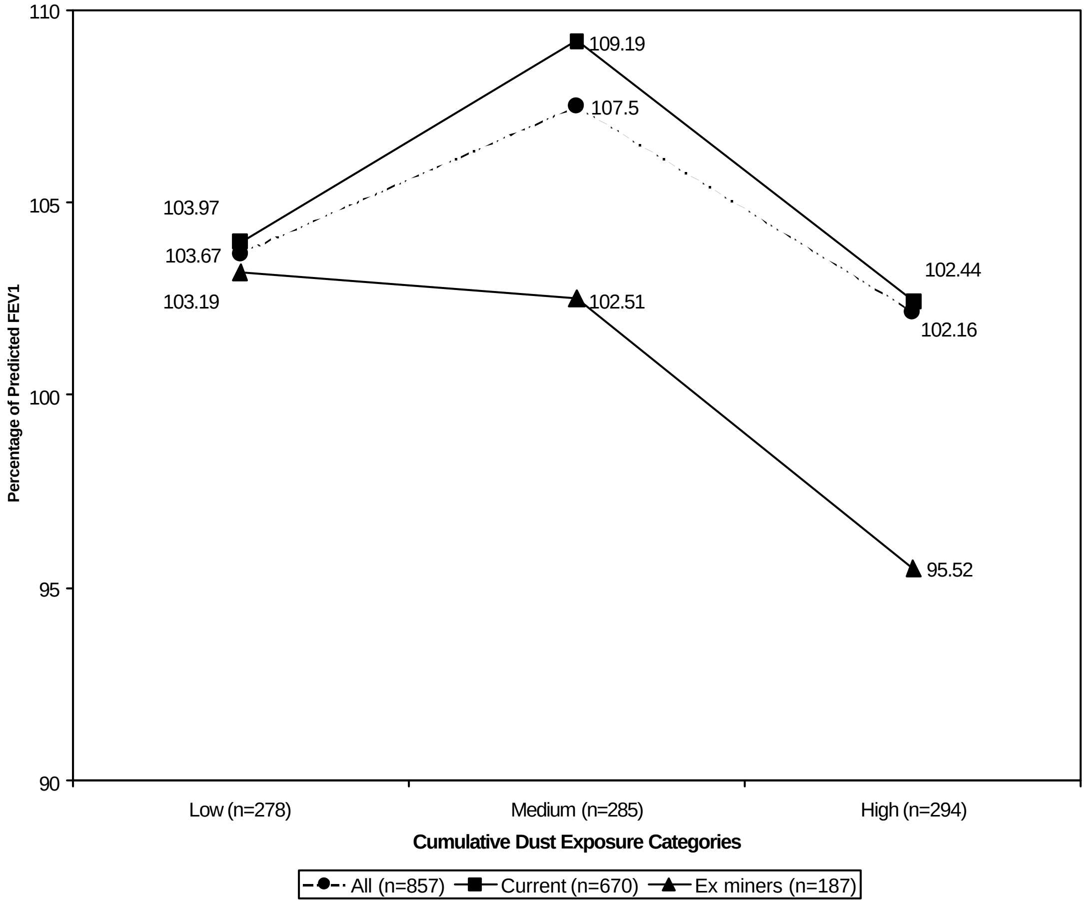

Figure 4.10.1.1 Respiratory health of South African Coalminers: percentage predicted FEV$_1$ for categories of cumulative dust exposure for all miners, current and ex – miners

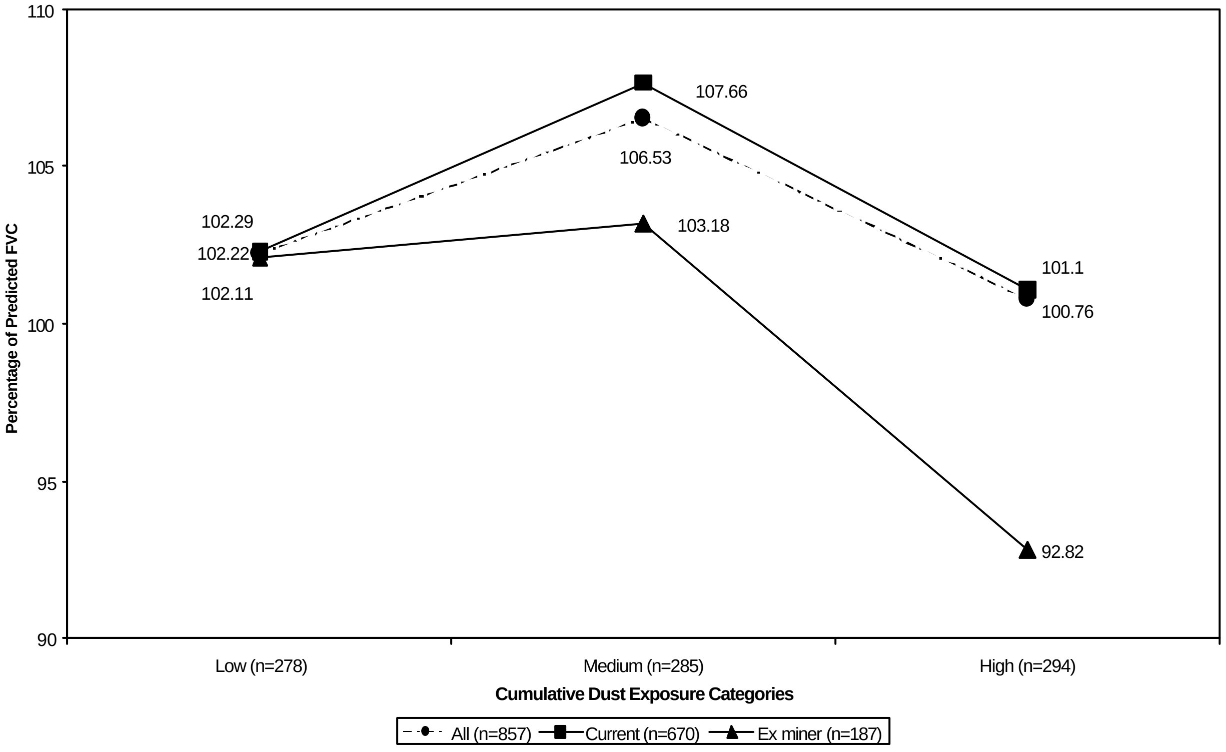

Figure 4.10.1.2 Respiratory health of South African Coalminers: percent predicted FVC for categories of cumulative dust exposure among all, current and ex – miners

Further investigation attempted to determine the relationship between employment status and lung function outcomes. Significant differences were seen between the medium vs high and medium vs low categories for percent predicted FEV_1 and FVC in those currently employed. No significant differences in the lung function outcomes were seen across the exposure categories in the ex-miners. This detail is contained in table 4.10.1.3 (in Appendix 8.6), and reflected in the figures, 4.10.1.1 and 4.10.1.2.

In order to determine whether there were differences between the employment status for each exposure category, differences in the means were analysed. Significant differences by employment status were seen with respect to percent predicted FEV_1 and FVC in the medium category between current and ex-miners (student t test p value=0.03). There were no other significant differences in the lung function outcomes in the different employment categories.

When examining lung function in underground and surface workers (i.e. a lifetime history of no underground exposure), statistically significant differences ($p<0.05$) were seen in the percent predicted FEV_1 and FVC between the two groups, with the lower values seen in the surface workers. This is shown in figure 4.10.1.4 (details in table 4.10.1.4 in Appendix 8.6).

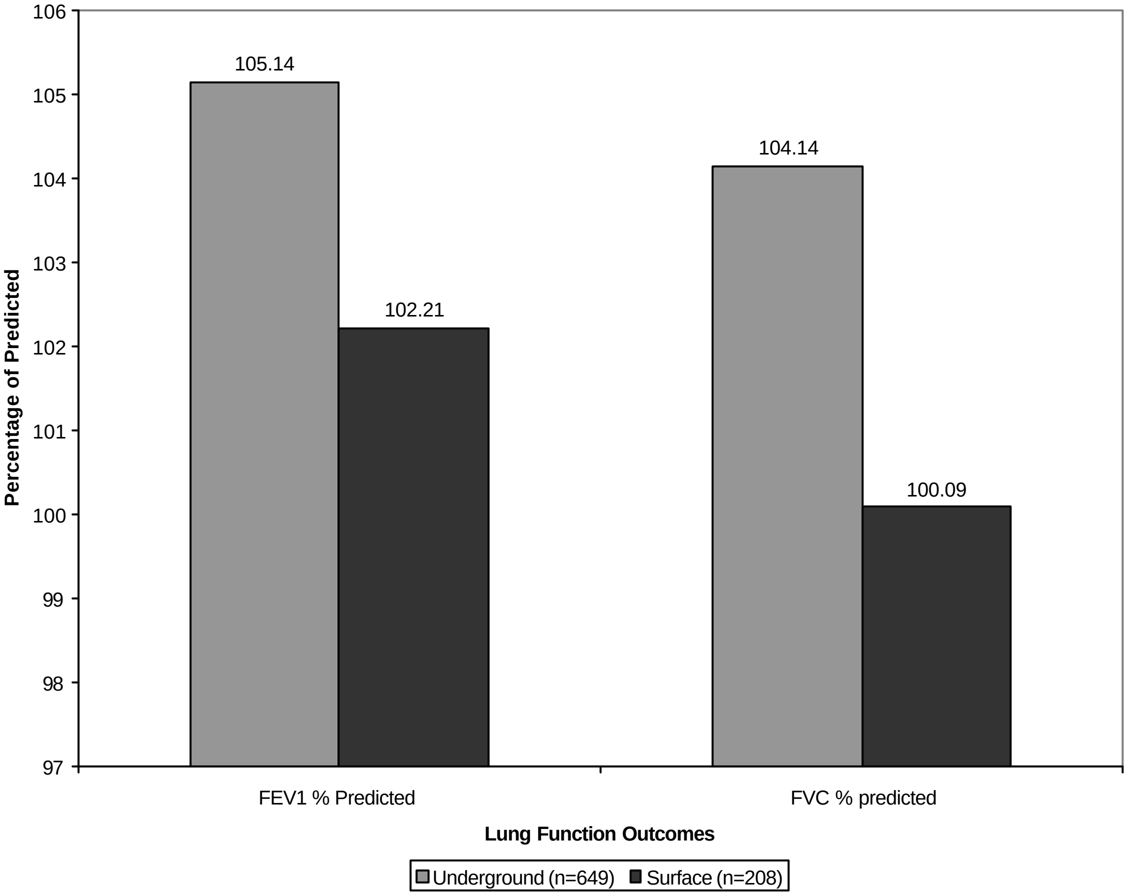

Figure 4.10.1.4 Respiratory health of South African Coalminers: lung function percent predicted FEV_1 and FVC stratified on exposure zone (underground/surface)

A good indication of the relationship between two variables is to calculate the correlation coefficient, which indicates how one variable changes with another on a linear scale. This was calculated for CDE and each of the lung function outcomes. Percent predicted FEV_1 for current and ex-miner were not statistically significant, but in the expected direction (increasing dust exposure results in declines in outcomes). These were relatively low correlation coefficients.

None of the coefficients for percent predicted of FVC were statistically significant. Table 4.10.1.5 provides these details.

Table 4.10.1.5 Respiratory health of South African Coalminers: correlation coefficients for cumulative dust exposure (mg-years/m^3) and lung function (% predicted) outcomes

Job Status	FEV_1 (p value)	FEV_1 % predicted r^2 (p value)	FVC (r^2 p value)	FVC % predicted r^2 (p value)
All miners	-0.09 (0.01)	-0.04 (0.06)	-0.07 (0.03)	-0.03 (0.36)
Current	-0.12 (0.01)	-0.06 (0.10)	-0.09 (0.02)	-0.06 (0.23)
Ex miner	-0.15 (0.04)	-0.07 (0.30)	-0.14 (0.05)	-0.05 (0.5)

Further analysis of the lung function outcomes using multiple linear regression models are presented in the later sections.

4.10.2 Lung function outcomes vs smoking

Lung function outcomes were analysed against smoking habits.

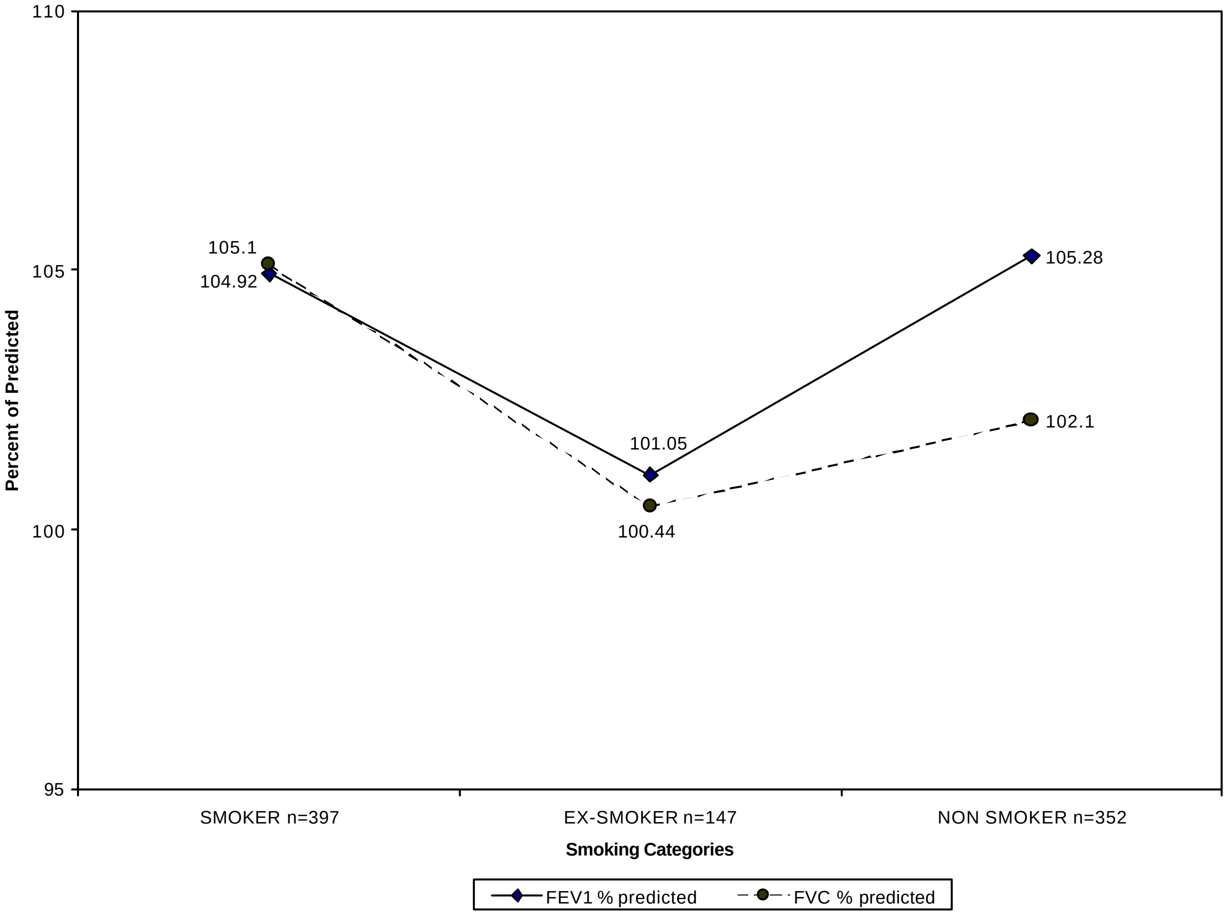

Figure 4.10.2.1. Respiratory health of South African Coalminers: smoking status vs percent predicted lung function outcomes

Analysis revealed significant differences in percentage predicted FEV_1 and FVC between current and ex-smokers, with current smokers having a higher percent predicted outcome than ex-smokers (shown graphically in figure 4.10.2.1, and detailed in table 4.10.2.1 (Appendix 8.6)). These results suggest that, in combination with the effects of coal dust exposure, those smokers with fewer adverse effects on lung function are more likely to continue to smoke than others, resulting in the relatively lower lung function among ex-smokers. There were no statistically significant differences between current and never smokers for percentage predicted FEV_1 (p value=0.5). The difference in percentage predicted FVC outcomes between current smokers and never smokers was significant (p value = 0.01).

There was a positive (and significant) correlation with percent predicted FEV_1 and pack years of smoking, i.e as pack years of smoking increased, a significant decline in percent predicted FEV_1 was noted (r^2 = -0.08, p value = 0.02). No significant relationship was seen with FVC.

4.10.3 Linear regression models for lung function outcomes

As discussed in section 4.10.0, a number of factors influence lung function of normal healthy individuals. As such, each absolute lung function test result (i.e. actual result produced by the tested individual) must be compared as a percentage against a set of “predicted values”. In this study we made use of the “prediction equations” developed by Louw et al (1996) to obtain the predicted values for our study participants. Having “standardised” our study population by making use of the percent predicted values of FEV_1 and FVC, we analysed our data to see what other factors (apart from gender, age, height and race) may influence our lung function outcomes. This is done through statistical modelling – the creation of a multiple regression models. This process is done by including probable influencing factors (such as cumulative dust exposure, history of TB, etc.) into a computer based model, and then evaluating the results of the model and assessing the model for accuracy. The advantage of using a multiple variable model is that you can assess the extent to which each variable influences the outcome, while controlling for other probably influential factors. Several models can be created and evaluated, depending on the research questions of interest, biological sense, previous research experience, etc. The detailed statistical steps that were used in this process are included in Appendix 8.3.

Following the statistical analyses and the various techniques of assessing whether the statistical models were appropriate, models for each of the lung function outcomes (percent predicted FEV_1 and FVC) were chosen. According to the statistical analyses, percent predicted FEV_1 and FVC were influenced by cumulative dust level, current smoking status, current employment status, previously diagnosed TB and pack years.

The actual models are represented by the following equations:
Selected model (Multivariate Model 14 from Table 4.10.3.1)

> **FEV_1 % predicted** = 105.68 – 0.04*(dust level (mg/m^3) x years of exposure) + 1.96*(current smoker) + 3.84*(current miner) – 21.04*(previously diagnosed TB) – 0.93*(pack years) + 0.71*(pack years x current smoker)

The actual models of percent predicted FVC:
Selected model (Multivariate Model 9 from table 4.10.3.2)

> **FVC % predicted** = 100.95 – 0.03*(dust level (mg/m^3) x years of exposure) + 5.32*(current smoker) + 3.68*(current miner) – 13.61*(previously diagnosed TB) – 0.21*(pack years)

MODEL INTERPRETATION GUIDE (REGRESSION EQUATIONS):

- Multiple linear regression models allow for determining the effect of one variable (a predictor) on a specific outcome, while holding the other variables (predictors) constant. Analysis that does not include all predictors does not take into account the simultaneous effect that predictors have on an outcome (e.g. bivariate analysis).
- Example of multiple regression: FEV_1 = y – x_1 (age) + x_2 (height) – x_3 (dust exposure level).
- Bivariate analysis of changes in absolute lung function in two exposure categories may show significant differences, but if in the higher exposure category workers are older and shorter, this may lead to a lower lung function, which maybe erroneously attributed to higher exposure. Multiple regression will allow for the analysis of the effect age, height and exposure category simultaneously.
- These equations produce “parameter coefficients” (x_{1-3} in the example above) (see Glossary), which predict how the outcome will vary when the predictor changes, while the other predictors are held constant. For example, let $x_1 = 2$, $x_2 = 5$ and $x_3 = 3$: this implies that for every increase of one year in age, there is a drop in FEV_1 by a factor of 2, assuming no change in the person’s height or exposure category. Similarly, for every increase by a single unit of dust level, the person’s FEV_1 drops by a factor of 3, assuming no change in age or height. (The arithmetic sign preceding the “coefficient” determines whether there is a drop or increase).
- Thus the multiple linear regression models for the outcomes of FEV_1 and FVC above have similar interpretations. For example, the model for FEV_1 implies that for every increase in dust level by 1mg/m^3 in each year, there is a drop in the percent predicted of FEV_1 of 0.04%, independent of the effects of smoking, past TB or current employment status. Similarly, if someone is currently a miner, then there is an increase in percent predicted FEV_1 by 3.96%.
- To know the full effect of the change in percent predicted FEV_1 in an individual, one has to calculate the effects of ALL the variables simultaneously, depending on how each predictor is present in that individual.
- For example, using the model for FEV_1 , in a current miner with 10 years of dust exposure at 1mg/m^3 with a previous history of TB and currently smoking with a 10 pack year history, percent predicted FEV_1 = 105.68 – 0.04 x (1mg/m^3 x 10 years) + 1.96 x (current smoker) + 3.84 x (current miner) – 21.04 x (previous TB) – 0.93 x (10 packyears) + 0.71 x (10 packyears x current smoker).
- This results in = 105.68 – (0.04x1x10) + (1.96x1) + (3.84x1) – (21.04x1) – (0.93x10) + (0.71x10x1) = 87.84.

4.10.4 Clinically important declines in lung function

This is discussed in the section 4.10.0 above. For each participant in the study, a lower limit of normal (LLN) was calculated. In terms of the calculation, 6.40% of workers had an FEV_1 that was below the LLN. This varied from 5.74% for currently employed, to 8.52% of the ex-miners. A similar percentage of workers fell below the LLN when the FVC criteria was used: 4.66% were in the “abnormal” category. This ranged from 4.73% for current miners and 4.48% for ex-miners. Similarly, a level of lower than 65% of predicted FEV_1 is likely to result in an interference with normal daily living. In this study, 2.82% (1.72% of current worker and 6.28% of ex-miners) of workers met this disability criterion. This data therefore indicates that an important category of workers in the sample is outside the accepted limits of normality.

4.11 Radiographic Outcomes

KEY FINDINGS (SECTION 4.11):

- Two experienced readers read the chest radiographs independently and blinded to exposure status of the participants. The films were read according to the ILO 1980 Classification of Pneumoconiosis.
- There was 98.88% agreement between the readers when profusion was graded as 1/1 (kappa statistic of 0.58). There was moderate agreement with regard to TB (kappa = 0.48).
- Prevalence of pneumoconiosis was low. For profusion grade $\geq$ 1/0, prevalence in the sample ranged between readers from 1.9 – 4.24%. The prevalence of TB was 5.40% (reader 1) and 3.60% (reader 2).
- A significant association and trend of increasing cumulative exposure (CDE) with increasing prevalence of pneumoconiosis was seen.
- Lung function outcomes were higher for those with profusion grades of $\leq$ 1/1.
- The findings of increasing prevalence with increasing exposure have been documented in several studies amongst coalminers. The levels of pneumoconiosis of approximately 4% diagnosed on radiographs is much lower than that seen amongst goldminers, with prevalence of silicosis of 14%. The prevalence of 4% compares with that of US studies of 6.8%.
- Hyperinflation on radiographs could act as a surrogate for emphysema. A significantly higher cumulative exposure was present amongst those with hyperinflation than those without. Smoking and lung function outcomes were not significantly associated with this variable, possibly due to the small sample size (n = 44).
- The findings suggest a dose related risk for pneumoconiosis, but an overall low risk for disease amongst South African coalminers.

4.11.1 Descriptive radiographic data

It has been well established in the scientific literature that in the reading of profusion scores on chest radiographs, there is considerable inter reader and intra reader variability. To control for inter reader variability, two readers were responsible for the reading of the chest x-rays. Professors White (UCT) and Solomon (NCOH) conducted the readings. Eight hundred and seventy two films were read by both readers according to the International Labour Organisation’s 1980 Classification of Pneumoconiosis.

Table 4.11.1.1 Respiratory health of South African Coalminers: findings on radiographs between two readers (n (%))

PATHOLOGY	READER 1 (N=872)	READER 2 (N=872)
Any abnormalities	106 (11.92)	192 (21.60)
TB	32 (3.60)	48 (5.40)
Large Opacities	1 (0.11)	6 (0.67)
Pleural abnormalities	4 (0.45)	7 (0.79)
Coalesced opacities	1 (0.11)	1 (0.11)
Bullae	0	17 (1.91)
Cancer	0	4 (0.45)
Effusion	0	2 (0.22)
Emphysema	0	215 (24.18)
Eggshell Calcification	1 (0.11)	2 (0.22)
Fractured ribs	22 (2.47)	20 (2.25)
Hilar nodes	0	3 (0.34)
Ill defined diaphragm	0	1 (0.11)
Fissure pleural thickening	3 (0.34)	6 (0.67)

For most radiographic outcomes, the readers seemed to be similar, with the exception of radiographic diagnosis of emphysema. The latter differences existed because of the definitions used by the readers. Reader 1 was of the opinion that in the absence of a lateral, commenting on emphysema on a antero-posterior film was of little scientific value. Previous studies have shown that a strong correlation between radiographic findings and pathological findings of emphysema only exists when the lung is more than 66% damaged. Reader 1 reflected his opinion on possible obstructive disease by referring to the lung fields as being “hyperinflated”. Relationships between this variable and cumulative exposure and lung function outcomes were investigated. Reader 2 used the symbol “em” on the ILO classification when the chest appeared hyperinflated, i.e. if there were 11 or more ribs evident posteriorly on the right or, more specifically, if more than half of the space between the tenth and eleventh ribs posteriorly on the right was seen above the dome of the diaphragm.

4.11.2 Reader agreement analysis

Because of the known inter-reader variability, it was important to compare how closely the two readers assessed the radiographs for the various outcomes. The statistical method for comparing is by determining the degree of agreement, and is represented by the kappa statistic.

4.11.2.1 Profusion

In order to determine degree of agreement between the two readers for various radiological findings, kappa statistics were estimated. Several different kappa statistics are presented, looking at different definitions of abnormality and precision between the readers. In looking for an exact match for level of profusion (i.e. all 12 points on the ILO system) on the films, the weighted kappa statistic was 0.30 (not shown in tables). This suggests a low to moderate level of agreement with each radiograph. Different kappa statistic values were obtained, depending on the definition of pneumoconiosis used. The data for pneumoconiosis defined as 0/1 or greater or greater than 1/1 is shown in Appendix 8.4. When using the cut off for positive pneumoconiosis as being 1/1, this statistic changes to 0.40 (CI = 0.232 – 0.568), a moderate level of agreement. At this cut off, 840 (96.52%) films were read in complete agreement. This is shown in table 4.11.2.2.

Table 4.11.2.2 Respiratory health of South African Coalminers: table of agreement between readers for ≤1/0 vs > 1/0

		READER 2		
		NEGATIVE	POSITIVE	TOTAL
READER 1				
NEGATIVE	N	829	26	855
	%	95.07	2.98	98.05
	Row %	97.02	2.98	
	Col %	99.41	70.27	
POSTIVE	N	6	11	17
	%	0.69	1.26	1.95
	Row %	31.25	68.75	
	Col %	0.59	29.73	
TOTAL	N	835	37	872
	%	95.76	4.24	100

Whichever definition of normality is used, it is obvious that the prevalence of pneumoconiosis in this population is low (1.03% – 4.24), unless the definition of >0/1 is considered, when the prevalence is 13.42%.

Analysis was conducted to determine exact differences between the readers using the ILO Classification. For 89.65% of films, the readers were only ½ point different from each other on the ILO 12 point scale. Only 20 (2.25%) films were read as extreme as four half point differences.

4.11.2.2 Shape and size of opacities on radiographs

The overwhelming majority of films were read as having rounded regular opacities. Reader 1 scored only four cases as being of irregular shape and size, while reader 2 scored eight in this category. The type most often associated with coaldust exposure is rounded opacities.

4.11.2.3 Tuberculosis

Kappa statistics were run for the diagnosis of TB on the radiographs between the two readers. The results are shown in Table 4.11.2.5. There is moderate agreement between the readers with regard to this diagnosis. In 849 (95.5%) films the readers were in complete agreement about the presence or absence of TB, with a kappa statistic of 0.48 (CI = 0.34 – 0.62).

Table 4.11.2.5 Respiratory health of South African Coalminers: table of agreement between readers for radiographic diagnosis of TB

		READER 2		
		NEGATIVE	POSITIVE	TOTAL
READER 1				
NEGATIVE	N	807	26	833
	%	93.19	3.00	96.19
	Row %	96.73	3.27	
	Col %	98.57	58.33	
POSTIVE	N	13	20	33
	%	1.50	2.25	3.81
	Row %	37.50	62.50	
	Col %	1.43	41.67	
TOTAL	N	820	46	866
	%	94.69	5.31	100

Once again, the prevalence of TB as diagnosed by x-ray was fairly low, with a range between readers of 3.81% - 5.31%. This is in accord with the low levels of previous TB reported by study participants during the interview. As the readers differed in the way they read emphysema, no kappa statistic was run for this outcome.

4.11.3 Radiographic outcomes vs Cumulative Dust Exposure (CDE)

The radiographic data was then analysed using the cumulative dust exposure (CDE) measures. For the purposes of this analysis, the readings of readers 1 and 2 (n=872) are shown separately. When CDE categories (excluding years of no exposure at the coalface) are used as an exposure measure, only pneumoconiosis (defined as >1/0 ILO scale) is strongly associated with exposure, and shows an increasing trend with increasing exposure. No such trends existed for radiological evidence of TB nor radiological evidence of emphysema. These are shown in figures 4.11.3.1 and 4.11.3.2 below (with details in the corresponding tables in Appendix 8.6).

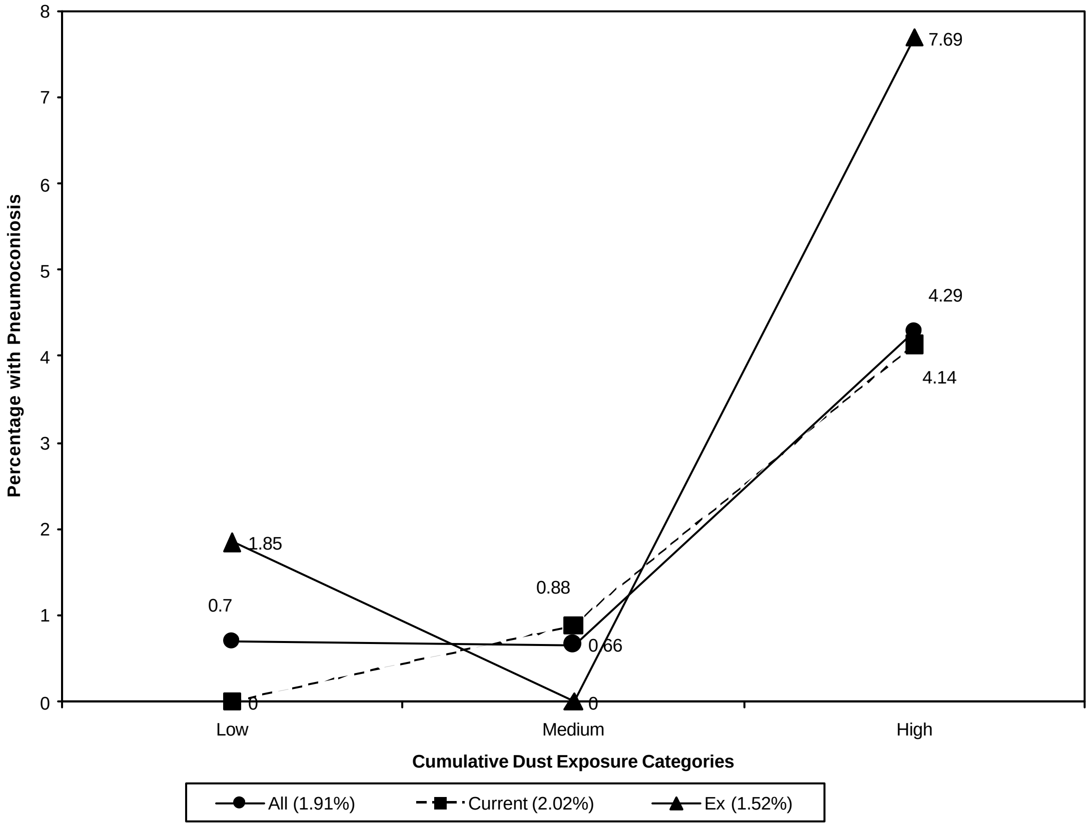

Figure 4.11.3.1 Respiratory health of South African Coalminers: trends for pneumoconiosis vs cumulative dust exposure for all, current and ex miners - Reader 1

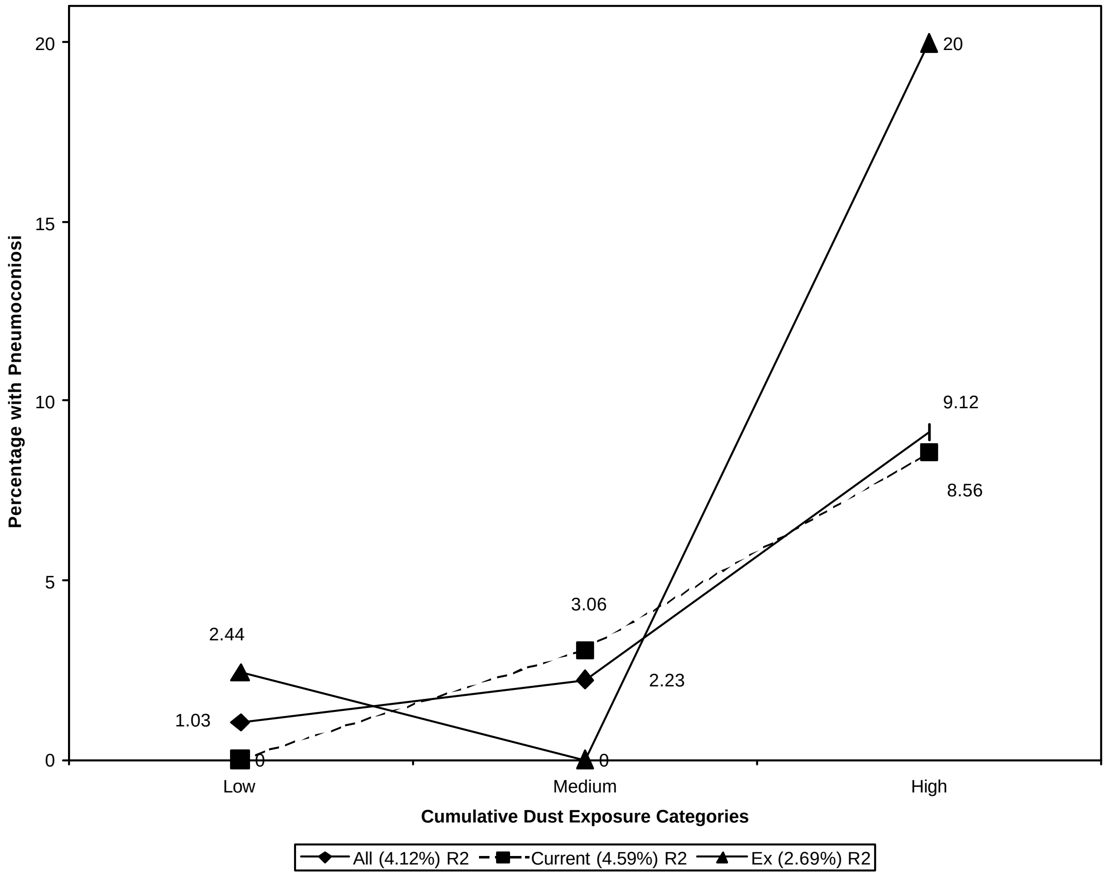

Figure 4.11.3.2 Respiratory health of South African Coalminers: trends for pneumoconiosis vs cumulative dust exposure for all, current and ex miners – Reader 2

Further analysis was conducted stratifying on the basis of employment (also refer to figures 4.11.3.1 and 4.11.3.2). When analysing only the current miners, pneumoconiosis retains its significance ($p < 0.001$), with TB also showing a significant trend (p value <0.03) but in a negative direction to exposure for reader 2 only (not shown). This finding may be a reflection of the current approaches on mines, where workers, when diagnosed with TB, are removed from the higher exposed areas. When reviewing ex-miners only, pneumoconiosis for reader 2 remained significantly associated with exposure (p value <0.001). However, the exposure response estimates for both readers are likely to be unstable because of the low number of individuals read as having pneumoconiosis.

4.11.4 Pneumoconiosis vs lung function outcomes

Analysis was conducted to determine whether any differences in the mean lung function outcomes for predicted percents of FEV_1 and FVC were seen in relation to pneumoconiosis. For both readers, those workers defined as having pneumoconiosis had lower mean percent predicted lung function outcomes. This was only statistically significant for reader 1. This is shown graphically in figure 4.11.4.1 and the details in the corresponding table in Appendix 8.6.

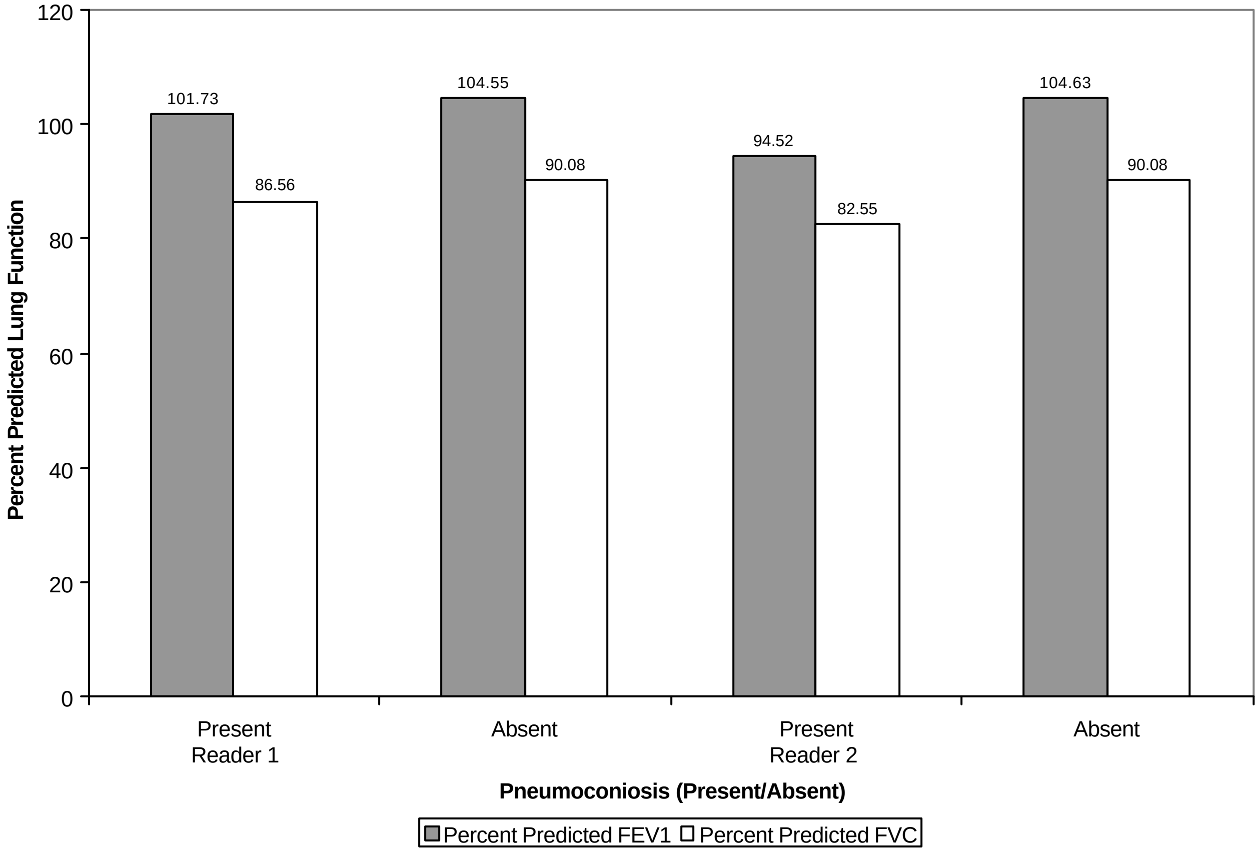

Figure 4.11.4.1 Respiratory health of South African Coalminers: means of lung function outcomes vs pneumoconiosis status for each reader

4.11.5 Radiographic outcomes vs smoking

Contrary to the dust exposure variables, TB and emphysema showed significant associations with smoking status, as shown in the tables 4.11.5.1 and 4.11.5.2.

Table 4.11.5.1 Respiratory health of South African Coalminers: association for categorical outcomes vs categories of smoking status (number (% within smoking category)) – Reader 1

RESPONSE (n=872) (n (%))	Smoker n=384	Ex smoker n=142	Never smoker n=346	Chi Square p value
Radiological evidence of TB (33 (3.71))	14 (3.66)	10 (7.14)	9 (2.45)	0.04
Pneumoconiosis (17 (1.90))	10 (2.72)	2 (1.41)	5 (1.30)	0.33

Table 4.11.5.2 Respiratory health of South African Coalminers: association for categorical outcomes vs categories of smoking status (number (% within smoking category)) – Reader 2

RESPONSE (n=871)	Smoker n=383	Ex smoker n=142	Never smoker n=346	Chi Square p value
Radiological evidence of TB (49 (5.48))	23 (5.99)	14 (9.86)	12 (3.26)	0.01
Radiological evidence of emphysema (216 (24.16))	123 (32.03)	37 (26.06)	56 (15.22)	<0.0001
Pneumoconiosis (38 (4.25)	15 (4.08)	9 (6.34)	14 (3.65)	0.40

Analysis of radiological outcomes with pack years of smoking showed a significant association and trend for emphysema.

Table 4.11.5.3 Respiratory health of South African Coalminers: association and trends for radiological outcomes vs categories of pack years – Reader 1

	CATEGORIES OF PACKYEARS					
RESPONSE (n (% of total respondents)) (n=872)	No smoking (n=346) (n (%))	Low (n=172) (n (%))	Medium (n=176) (n (%))	High (n=178) (n (%))	Chi square p-value	Trend test p value
Radiological TB (33 (3.71))	9 (2.45)	10 (4.31)	8 (4.00)	6 (6.67)	0.25	0.04
Pneumoconiosis (17 (1.90))	10 (2.72)	1 (0.58)	1 (0.57)	5 (2.51)	0.15	0.43

Table 4.11.5.4 Respiratory health of South African Coalminers: association and trends for radiological outcomes vs categories of pack years – Reader 2

	CATEGORIES OF PACKYEARS					
RESPONSE (n (% of total respondents)) (n=872)	No smoking (n=375) (n (%))	Low (n=172) (n (%))	Medium (n=176) (n (%))	High (n=178) (n (%))	Chi square p-value	Trend test p value
Radiological TB (49 (5.49))	12 (3.26)	16 (9.30)	12 (6.82)	9 (5.08)	0.03	0.32
Radiological emphysema (216 (24.19))	56 (15.22)	41 (23.84)	61 (34.66)	58 (32.77)	<0.001	<0.001
Pneumoconiosis (38 (4.26))	15 (4.08)	9 (5.22)	4 (2.27)	10 (5.65)	0.40	0.31

4.11.6 Analysis of “Hyperinflation” (Reader 1) and “Emphysema” (Reader 2)

As explained in the introduction to the section, each reader adopted a different approach to the diagnosis of emphysema on chest radiograph, with reader 1 abstaining from making such diagnosis. Using reader 2’s diagnoses of emphysema, there were no statistically significant associations with exposure or trend in either the entire cohort, the subsets of current or ex-miners (all p values >0.2).

Because the possible correlation between emphysema (as a pathological entity) and the radiographic findings of hyperinflation, separate analysis was run on those films which included the comment “hyperinflation” and “overinflation” by reader 1 (n=44).

Table 4.11.6.1 Differences seen among those with and without radiographic findings of hyperinflation

	Hyperinflation	No Hyperinflation	T test p value
FEV_1 % predicted (SD)	105.20 (25.05)	104.39 (17.95)	0.80
FVC % predicted (SD)	93.56 (18.34)	89.75 (13.67)	0.17
Mean CDE ($mg/m^{3.}$years (SD))	79.36 (68.30)	56.98 (50.88)	0.03
Pack years (SD)	5.93 (6.82)	4.26 (6.90)	0.12

The extremely small sample size does not allow for any meaningful conclusions, but the fact that the cases with no radiological evidence of hyperinflation had a statistically significant lower cumulative dust exposure, suggests that a possible relationship exists between dust exposure and this radiological finding. The lack of significant finding in percent predicted may be due to the small sample size or related to the pathology of coal related lung disease and the development of the radiological findings of hyperinflation. In the introduction to the report (Section 1), a brief explanation was provided on the development of coal related pathology. The reaction of the lung to coal dust exposure results in the development of a coal macule, and subsequently surrounding tissue damage causing emphysema. Emphysema, which is the enlargement of the airspaces in the lungs, will show up as “hyperinflation”. This may be present in the absence of loss of lung function, hence the non-significant relationship between FEV_1 and hyperinflation. Parkes (1994) quotes a study by Lohela in which postero-anterior radiographs of lungs during life, where compared with post mortem findings, showed a 77% accuracy for the diagnosis of moderate to severe emphysema.

4.12. Autopsy database analysis

KEY FINDINGS (SECTION 4.12):

- The PATHAUT database consisting of statutory autopsies performed on miners according to the Occupational Diseases in Mines and Works Act was analysed for this study. This database is housed in the National Centre for Occupational Health (NCOH). The analysis was restricted to the years 1975 (first year of electronic capture of data) to 1995.
- In order to assess the validity of the diagnoses of concern contained in the database, an evaluation was done by three pathologists with international experience in coalminer lung pathology. Their systematic review showed a high degree of agreement between the reviewers and the diagnoses captured on PATHAUT.
- Although PATHAUT provides information on the **grade** of emphysema, which the reviewers found acceptable for analysis, they advised that the diagnosis of emphysema made on whole mount sections is the most appropriate for analysis.
- The exposure variables contained in PATHAUT were of limited quality. Ever exposure and years of exposure were available, with no details on job description, face or surface activity. Of the 7760 cases with some exposure to coal in their lifetime, 2046 (26.37%) had no information on the number of years of coaldust exposure. A total of 3176 (40.92%) cases were exclusively exposed to coaldust AND had information on years of exposure to coal.
- Information on smoking was also limited. In the entire dataset, 67% had no information on smoking status. For those with smoking history, only 63 cases had information on the number of years smoked, hence making the calculations of pack years an unreliable variable. Only 18 black (African) workers had smoking histories.
- Amongst those with exclusive coal exposure, TB was present in 5.21%, CWP: 7.37%, silicosis: 10.86%, significant emphysema: 6.45% (all emphysema: 31.33%), cancer 2.24%.
- All outcomes, except TB, showed a significant upward trend with increasing years of exposure. Similarly, there was a statistically significant greater years of exposure amongst those with disease compared to those without. The grade of severity of emphysema was strongly correlated with increasing years of exposure (correlation coefficient = 0.43). The mean number of years of exposure amongst those without emphysema was 7.85 years; insignificant: 16.87, moderate: 21.84 and marked: 25.82.
- Smoking was strongly associated with TB, silicosis, emphysema and cancer, with higher prevalence seen in ex-smokers compared to current smokers.
- Race – most probably acting as a surrogate for unmeasured covariates such as intensity of exposure, living conditions, nutrition, health care access – was significantly associated with the various outcomes. Black workers were at an increased risk for TB (6.59 times greater) and CWP (1.35 times) when compared to white miners, while white miners were at increased risk for silicosis (1.28 times), emphysema (5.26 times) and cancer (3.33 times).
- Logistic regression analysis allows the calculation of odds ratios, controlling for covariates. While controlling for smoking, there was a 5.68 greater odds of silicosis amongst those with high exposure compared to low exposure. The highest exposed workers had a 9.59 increased odds for developing significant emphysema compared to the low exposed workers. When controlling for dust exposure, current smokers had a 3.60 increased odds of developing significant emphysema compared to never smokers.
- Cases of full and partial post mortems, in which whole mount preparations of lung sections were done, were further analysed for emphysema outcomes, because of the high accuracy of this diagnosis with this technique. However, this resulted in a dataset of n=100. No statistically significant associations or trends were seen with exposure or smoking, most probably due to the small sample size.
- The prevalences for the various disease outcomes diagnosed at post mortem are generally similar to those seen for South African goldminers, with the notable exception of emphysema (26% in goldminers, compared to 14% in coalminers). Of note, however, is the increased dose related dust risk for the development of all diseases, especially emphysema, which seems to be at least as high as amongst goldminers.

4.12.0 The pathology of emphysema

Emphysema is amongst the most common pathological disorders of the lung, even amongst non-occupationally exposed populations. It can therefore present as an incidental finding in workers with occupational diseases. As discussed previously, it cannot be assessed with accuracy clinically or radiologically. The most accurate method of assessing emphysema is by reviewing the lungs at post mortem. However, even in the latter case, the lungs have to be properly prepared for an accurate assessment to be made (this is discussed below). Emphysema is therefore defined according to pathological findings made at post mortem. It is defined as a condition characterised by an abnormal and permanent enlargement of the airspaces in the lung in the portion of the airways beyond that referred to as the "terminal bronchioles" (the latter is the part of the airways just before exchange of gases between the lungs and the blood vessels in the lungs take place). There are two subcategories of emphysema, and these are specific to the precise location of the pathology within the lungs: panacinar and centriacinar emphysema, the latter being the type most related to coal dust exposure ("focal emphysema").

In most cases of severe disease, patients will present with features of chronic airflow obstruction (shortness of breath, wheezing etc) which is not responsive to bronchodilator therapy as used in reversible obstructive airways disease (e.g. asthma). The panacinar type is associated with a gradual increase of symptoms of breathlessness initially on exertion, and eventually even at rest. The centriacinar type rarely causes symptoms, and breathlessness, if present, may be due to other lung pathology. Standard lung function testing may not detect any abnormality, unless special gas diffusion tests or advanced disease is present. Radiographs show some sensitivity for moderate to severe disease, especially the panacinar type.

Some known risk factors for the development of emphysema are smoking and the lack of an enzyme, α_1 antitrypsin. Some studies have shown that the relative frequency of both types of emphysema in coalminers, increases with age and smoking (Ruckley et al, 1984). Age, smoking and exposure to dusty jobs (independent of silicosis severity) were shown to be important predictors of the development of emphysema among South African goldminers (Becklake et al, 1987).

4.12.1 The pilot study

The following results are the findings of the pilot study that was conducted by the three reviewers. The first review was done on 30 randomly selected cases that were independently reviewed by the reviewers. The first identified issue was that the population chosen consisted predominantly of miners with mixed exposures i.e. coal plus gold, platinum, etc. Exposure times ranged from a few months to 40 years. Two cases were excluded because of missing files.

Agreement between the consensus of the reviewing pathologists and the PATHAUT diagnosis is shown in Table 4.12.1.1. The only differences in the reviews were that, in each case where the PATHAUT pathologist scored pneumoconiosis as absent, the consensus of the reviewing pathologists was that "trivial" emphysema was present. This difference is most likely due to the fact that the PATHAUT classification determines whether workers receive compensation from the statutory Compensation Fund for occupational diseases. Because of these financial imperatives, the PATHAUT pathologists are more likely to record cases as having no pneumoconiosis when there is a mild case of pneumoconiosis.

Table 4.12.1.1 Respiratory health of South African Coalminers: agreement on pneumoconiosis amongst reviewers and PATHAUT pathologists

	Pneumoconiosis		
	Present	**Trivial**	**Absent**
PATHAUT pathologists	18	0	10
Reviewing pathologists	18	10	0

Table 4.12.1.2 in Appendix 8.5 shows the number of diagnoses by each reviewing pathologist (n=28). When using the previously discussed kappa statistic to determine degrees of agreement among the reviewing pathologists and between the reviewers and PATHAUT, there was moderate to excellent agreement among the reviewers (with a perfect score for pneumoconiosis), but agreement with PATHAUT ranged from poor to very good (this is shown in table 4.12.1.3 in Appendix 8.5).

The second review was conducted on 31 cases of pure coal mine dust exposure using the same criteria as per first review. Agreement between the consensus of the reviewing pathologists and the PATHAUT diagnosis is shown in Table 4.12.1.4. (Appendix 8.5). As for the first review, there was complete agreement between reviewers and PATHAUT for positive pneumoconiosis; however, all cases indicated as absent by PATHAUT were diagnosed as being “trivial” by the reviewers.

As for the agreement among reviewers and between reviewers and PATHAUT for the various diagnoses, the kappa scores ranged from moderate to excellent. The lower scores were reflective of the different criteria used for borderline disease (table 4.12.1.5, Appendix 8.5).

Based on the above review of the histological specimens and the comparison with the diagnoses captured on the PATHAUT database, the reviewers concluded that PATHAUT can be used with confidence to establish a diagnosis of moderate to severe grades of coal workers’ pneumoconiosis, while noting that minimal disease is reported as negative for pneumoconiosis on the PATHAUT dataset. It was noted that “Coal workers’ pneumoconiosis” includes silicosis and mixed dust pneumoconiosis in this dataset.

4.12.1.2 Emphysema

As one of the key outcome variables in the study was emphysema, the reviewers also considered this diagnosis on the PATHAUT database. Two important sets of data are used in PATHAUT to describe emphysema, namely the **grade** and the **type**. As emphysema is compensable under the Occupational Diseases in Mines and Works Act (ODMWA), information as to the presence or absence of emphysema is captured, and graded. Thus **all** post-mortem assessments receive an emphysema grade. Because of the issue of validity of microscopic recognition of emphysema, the **type** is only classified when whole lung sections, prepared appropriately (GOUGH-WENTWORTH technique), are available for review.

The PATHAUT system uses a grading system of insignificant (score <33), moderate (score 33-66) and marked (score>66). These categories are based on either an evaluation of a properly prepared whole lung section (for autopsies done at the NCOH (n=805)), or an evaluation of a sagittal slice of the wet (fixed) lung (for cases autopsied at peripheral locations (n=6800) and transported to Johannesburg for evaluation by the NCOH pathologists). If a whole lung section is available, the recommended approach uses a 20 segment grid and reads each segment 0-5 for a total score of 100, although numerical scores are not usually recorded in the database. If a whole lung section is not available, categorisation is done by the pathologists by a macroscopic assessment of the lung slices.

The PATHAUT pathologists also categorise the emphysema into five types. These are: panacinar, centrilobular, focal, irregular and combined panacinar and centrilobular. These are appropriate categories for a study of dust exposed populations. Centrilobular emphysema is the characteristic type for smokers, panacinar for smokers and alpha_1 anti trypsin deficiency. Focal is specific for coal workers (but is similar to centrilobular). Irregular is associated with scars.

In order to validate the PATHAUT system on GOUGH-WENTWORTH sections the reviewers independently reviewed 31 whole lung sections using the PATHAUT criteria. The non-NCOH reviewers were briefed on the PATHAUT scoring and diagnostic process.

The reviewing pathologists graded (absent, insignificant, moderate, marked) the sections. These findings were then compared to the data contained in PATHAUT. Of the 31 cases reviewed, in 27 (87%), there was complete agreement by the reviewers with PATHAUT.

The three reviewing pathologists attempted to classify the type of emphysema into four major categories: centrilobular, panacinar, focal and irregular. There was no prior review of the diagnostic criteria. Overall there was agreement between the three in 11 cases (35%). In 20 cases, two of the three pathologists agreed. Subsequent review of the cases with disagreements showed that these were largely due to poor specimen preparation.

The reviewers concluded that the PATHAUT grading system for emphysema is simple and reproducible; however, the readings only give a relatively crude measure of emphysema. The PATHAUT data for grade of emphysema (but not type of emphysema) is of sufficient quality to be used for epidemiological purposes. However, the reviewers further recommended that, even for epidemiological studies, strong preference should be given to cases with the properly prepared whole lung sections. As emphysema is an important health outcome amongst coal workers, and has been shown in other studies to have a dose response relationship with coal dust exposure, it was felt that further investigation may be necessary to complete our understanding of the disease process amongst South African coalminers. However, as indicated above, the PATHAUT database was not ideal for this investigation. The data contained in the Medical Bureau for Occupational Diseases' files has details on the exposure history (years/months working in a specific job description in a specific mine); fairly detailed smoking history; lung function test results; whole lung section plates and the pathology report (with more details than the PATHAUT database).

Thus, although the reviewers concluded that the **classification of emphysema type** is only possible using the Gough-Wentworth whole mount technique, PATHAUT also records the **grade** of emphysema, irrespective of postmortem type. This latter grading was used in the subsequent analysis in view of the desire to have an adequate number of cases for reasonable statistical power. Because the non-mounted evaluation of grade is likely to underestimate the degree of emphysema (personal communication, Head of Pathology, National Centre of Occupational Health), association with exposure is likely to be underestimated.

4.12.2 Descriptive analysis of the PATHAUT database

This pilot study validated the diagnoses of pathological outcomes contained in the database. A total of 7760 autopsies were reviewed for this analysis. These included workers with exclusive coal exposure (n= 5077 (65.43%)) and those with coal plus other mining exposure (n=2683 (34.57%)).

4.12.2.1 Exposure variables

Because of the restricted information contained in the database, the primary exposure variable was years exposed to coal. This variable was further categorised to determine if any trends were detectable with increasing exposure. As this was a subset of the main PATHAUT database, all the cases (n=7760) on the dataset were exposed to coal during their lifetime for variable periods. Of these, 2046 cases (26.37%) had no information as to the number of years exposed to coal. These cases subsequently had to be excluded from analysis involving years of exposure. The mean number of years of exposure to coaldust amongst those autopsied (for whom years of exposure was available (n = 5714 (73.63%)) was 9.10 with sd 10.34.

For those workers who were exclusively exposed to coal (and for whom years of exposure was available (n= 3176(40.92%)), the mean years exposed to coaldust was 10.96 (sd=11.30). For analysis of association and trend the four categories of exposure were: low (0.1 – 2.5 years of exposure, n= 786), medium low (>2.5 – 7 years of coaldust exposure, n= 783), medium high (>7 – 15.9 years of exposure, n = 801) and high (>15.9 – 55 years of exposure, n = 795). The choice of four categories for trend analysis reduces the chance that any one category can influence the direction of the trend. Three categories of years of exposure were developed and used in the logistic regression analysis: low exposure (0.1 – 3.5 years); medium (3.6 – 11.9 years) and high exposure (12 – 55 years). The use of three categories allows for easy interpretation when terms are entered into a regression model (comparing low with medium or low with high categories). Using these categories, there were 1054 autopsies done in the low category, 1059 in the medium and 1057 in the high category.

The following figure shows the subsetting of the PATHAUT dataset on the basis of available information for the critical exposure and outcome variables.

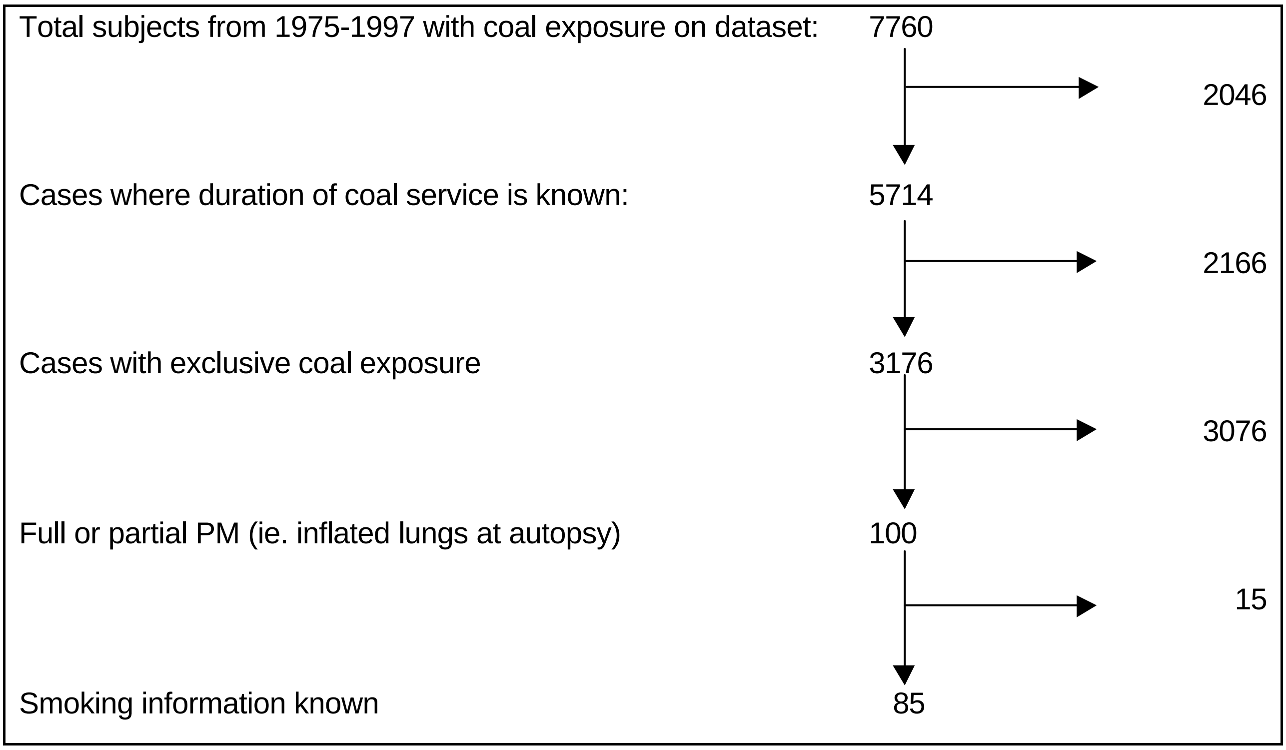

Figure 4.12.2.1 Respiratory health of South African Coalminers: subsetting the PATHAUT data

4.12.2.2 Mining exposures other than coal

Table 4.12.2.2 Respiratory health of South African Coalminers: other mining exposures and mean years of exposure

MINE TYPE	NUMBER OF MINERS	MEAN EXPOSURE YEARS
Gold	2293	3.83
Asbestos	299	0.17
Platinum	299	0.16
Copper	197	0.14
Diamond	145	0.10
Iron	39	0.02
ISCOR	83	0.08
Other	221	0.08

The number of miners in each mine type is not completely independent of the number of miners in other mine types as many miners have had several types of exposures. This table excludes those for which no information was provided for the duration specific exposure.

4.12.2.3 Potential confounding by smoking

Smoking, race and age were variables in the database identified as important potential confounders in the analysis. Data on smoking was absent for a large number (5349 (68.93%)) of the workers on whom autopsies were conducted. In addition, on those autopsies where data was available, only 63 cases had information on the number of years of smoking, thus making the calculation of a pack year variable unreliable. Those on whom data was available:

Table 4.12.2.3 Respiratory health of South African Coalminers: smoking data from database for the 2411 cases for which smoking information was available

SMOKING STATUS	NUMBER (%)
Cigarette smokers only	1294 (24.19)
Pipe smokers only	90 (1.68)
Smoker of both	127 (2.37)
Ex-smokers	500 (9.35)
Never smoker	272 (5.09)
Smoker with insufficient information	128 (2.39)

4.12.2.4 Age

Age data was available for 7534 (97.09%) cases. The mean age was 45.47 (sd=16.23). Amongst those with exclusive coal exposure, the average age was 41.05 (sd=14.72), and with mixed exposure, 53.62 (sd = 15.71). There was also a statistically significant difference in the mean ages between black (38.69, sd = 12.35) and white miners (53.95, sd = 17.92).

4.12.2.5 Race Data

Figure 4.12.2.5 shows that the overwhelming majority of cases in the dataset were black miners (66.13%), white miners 33.60%, and a negligible amount of coloured miners (0.27%)

Data on the number of years exposed to coal was available for 3176 (40.72%) of the miners in the entire dataset, including 3316 black, 2381 white and 17 coloured. A smoking history was available for only 18 black miners and 13 coloured miners, as compared to the 2380 white miners.

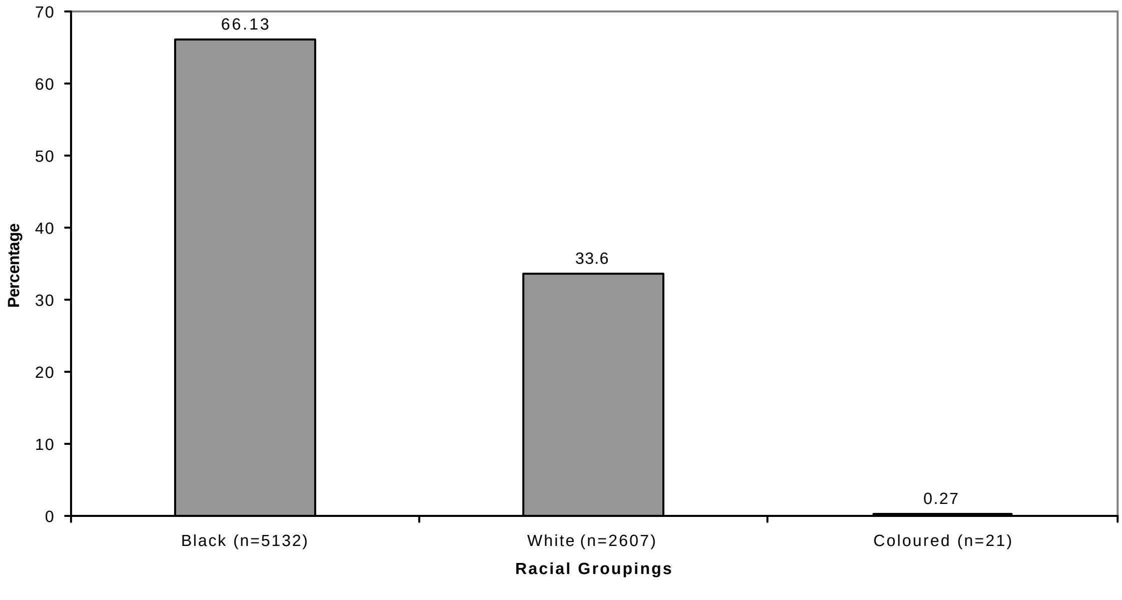

Figure 4.12.2.5 Respiratory health of South African Coalminers: race breakdown in dataset

4.12.2.6 Outcome variables

The following were considered as important outcome variables of interest:

- TB
- Silicosis
- Coal Workers' Pneumoconiosis
- Emphysema
- Progressive Massive Fibrosis
- Lung Cancer

Table 4.12.2.5 shows the number of cases with specific outcomes contained within the database.

Table 4.12.2.5 Respiratory health of South African Coalminers: autopsy outcomes from database

Autopsy outcome	**Number (%)**
Silicosis	1424 (18.35)
TB	411 (5.30)
Coalworkers' Pneumoconiosis	422 (5.44)
Emphysema	599 (7.72)
Progressive Massive Fibrosis	76 (0.88)
Lung Cancer	210 (2.71)

The definition of TB used in the study included cases diagnosed as having the presence of TB either in the regional glands, pleura or lungs. The table shows 599 (7.72%) cases were diagnosed as having moderate or marked emphysema (the definitions of insignificant, moderate and marked emphysema is stated in Section 2.9). When full or partial post mortems are conducted, the lungs are inflated and the grade of emphysema is based on the grid system of 20 radiating zones, each of which is allocated a score. The latter score is summed and expressed as a percentage, with insignificant < 33%; moderate 33-66% and marked >66%). If those with insignificant degree of emphysema were included, this increased to 2622 (33.79%). Of the latter, 1316 (51.57%) were considered to be the panacinar type 701 (22.47%), centrilobular; 199 (7.80%) focal; 79 (3.10%) irregular and combined (panacinar and centrilobular) was 257 (10.07%).

For the purposes of investigating the relationships of emphysema with exposure, analyses were conducted firstly with emphysema dichotomised as absent versus present (including insignificant, moderate and marked), and secondly with emphysema dichotomised as non-significant (absent and insignificant) versus significant (moderate and marked). The latter is referred to in the text of this report as "significant emphysema". It was decided to include analyses using both definitions of "emphysema" because neither was considered ideal: the inclusion of the insignificant grade of emphysema may underestimate the exposure-outcome association, as explained previously, and its exclusion from "significant emphysema" results in loss of data affecting the power to detect associations. Emphysema was further examined by looking at only those cases in which a full or partial postmortem was conducted, thus allowing for inflation of the lungs. The latter is the most appropriate method of grading emphysema, but results in severe loss of power because of the low percentage of total autopsies for which inflated whole lung sections were available, as per the flow chart (figure 4.12.2.1).

There were 13 cases of mesothelioma (0.17%) and 79 of asbestosis (1.02%). Of these, eight (0.16%) mesothelioma cases and 27 (0.53%) asbestos cases were seen amongst those workers with exclusive coal dust exposure. This may suggest that these workers were exposed to asbestos fibres during the course of their coalmining employment. As these were not key outcome variables for the study, they have not been considered any further.

4.12.3 Categories of years of exposure vs pathological outcomes

4.12.3.1 Analysis of workers with mixed exposure

Analysis was conducted to determine whether any relationships and trends existed between the pathological outcomes and categories of years of exposure as described above for the full dataset (which included coal miners with other exposure and miners with exclusive coal exposure). Emphysema, CWP and cancer showed a strong positive association and trend with increasing exposure (p values < 0.001). No significant trend was seen for silicosis (p value =0.19). (Actual values are shown in table 4.12.3.1 in the appendix, together with the p values). Because the associations of key interest are those of specific exposures occurring in coal mining with various outcomes, key analyses were restricted to the part of the sample reported to have worked only in the coal mines. In the section below, occasionally, information is also presented about coal miners with exposure to other types of mining for comparative purposes.

4.12.3.2 Analysis of those with exclusive coal dust exposure

In order to control for those with multiple mine dust exposure, the analysis for association and trend with increasing exposure was repeated for those with exclusive coal dust exposure. The trend curve for these outcomes is shown in figure 4.12.3.2.

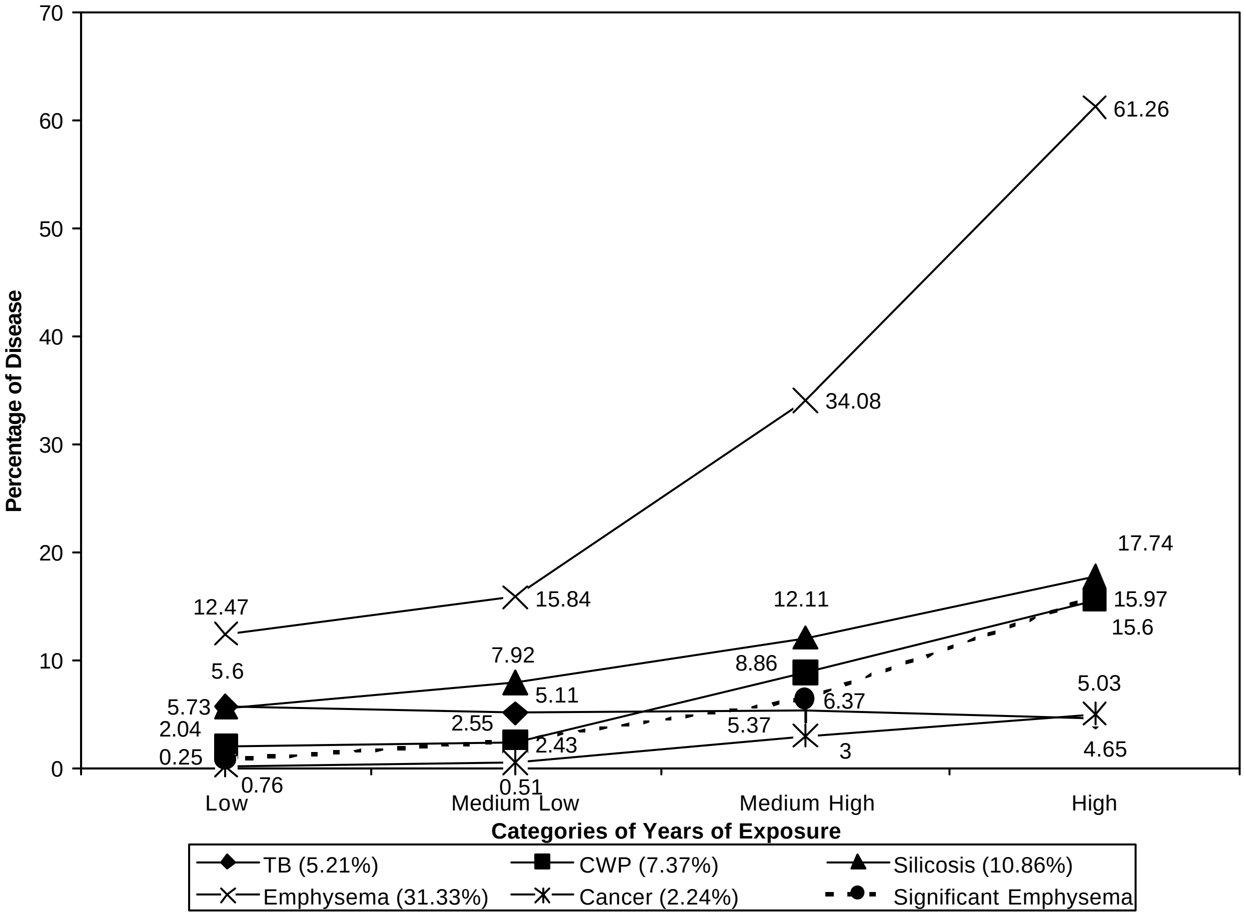

Figure 4.12.3.2 Respiratory health of South African Coalminers: autopsy outcomes vs categories of years of exposure – exclusively coal exposure

All of these outcomes other than TB were statistically significantly positively associated (p <0.0001) with exposure as well as an increasing trend with increasing exposure (p< 0.0001). Notably, silicosis, which showed an ambiguous trend in the combined exposures group, became statistically significant in the exclusive coal exposure group. The differences in the mean years of exposure between the diseased and non-diseased were analysed and is shown in table 4.12.3.3.

Table 4.12.3.3 Respiratory health of South African Coalminers: means years of exposure amongst those with and without disease.

Outcome	Mean years exposure		T test p value
	Disease (sd)	No disease (sd)	
CWP	17.07 (10.89)	9.94 (10.96)	0.0001
Silicosis	16.24 (13.32)	10.29 (10.77)	0.0001
Emphysema	18.15 (12.98)	7.69 (8.55)	<0.0001
Significant Emphysema	21.91 (12.86)	10.19 (10.71)	<0.0001
Cancer	20.68 (12.38)	10.62 (11.11)	<0.0001

To examine further relationships between exposure and emphysema, the correlation coefficient between increasing severity grade (NOT type) of emphysema and years of coal exposure was examined. The correlation coefficient was 0.43 (p value <0.0001). Figure 4.12.3.5 shows the increasing mean years of exposure for each grade of emphysema.

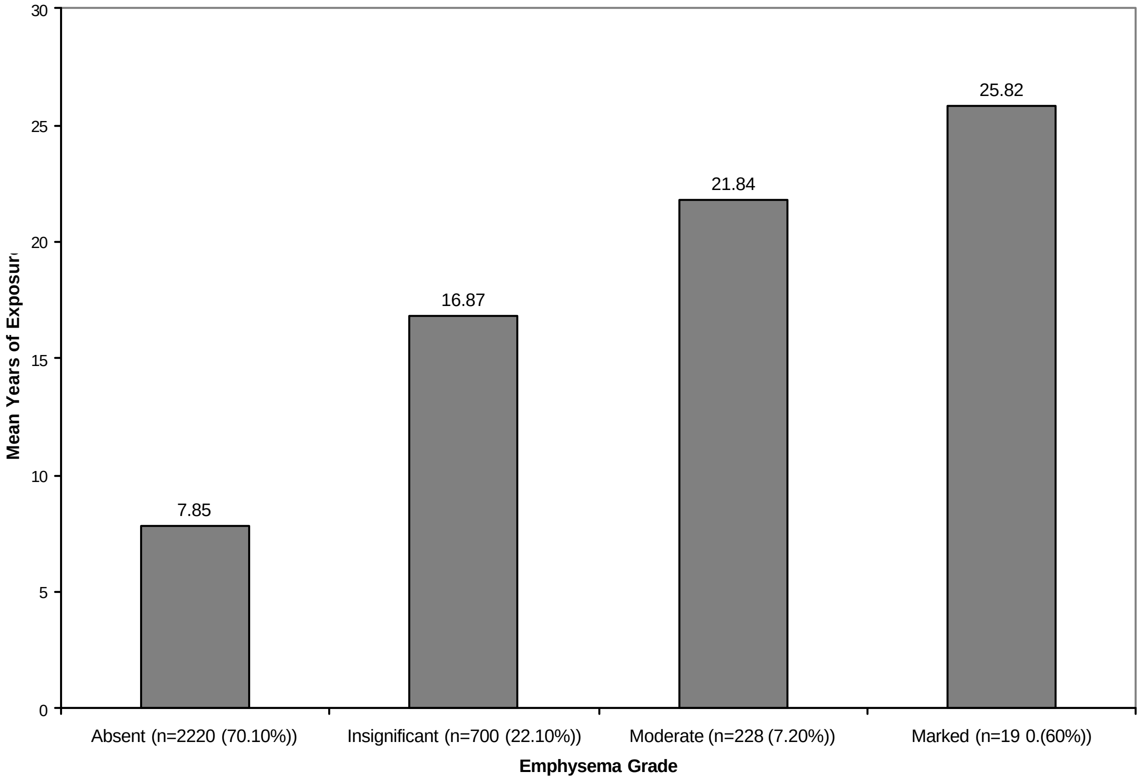

Figure 4.12.3.5 Respiratory health of South African Coalminers: means years of exposure for different grades of emphysema

4.12.4 Association between pathological outcomes and smoking

There was a lack of adequate smoking information on the database - only 2411 cases had data on smoking. Associations were assessed between smoking status (current, ex and never) and pathological outcomes. The values shown in Fig 4.12.4.1. are the percent with the diagnosis within the smoking category – e.g. amongst never smokers, 35% had silicosis).

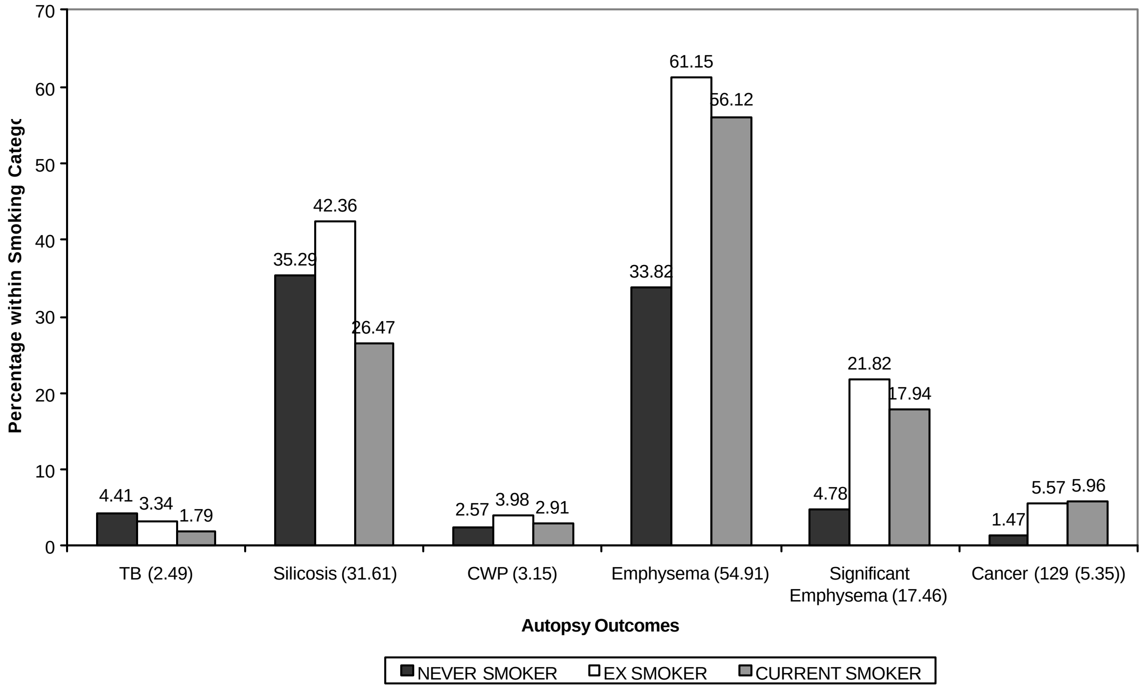

Figure 4.12.4.1 Respiratory health of South African Coalminers: autopsy outcomes vs smoking status

The data (Table 4.12.4.1 in Appendix 8.6 contains actual values including chi square p values) shows a significant relationship between smoking and most of the autopsy outcomes (chi square p values <0.01). CWP showed no significant relationship (p value =0.37). For most outcomes, a higher prevalence was seen amongst ex-smokers than current smokers.

Analysis to determine relationships between coal exposure and emphysema grades, adjusting for smoking was done. Smoking (ex- and current vs never smoker) and exposure (low vs high) were dichotomised. A statistically significant association (p value <0.0001) and trend (p value <0.0001) was seen with increasing grades of emphysema in the high exposure group.

4.12.5 Associations with race in the pathology data

Analysis to determine whether associations existed between race and pathological outcomes were conducted. Because of the small number of coloured workers, this analysis was restricted to African (black) and white workers.

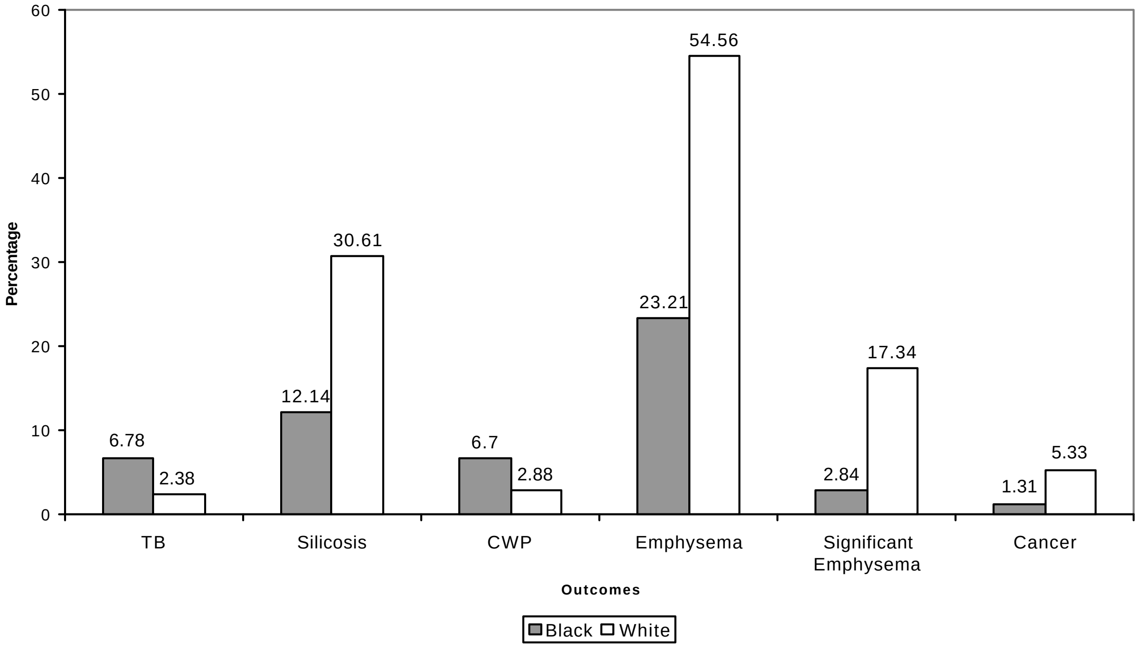

Figure 4.12.5.1 Respiratory health of South African Coalminers: differences in pathological outcomes between race groups (full dataset)

Figure 4.12.5.1 (corresponding table with actual numbers and p values for association and trend in Appendix 8.6) indicates that race is strongly associated with pathological outcomes, but which race has a higher risk varies across the outcomes. Black miners have a greater risk for TB and CWP, while white miners have an increased risk for silicosis, emphysema and cancer. Further analysis looking at exposure and autopsy outcomes while stratifying for race is shown later. The relative risks shown in table 4.12.5.1 (in Appendix 8.6) compares black miners to white miners. Black miners had in excess of twice the risk for TB and CWP compared to white miners. All the relative risks were statistically significant.

When coal only exposed workers were analysed (see figure 4.12.5.2, with corresponding table in Appendix 8.6), the relationships between race and outcomes remained significant, but for silicosis and CWP there were important declines in the risk effect compared to the mixed group: white miners in the mixed exposure group had a 2.5 times greater risk for silicosis compared to black miners, but only a 1.3 times greater risk when only coal exposed workers were considered. Similarly, for CWP, the relative risk declined from 2.33 to 1.35 for black miners compared to white miners. The risk for TB amongst Black workers increased from 2.85 to 6.59, when compared to white miners.

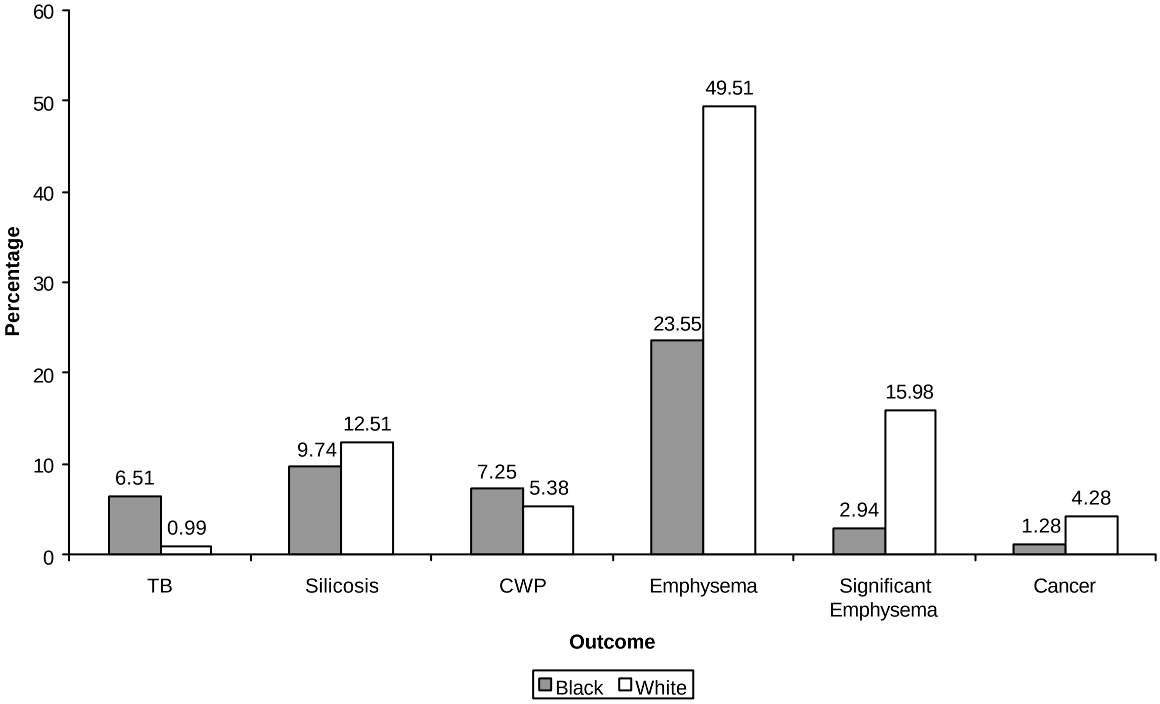

Figure 4.12.5.2 Respiratory health of South African Coalminers: differences in pathological outcomes between race groups (coal exposure only)

4.12.6 Logistic regression for pathological data

In order to control for all the covariates of interest within the PATHAUT dataset, logistic regression models were run for the various pathological outcomes. The exposure covariates of interest were the categories of years working in coal, categories of smoking status and race. Logistic regression models were run for the subset of cases with only coal exposure AND on whom history on years of exposure to coaldust was available (n=3167). The statistical procedure was conducted for the outcomes of TB, silicosis, coalworkers' pneumoconiosis, emphysema and cancer, with separate models including and excluding smoking variables. Further details of the analytic procedure are contained in Appendix 8.5. Table 4.12.6.1 shows the odds ratios for the various logistic regression models.

Table 4.12.6.1 Respiratory health of South African Coalminers: odds ratios from logistic regression models of exclusive coal exposed cases on PATHAUT for pathological outcomes (each row represents a separate logistic regression model)

Outcome	Odds Ratios (95% Confidence Intervals)		
	Black Miner	Medium Exposure	High Exposure
TB	9.55 (4.37 – 20.86)	1.20 (0.82 – 1.75)	1.62 (1.08 – 2.43)
Silicosis	1.09 (0.83 – 1.43)	1.81 (1.31 – 2.51)	3.33 (2.41 – 4.61)
CWP	2.66 (1.88 – 3.75)	2.87 (1.73 – 4.78)	11.98 (7.43 – 19.32)
Emphysema	0.54 (0.45 – 0.65)	2.20 (1.75 – 2.78)	7.14 (5.65 – 8.99)
Significant Emphysema	0.30 (0.21 – 0.41)	5.14 (2.50 – 10.56)	10.87 (5.41 – 21.84)

MODEL INTERPRETATION GUIDE (TABLE 4.12.6.1):

- Logistic regression models provide the odds ratio (the odds of risk factor *x* resulting in an outcome compared to risk factor *y*) for the various outcomes compared to exposure.
- The regression model allows for simultaneously accounting for the other potential risk factors (as compared to the calculations of relative risks in the previous section, 4.12.5 when, apart from race, no other factor was simultaneously considered)
- Each factor is compared to its opposite, which is excluded from the model, i.e. black worker compared to white, medium exposure with low, high exposure with low.
- Interpretation of emphysema in table 4.12.6.1: the odds are 7.14 greater of those workers with high exposure having emphysema compared to those with low exposure, irrespective of their race.
- When the odds ratio is less than one, then the interpretation is more easily understood by considering the opposite risk factor which is not included in the model, and using the inverse of the odds ratio – e.g. for emphysema and race: white workers (not in model) have a 1.85 (inverse of 0.54) greater odds of having emphysema compared to black workers, irrespective of the extent of their dust exposures.

High exposure to coaldust was significantly related to TB, and shows 1.62 greater odds for those exclusively exposed to coal, while black miners when compared to white miners have increased odds of 9.55. Exposure variables showed a 1.81 (medium exposure) and 3.33 (high exposure) greater risk for silicosis, when compared to the low exposed category. There is also a considerable increase in the odds for emphysema amongst the higher exposed workers when compared to the low exposed. Although these models do not control for smoking (due to the limitations of the dataset), this is reasonable evidence that coaldust exposure is an important factor in the development of emphysema.

When age was introduced into the above models, it had a consistent effect of increasing the odds of black miners when compared to white miners in the various outcomes (table 4.12.6.2). For TB, there was a statistically significant increase to 12.61 for black miners and for CWP the increase was from 2.66 to 5.08. It furthermore caused a consistent decrease in the odds of the exposure variables for all the outcomes, with this drop maintaining statistical significance for CWP and emphysema amongst the high exposed group. It should be recognised that, because of the positive correlation between age and exposure (r=0.68), these lower odds ratios may represent an inappropriate dilution of the exposure effect.

Table 4.12.6.2 Respiratory health of South African Coalminers: odds ratios from logistic regression models of exclusively coal exposed cases on PATHAUT for pathological outcomes, including AGE term

Outcome	Odds Ratios (95% Confidence Intervals)			
	Age	Black Miner	Medium Exposure	High Exposure
TB	1.02 (1.01 – 1.04)	12.61 (5.64 – 28.19)	1.12 (0.75 – 1.66)	1.20 (0.74 – 1.93)
Silicosis	1.07 (1.06 – 1.08)	2.43 (1.76 – 3.35)	1.18 (0.84 – 1.66)	1.11 (0.76 – 1.61)
CWP	1.04 (1.04 – 1.06)	5.08 (3.40 – 7.58)	2.05 (1.22 – 3.45)	5.50 (3.28 – 9.22)
Emphysema	1.07 (1.06 – 1.07)	1.12 (0.89 – 1.41)	1.42 (1.11 – 1.83)	2.24 (1.71 – 2.93)
Significant Emphysema	1.07 (1.05 – 1.08)	0.64 (0.44 – 0.94)	3.31 (1.59 – 6.88)	3.29 (1.57 – 6.88)

To determine the effect of smoking, models with smoking variables were developed. As mentioned previously, a significant percentage of the cases did not have smoking histories. These models were problematic in that the overwhelming majority of cases without smoking history (n=2442, 77.11%) were black miners (n=2382, 97.54%). This meant the models excluding smoking history had to exclude the race variable. Outcomes which were seen almost exclusively in black miners (TB and Coal Workers' Pneumoconiosis, CWP) were difficult to assess - models with TB and CWP were run including exposure and smoking variables (excluding cases with missing smoking data); however, because of the small number of black miners included in the analysis, the results showed a minute odds ratio (<0.001) for exposure with confidence limits from <0.01 - >999.99). The other results are shown in the table 4.12.6.3.

Table 4.12.6.3 Respiratory health of South African Coalminers: odds ratios from logistic regression models of exclusively coal exposed cases on PATHAUT for pathological outcomes (each row represents a separate logistic regression model)

Outcome	Odds Ratios (95% Confidence Intervals) of terms in model			
	Medium Exposure	High Exposure	Ex-smoker	Current Smoker
Silicosis	0.64 (0.13 – 3.23)	5.68 (1.74 – 18.50)	0.79 (0.39 – 1.59)	0.55 (0.29 – 1.03)
Emphysema	2.75 (1.23 – 6.15)	15.52 (1.17 – 32.00)	2.11 (1.17 – 3.80)	2.24 (1.34 – 3.73)
Significant Emphysema	4.23 (0.92 – 19.47)	9.59 (2.31 – 39.85)	2.76 (1.01 – 7.56)	3.60 (1.41 – 9.19)
Cancer	2.61 (0.29 – 23.83)	4.13 (0.55 – 31.01)	2.44 (0.51 – 11.66)	2.03 (0.47 – 8.81)

Once again, high exposed workers are at a greater risk than low exposed workers for silicosis outcomes. "Significant emphysema" showed a statistically significant odds of 9.5 times greater (95% CI = 2.31 – 39.85) when compared to low exposed workers, while controlling for smoking outcomes. This was several fold greater than the increased risk of emphysema due to current smoking status. The model for cancer was not significant although in view of the small numbers reflected in the wide confidence intervals, no clear conclusions can be drawn about this outcome.

When age was introduced in the model, it had the same effect as the previous analysis in that it caused a consistent decline in the effect of the exposure variables with a reduction in the odds of outcomes. However, importantly for the outcome of emphysema, the reduction of the high exposure odds to 4.84 (95% CI = 2.20 – 10.64) from 15.52 was still higher than the increase in the current smoker odds from 2.03 to 3.37 (95% CI = 1.89 – 6.01). For significant emphysema, the introduction of age in the model resulted in point estimates slightly less than three which were no longer statistically significant. These high estimates were quite similar to those for ex-smoker versus non-smoker, but were substantially lower than those for current smoker versus non-smoker (slightly less than six).

Table 4.12.6.4 Respiratory health of South African Coalminers: odds ratios from logistic regression models of exclusively coal exposed cases on PATHAUT for pathological outcomes, including AGE term

(each row represents a separate logistic regression model)

Outcome	Odds Ratios (95% Confidence Intervals)				
	Age	Medium Exposure	High Exposure	Ex-Smoker	Current Smoker
Silicosis	1.08 (1.07 – 1.08)	0.60 (0.46 – 0.78)	2.08 (0.59 – 7.31)	0.79 (0.39 – 1.61)	0.65 (0.34 – 1.25)
Emphysema	1.07 (1.06 – 1.09)	2.04 (0.86 – 4.89)	4.84 (2.20 – 10.64)	2.12 (1.12 – 4.02)	3.37 (1.89 – 6.01)
Significant Emphysema	1.06 (1.04 – 1.08)	2.93 (0.61– 13.97)	2.82 (0.64 – 12.37)	2.91 (1.04 – 8.14)	5.97 (1.96– 13.63)
Cancer	1.03 (1.00 – 1.06)	2.11 (0.23-19.64)	2.15 (0.26 – 17.81)	2.37 (0.50– 11.35)	2.29 (0.52– 10.03)

Because of the large differences seen when age was introduced into the model, it was necessary to examine whether it was influencing any of the important exposure variables. Correlation analysis revealed that the correlation coefficients for age vs years of coal exposure was 0.40 (p value < 0.0001) for the entire dataset, and 0.68 (p value <0.0001) for only coal exposed workers. This suggests that in the exclusive coal exposed workers, by introducing age into the model, any real exposure effect is likely to appear reduced.

4.12.7 Emphysema amongst those with full or partial post-mortems

Because of the nature of the dataset, a separate analysis was conducted on this subset and is detailed in Appendix 8.5. There were no statistically meaningful associations seen, probably due to the small subset (n=100), with only 21 cases of significant emphysema. Logistic regression models were also developed, but probably for similar sample size reasons, were non-significant.

4.12.8 CWP as a predictor of emphysema

Pathologically macules in coal workers' pneumoconiosis have a degree of focal emphysema as part of the lesion. Logistic regression models (not shown in tables) using CWP (together with dust exposure and smoking variables) as a predictor for emphysema were developed. While the exposure and smoking variables showed significant odds for the development of emphysema when compared to low exposure (high exposure OR= 9.93, CI = 2.39 – 42.32) and never smokers (current smoker OR = 3.51, CI = 1.37 – 8.97) respectively, CWP was statistically non-significant (OR=0.45, CI= 0.17 – 1.17). The introduction of an age variable into this logistic model resulted in only smoking variables retaining significance. Coal workers' pneumoconiosis became statistically significant (OR=0.34, CI = 0.13 – 0.89) – but showing a protective effect for emphysema.

4.12.9 Summary of the autopsy analysis

Notwithstanding the limitations of the autopsy data, especially with regard to important exposure variables and covariates such as smoking, there seems to be significant associations of key outcomes, such as emphysema, with coal dust exposure. These associations seem to be dose related, with greater odds amongst the workers with the higher categories of exposure.

There were other important biases present in the autopsy dataset that were mentioned in section 2.9, primarily related to how miners present to autopsy. The effect of these biases are discussed in the following sections of the report.

5. Discussion of Results

DISCUSSION SUMMARY

- All measured dust levels and most historical were below the South African standard of 2mg/m^3. Silica content was below the international standard of 3%.
- Ex-miners reported more symptoms than current miners, with ex-miners showing an increasing prevalence of symptoms with increasing exposure. This was not seen amongst current miners.
- Ex and non-dust exposed workers had lower lung function outcomes than currently employed or underground miners.
- The estimated dust related decline in FEV$_1$ is 1.33 per mg/m3*years. At current mean levels of exposure at the coal face (1.91 mg/m3), dust related declines accounted for 2.54ml per year loss in FEV$_1$ and 2.36ml per year of FVC while controlling for declines resulting from age, employment status, smoking and past TB (using a 40 year old, 170cm tall man as a standard).
- Ex-miners had a FEV$_1$ of 128ml and FVC of 151ml lower than that of current miners, controlling for the above variables.
- At least 6% of workers had abnormal FEV$_1$ and 5% abnormal FVC, according to the lower limits of normal criteria (5th percentile) using the Louw equations. These are similar to the prevalence of those classified "abnormal" among goldminer populations. Approximately 3% of workers had lung function impairment that would be expected to interfere with activities of daily life, i.e., <65% of predicted.
- TB and smoking were important contributors to lung function declines.
- Prevalence of radiographic evidence of pneumoconiosis was low, not exceeding 4.16%. However, those with the highest exposure had a 6.5 times greater risk of having the disease than those with moderate exposure.
- The autopsy outcomes of silicosis, CWP and emphysema increased with increasing years of coaldust exposure. Workers with high exposure (12-55 years) had a 9.6 fold risk for "significant emphysema" while controlling for smoking, compared to workers with low exposure (0.1 - 3.5 years).
- The findings of this study appear quite consistent with those seen amongst coal miners in other parts of the world. As compared to SA goldminers rates of TB prevalence and percent of workers below the lower limit of normal in lung function were similar, but prevalences of emphysema and radiological pneumoconiosis are considerably higher amongst goldminers.
- Although there is an overall relatively low prevalence of disease, there is sufficient and complementary evidence from both the living and deceased miners components of this study, that at dust levels to which South African coalminers are currently exposed, important adverse respiratory health outcomes are occurring.

5.1 Summary of Key Findings

[NOTE: In discussing the lung function findings, to allow for the illustration of arbitrary values such as percent predicted, the latter has been translated as outcomes for a 40 year old 1.7m tall man exposed to average concentration of 1.91 mg/m^3 at the face. According to the Louw predictor equations, the expected values for such an individual are: FEV$_1$ = 3.32L and FVC = 4.12L].

The study of a sample of current and former employees was conducted on three mines. It is unknown how representative of conditions throughout the SA coal mining industry these three mines are, though there is no obvious reason to expect they are not typical. Dust levels measured at the mines were below the South African standard of 2mg/m^3 respirable dust level in all dust samples taken by the investigators and most historical data available. The percentage of silica content of the dust was always less than 3% in all samples taken.

Ex-miners reported significantly more symptoms and a higher doctor diagnosed prevalence of asthma and bronchitis than current miners. Analyses of current and ex-miners combined showed a declining trend in the prevalence of symptoms with increasing categories of exposure. This trend however, disappeared, when the participants were stratified into employment groupings (current and ex). When only ex-miners were analysed, a greater prevalence was seen amongst the higher exposed categories. Ex-workers had a several fold greater risk of developing the various respiratory symptoms than current miners – with a range from 5 – 12, depending on the symptom. These findings support the argument of a “healthy worker survivor effect” present in the data. If the latter assumption is correct, this would imply that the true magnitude of any dust related effect is likely to be greater than that estimated from the data available in this study.

Ex-miners and non-dust exposed miners had lower lung function outcomes than currently employed or underground miners. Bivariate analyses showed that a 40 year old 1.7m tall man currently employed had a FEV$_1$ of 310ml greater than that of a similar age and height ex worker, if both had worked in the highest exposure category (with a mean dust level of 1.91 mg/m^3). A 40 year old 1.7m tall man with no coaldust exposure (lifetime surface worker), has a 157ml lower FEV$_1$ compared to similar individual with underground exposure. This suggests that a healthy worker selection (into initial employment) and/or healthy worker survivor effect may exist when comparing underground to surface workers (i.e., need to be healthier to be selected for and/or remain on underground work as compared to surface work).

Our estimate of coal-dust related effect on FEV$_1$ is 1.33ml per mg-years/m^3 and for FVC is 1.24ml per mg-years/m^3. For a coalminer with average current exposure at the face (1.91 mg/m3), this translates into a 2.54ml loss in FEV$_1$ and a 2.36ml loss in FVC for each year of exposure. An ex-worker had losses of 127.49ml FEV$_1$ and 152ml FVC greater than that of current workers. Both these findings were seen while controlling for smoking and previously diagnosed TB. The applicability of these findings to longitudinal lung function loss is discussed in greater detail below. The study findings predict that at least 6% of workers are below the 95th percentile and perhaps likely to experience some form of exercise intolerance, based on the lower limit of normal lung function. This is only marginally higher than the expected from the population. It is probable that the countervailing tendencies of the healthy worker effect and the dust related effects are reflected in this percentage. In other words, the prevalence of lower FEV$_1$ values in the study population is modulated by the selection of healthier miners to work and remain underground.

Pneumoconiosis prevalence was low, with a range between readers of 1.01% to 4.2%, depending on the reader and the definition used. The prevalence of pneumoconiosis increased with increasing exposure, with the highest cumulative exposure (72.01 – 258.70 mg-years/m^3) group having a 6.5 times greater risk of pneumoconiosis than the medium cumulative exposure group (19.39 – 72.01 mg-years/m^3). Lower lung function outcomes were seen in those with profusion grades greater than 1/1 when compared to those with less than 1/1.

The pathological database analysis showed that the prevalence (amongst workers coming to autopsy who have only coal exposure) of TB was 5.21%, CWP – 7.37%, silicosis – 10.86%, significant emphysema – 6.45% and cancer – 2.24%. The outcomes of silicosis, CWP and emphysema increased with increasing years of coaldust exposure: A worker with greater than 12 years of exposure has an almost 12 times greater risk of developing CWP when compared to those with the lowest exposure group (1-2.5 years). Similarly a 5.7 times greater risk exists for silicosis, and a 9.6 fold risk for "significant" emphysema, while controlling for smoking. The severity of emphysema increased with increasing years of exposure, with those with marked emphysema having 25.82 years of exposure compared to those without emphysema having 7.85 years of exposure.

5.2 Study of current and ex-miners

The health outcomes examined for the sample study appear to have substantial face validity. Information on symptoms, pulmonary function testing, and chest radiography were all collected and interpreted using standard methods following current recommendations for epidemiological studies.

Substantial effort was also devoted to the development of valid and reliable estimates of lifetime cumulative dust exposure. Historical data collected by the mine owners was available from approximately 1991 forward in a large variety of jobs with a particular emphasis on high exposure jobs at the coal face. This data was sufficient to assess time trends during the period 1991 through 1998. This assessment indicated a lack of consistent trend of change in exposure means over this time period. It should be noted that this data was collected using a sampler, the CIP10, the capture characteristics of which are still under review by the European agencies. Moreover, there appears to be no simple formula to translate values derived from the CIP10 sampler into those using a cyclone.

The available historical sampling data was supplemented by extensive sampling of current exposures in all three participating mines, conducted by the investigators. This sampling used the recommended cyclone sampler. Thus, there existed a substantial body of historical and current sampling data from which to derive cumulative dust exposure estimates. The major concern with the accuracy and robustness of these estimates relates to exposures occurring prior to 1991 which constitute 46.51% percent of the total exposure years of the sample. However, a sensitivity analysis was done which compared the key exposure outcome regression models under a variety of assumptions about the relationship of the pre-1991 exposures to later exposures, which showed effect estimates that were quite stable across these different assumptions. Also, as is described below, exposure response estimates for a number of outcomes (although not all) were in the expected direction and the range seen in comparable studies from other countries offers further reassurance that cumulative exposures were not grossly misclassified. It should be noted that, to the extent that cumulative dust exposures were non-differentially misclassified (i.e. any error was unrelated to the outcome), this would tend to lead to an underestimate of exposure response effects (i.e., bias toward the null). On the other hand, if it were to be true that the post-1991 exposures were systematically underestimated, this would tend to lead to an overestimate of exposure response effects (because the assumed dose necessary to produce a certain response would tend to be systematically underestimated). It is uncertain which of these two potential counterbalancing effects predominates.

The development of more comprehensive exposure indices, especially for periods prior to the 1990s must be given consideration. Although the mines have been collecting this data for legal reasons (compensation levy based) under the Minerals Act for several decades, only a limited back period of information is available from mining operations themselves. The database of the

DME is not in a readily usable form. The use of historical dust data allows for more accurate characterisation of past exposure and permits the calculation of cumulative exposure, without having to rely on statistical modelling. The lack of dust data prior to 1991 was a limitation in this study. Further research of the information in the DME database may be important to determine its ability to provide historical dust data.

The coal dust related outcomes for which objective, quantitative results are available, which tend to have direct clinically interpretable relevance, and for which there remains some degree of controversy in the international literature, are the spirometry outcomes, i.e. FEV_1 and FVC. The key findings of this study with respect to these outcomes are contained in the final best linear regression models presented in tables 4.10.3.1 and 4.10.3.2. For FEV_1, the best models which controlled for smoking status and history of doctor diagnosed TB, indicated a cross-sectional loss of 0.04 % in predicted FEV_1 per mg-year/m^3.

According to our data, at the average levels of dust exposure recorded at the face during the research (1.91mg/m^3), an estimated dust related loss of at least 2.54ml per year in FEV_1 and 2.36ml in FVC was seen – while controlling for smoking habits and previous TB. [This is based on outcomes in a 40 year old 1.7m tall man, using the Louw predicted equations, with an expected FEV_1 = 3.32L and FVC = 4.12L]. The review of differences between current and ex-miners showed important differences, while controlling for cumulative exposure, smoking and past TB. A cross sectional decrease of 128ml in FEV_1 and FVC 152ml was seen amongst ex-workers when compared to current miners. Thus, workers who are no longer working on the mines show a higher level of loss of lung function than those still employed. This suggests that an important higher actual coal dust effect on lung function might be present were the data not being influenced by some unmeasured factors represented by “employment status”. However, this interpretation of the data must be done cautiously. Several biases are likely to operate within such an “ex-miner” population: healthier workers may be currently employed elsewhere, and not have presented to the study, and those presenting may have done so because of medical problems. Attempts at controlling for these biases during the study were done by inviting participation, rather than a public announcement attracting participants. Notwithstanding this, it is recognised that absolute control for such biases is not possible.

In the study, at least 3% of workers suffer from respiratory impairment which is likely to have an important bearing on their daily lives. The mean loss in FEV_1 for a worker at the coalface with an average of 1.91mg/m^3, over an approximate 30 years underground, is approximately 90ml - a seemingly low figure which, however, is equivalent to approximately a five year loss due to age alone in a non-exposed man. Additionally, some individuals are likely to be more susceptible to having substantially greater effects than this predicted mean loss. Workers with already compromised lung function might be driven toward the 65% of predicted level, resulting in disability.

Our pulmonary function data are cross-sectional, whereas, coal related decrements longitudinally in the same individuals is the parameter of greatest interest. Thus it is worth considering the relationship between cross sectional and longitudinal measures of pulmonary function. There have been several investigations into the reliability of the use of prediction equations and data derived from cross sectional studies for the prediction of longitudinal declines in lung function (Glindmeyer et al, 1982; Louis et al, 1986; Ware et al, 1990; Vollmer, 1993). Vollmer defines several reasons why the applicability of cross sectional data to assuming longitudinal declines in lung function may be inappropriate. These include the use of different statistical models, researchers assuming that lung function declines constantly with age, while the longitudinal decline accelerates with age, all of which may result in incorrect estimates of annual rate of loss in a sample. Survey (“learning”) effects where workers perform in subsequent tests better because of familiarity with the procedure, and cohort effects, where studies assume that a 20 year old today will have the same lung function 30 years from now as a 50 year old today (Vollmer, 1993), result in the difficulties in translating cross sectional derived predicted equations to longitudinal effects.

In comparing repeated cross sectional and longitudinal data generated from the same population (an asymptomatic never smoking population), Ware et al (1990, Six Cities Study) showed that the model from the cross sectional data indicated a greater estimated rate loss of lung function than the longitudinal data, and this was reversed in the older age categories. However, their data showed that for the middle age ranges, there is little differences between cross sectional and longitudinal data. Glindmeyer et al (1982) showed, in a study of 52 adult males, almost a two fold discrepancy between cross sectional and longitudinal data. There is a strong possibility that given the small sample size, these findings were due to chance. However, there is considerable inconsistency between study findings, which implies that it is not always accurate to use one type of model to predict outcomes for which that model is not specific.

In summary, the relationship between cross sectional and longitudinal data is likely to be complex with some studies showing greater decrements with longitudinal data and others greater decrements with cross sectional. In any event, pending a prospective study with repeated measures of pulmonary function on the same individual, our cross sectional data are the best available estimates for decrements among South African coal miners.

Our findings of 0.04% per mg-years/m^3 and 0.03% per mg-years/m^3 loss in predicted FEV$_1$ and FVC respectively (equivalent to 1.33ml FEV$_1$ and 1.24ml FVC in a 40 year old 170cm tall man) are comparable to those found in the international literature. The study by Henneberger (1996), in analysing the NSCWP data, showed statistically significant declines of 1.20ml per mg-years/m^3 in FEV$_1$ in a cohort of experienced miners with a mean employment history of 15 years. Studies among British coalminers have shown losses of 1.6ml per mg-years/m^3 in FEV$_1$ (Soutar, 1986). Further analysis of the US National CWP Surveillance data of new miners by Seixas et al (1993) showed a 27.5ml per mg-years/m^3 and 30.4ml per mg-years/m^3 dust related declines in FEV$_1$ and FVC respectively. These were higher than the usual findings seen in other studies. The authors suggested that this may have been due to this cohort having a relatively shorter duration of employment or exposure. More experienced miners had a loss of 6ml in FEV$_1$ per mg-years/m^3. The study of Sardinian coalminers showed a decline of 10.9ml (absolute) per mg-years/m^3 in FEV$_1$ and 4.5ml (absolute) per mg-years/m^3 of coaldust exposure.

The finding of the expected association of radiological profusion score of opacities with cumulative dust exposure estimates lends additional support to the validity of the dust estimates and findings regarding impact on the lungs of coalminers. The findings in the study of predominantly rounded opacities is supported by other studies amongst coalminers (Parkes, 1994). Some studies have shown that up to 6% of coalminers may have irregular opacities (Amandus, 1989). The prevalence of 4.16% of radiologically diagnosed pneumoconiosis, compares with other studies amongst US coalminers, which have found ranges of 4.5% - 6.8% prevalences (Attfield et al, 1995). These studies differ from the findings in South African goldminers, with reports of 14% of workers with radiological evidence of silicosis of ILO grade greater than 1/0 (Hnizdo, 1998). This is most likely due to the high levels of silica dust to which goldminers are exposed, as compared to coal miners.

The response of the TB variable to lung function outcomes deserves further comment. For pulmonary function outcomes, a history of previous doctor diagnosed TB was associated with a highly significant and marked relationship to outcomes (a loss of 699ml FEV$_1$ and 536ml FVC, in a 40 year old 170cm tall man). This striking finding may be related to the high prevalence of TB found among South African miners and provides strong evidence that there is a significant functional effect due to TB among coalminers. These findings must be compared to those of Hnidzo et al (Thorax, 2000), who found increasing declines in lung function between the number of episodes of TB and between the increasing period from diagnosis to subsequent lung function test. The study, conducted amongst South African gold miners, found a range of loss of FEV$_1$ from 180 ml (for a single episode of TB) through to 964ml (for four or more episodes of TB). Although the study did not control for dust exposure or smoking history, there seems to be support that TB is a significant contributor to important lung function changes. In another study of tuberculosis amongst goldminers exposed to silica dust, an increased relative risk of 1.1 was found for TB amongst those without radiological evidence of TB, with an increasing risk with increasing quartiles of cumulative dust exposure (Hnidzo and Murray, 1998).

Our study, while showing low prevalence of past TB (overall 2.3%), showed a significant effect of the disease on lung function changes, while controlling for the effect of dust and smoking. When excluding ex-miners a statistically significant increase in prevalence with increasing cumulative exposure (table 4.9.2.2) was noted. Together with other studies supporting a dust related increase in TB prevalence, there is strong evidence for promoting TB prevention and other intervention programmes on the mines.

Another striking finding when looking at the entire sample, was the inverse relationship between most of the reported symptoms and estimates of cumulative dust exposure. These findings were echoed in the bivariate stratified analyses between exposure and lung function outcome, stratified by employment status (see table 4.10.1.2). This is not in keeping with other international studies. A study by Rae et al resulted in a 38% prevalence of bronchitis amongst 4122 coalminers, with a significant increase with increasing exposure. Carta and co-workers (1994) found an increased odds of 2.26 for the development of any respiratory symptom amongst the higher exposed coalminers. It is notable that, in the current study, these inverse relationships disappeared, and in some instances, were actually reversed when analyses were stratified upon current work status. These findings are indicative of a substantial healthy worker survivor effect in this population. Most likely controlling for work status diminishes this effect but does not eliminate it entirely resulting in some underestimation of exposure response relationships even in analyses stratified on work status. A similar finding has been demonstrated by Hnidzo et al (1999) in a study of goldminers. The latter study found that cumulative dust exposure was not associated with symptoms of chronic obstructive airways disease, and even found a non-significant positive trend between increasing CDE and lung function, and postulated that the healthy worker effect may have influenced the data.

A closely related phenomenon in this data set was a substantial "healthy smoker effect", i.e., current smokers tended to have fewest symptoms. This phenomenon has been described by other authors in the context of South African goldmining. This is relatively unusual to see even in an active working population and suggests that an interactive, or at least additive, effects of smoking plus coal dust exposure are causing respiratory symptoms and disease leading to strong selection out of continuing employment in the coal mines.

Smoking is recognised as an independent contributor to declines in lung function or emphysema. This was seen in our study. Smoking in this sample was generally low (mean pack years = 4.34), with over 40% of the entire sample having a lifetime never smoking history. Symptoms were strongly associated with smoking, with higher prevalence seen in the current smoker, with a statistically significant trend seen with symptoms and increasing number of pack years. In the multivariate modelling, packyears was statistically significantly associated with declines in lung function - a marginally bigger effect than that of coal dust: each packyear of smoking contributed to a 8.6ml decline in the predicted FEV_1 (for a 40 year old, 1.7m tall man) – an average lifetime loss in FEV_1: 8.6ml x 7.34 packyears = 63.12ml (compared to loss due to dust exposure: 1.33ml x 1.91mg/m^3 x 15.89 average years worked in the mines = 40.37). Given the overall low prevalence of smoking, and the associated statistically significant outcomes, smoking amongst this sample may have a reasonably similar effect on declines in lung function to that of dust exposure.

The findings suggesting a significant healthy worker survivor effect are important in considering the clinical significance of the findings in this study. It must be borne in mind that the average length of underground exposure in this sample was relatively modest (10.49 years). In addition, individual variability in sensitivity to the effects of dust exposure can be expected across the population of coal miners. Thus, the findings are suggestive that, over a full working lifetime in coal mining, substantial and clinically significant decrements in pulmonary function attributable to work exposures could be expected in a significant fraction of such exposed miners. This is indicated by the percentage of workers that were classified as abnormal on the basis of the lower limit of normal criterion – approximately 6% fell into this category, compared to between 3 – 8% reported for goldminers (Hnidzo, 2000).

5.3 The Autopsy Study

The findings of the sample study are complemented by the pathology study that was carried out in parallel. This study made use of the unique and very large data base available through the National Centre for Occupational Health. This resulted in an autopsy study which was able to include much greater numbers of coal miners than any previous studies reported in the literature. Notwithstanding the strengths of the PATHAUT database, it has several limitations, which are discussed below, including an absence of the emphysema score (a numerical value for the grading of emphysema), crude coal exposure variables (years of exposure) and absence of pack years of smoking.

A crucial important bias in the autopsy dataset is mentioned in Section 2.9, in the review of PATHAUT, and may have a differential misclassification. This bias relates to how miners present for autopsy. Although studies have shown that between 86% - 91% of white miners receive autopsy upon death, this is not similar for black miners. This is primarily because retired and ex- white miners are more familiar with their legal rights than are black miners. White miners receive autopsies if they have not been compensated in life. Those that receive maximum compensation are not likely to present to autopsy. Most autopsies conducted on black coalminers are those that die while in service. Thus the age of black miners at autopsy is much lower than that of white miners (see section 4.12.2.4). This may imply a “healthy lung bias” in the presentation of the post mortem data (i.e. black miners having autopsies at an age when there is a lower likelihood for disease, while white miners with respiratory pathology in life will present for autopsy at death). Theoretically this may have led to an overestimation of the findings. However, the logistic regression models were run with black miners (tables 4.12.6.1 and 4.12.6.2), and subsequently without black miners (4.12.6.3 and 4.12.6.4). Although the magnitude of the effect from exposure varies between the models, the direction and statistical significance of the effect is nevertheless the same. Thus the relationship between dust exposure and the outcomes of interest is still valid.

Because for this study, the outcomes of interest were extracted from historically collected and analysed data, the quality and usefulness of this data for the performance of exposure/outcome response estimates was uncertain initially. For this reason, a validation exercise comparing readings in the historical database to those of three highly experienced pathologists was conducted. Overall the results of this validation exercise were quite reassuring with respect to almost all of the outcomes of interest, i.e., substantial agreement existed between the findings of the three pathologists and the historical data set for most of the outcomes. It is particularly notable that the outcome of special interest for this study which might be expected to be related to pulmonary function decrements in the miners, i.e., significant autopsy-diagnosed emphysema, showed excellent agreement between the three pathologists and the historical data set.

The exposure and covariate information in this historical data set was, as expected, lower in detail and quality than the disease outcome data. Specifically, only years of exposure in coal mines, as well as, separately, in the other mines, was available with no exposure intensity estimates included. Moreover, data on tobacco smoking was recorded for the most part only for the white miners in the data set; and even for the white miners, pack year estimates were generally unavailable. The predictive validity of the smoking variable was supported by its positive association with emphysema and lung cancer, while showing no association with silicosis. Nonetheless, the results of exposure health outcome analyses discussed below indicate that the available exposure estimate, years worked in mines, performed quite reasonably as a surrogate for cumulative exposure.

In the South African mining context, race is an important variable. Hence, where possible (based on the robustness of the data), this was included in the analysis. Factors such as income, living conditions, access to medical care, nutrition, exposure to pathogens, and occupational exposure intensity are likely to have differed considerably between black and white miners, the inclusion of the race variable acts as a surrogate for these unmeasured covariates.

There are important limitations of the PATHAUT database in the diagnosis of emphysema, its grading and typing. The most appropriate method of grading is based on the whole mounted sections, using the Gough Wentworth technique. When analyses were restricted to the small fraction of cases prepared in this manner, the results were ambiguous owing to the small sample size. On the other hand, diagnosis of emphysema based only on formalin prepared lung slices, which is what was available for the large majority of cases, is expected to generally result in the underestimation of grade of emphysema.

The results for the subset of workers who had worked exclusively in coal mines were of greatest interest because of the freedom from the potential confounding effects of exposures while working in other types of mines. The key results for this group concerned the very strong, statistically significant associations of emphysema with exposure measures. As shown in Table 4.12.6.1, those in the highest tercile of exposure were more than seven times as likely to develop emphysema as those in the lowest tercile. Strikingly, for an analysis which included smoking (and therefore was necessarily restricted to white miners), the statistically significant estimate for the odds ratio of high exposure versus low exposure was even greater at above 15 whereas ex- and current smokers had odds ratios of only slightly > 2 as compared with never smokers. These results suggest that coal miner work exposures are very significant predictors of emphysema, and in fact are more important than the contribution of smoking in this group. Because of the limitation of the dataset, further investigation of the relationship between smoking and dust exposure, such as interaction, was not possible. It should be noted that when age was included as a covariate, the odds ratios for emphysema were substantially reduced although in the model including smokers it remained close to 5 and was substantially higher than the odds ratio for being a current smoker. The results for the analyses of "significant emphysema" are a bit less clear with respect to the relative contributions of dust exposure in smoking, i.e., in analyses excluding age, exposure appeared somewhat more important, but in those including age, smoking appeared more important. In view of the high correlation of age with years of coal exposure in the group who worked only in coal mines ($r = 0.68$), the effects of exposure and age are difficult to separate. It is likely that the true magnitude of the effect of exposure lies somewhere between the estimated effects in the models that include age and those that exclude age.

The literature examining the influence of age on the pathogenesis of emphysema is unclear. While studies have clearly shown that the loss in lung function amongst those with chronic bronchitis is greater than that of age alone, similar studies on emphysema are generally complicated by lack of agreement on clinical and diagnostic criteria and its general coupling with the symptoms associated with chronic bronchitis. A study by Piitulainen et al (1997), on emphysematous individuals with alpha 1-antitrypsin deficiency, did however show an age related decline in the percent predicted FEV_1, while controlling for occupational exposures and gender. Age was also shown to be a strong independent predictor for emphysema in gold miner autopsy studies in South Africa (Becklake et al, 1987).

The logistic regression models also showed a strong association of coalworkers pneumoconiosis with exposure years. This finding was to be expected and offers reassurance that exposure year measures were not greatly misclassified.

These findings on emphysema echo those of the international literature. Cockcroft (1982) showed that the odds for emphysema amongst coalworkers, compared to non-coal workers was 10.95 times greater. Dose response relationships between increasing grades of emphysema and dust have been also reported by Ruckley, 1984. The latter study was conducted on the post mortems of 450 coalminers, on whom reliable cumulative dust estimates (in gram-hours/m^3)

were available. Increasing cumulative exposure was related to the grade of histological diagnosed emphysema, with a range of 0.001 gh/m^3 for the smaller lesions to 0.005 gh/m^3 for the larger lesions, while controlling for smoking history and exposure to ash dust. Leigh (1982) in a review of 886 coalminer autopsies, showed that a strong relationship with emphysema existed with years spent on the coalface, with an increase in emphysema score of 0.047 significantly associated with each year of coalface exposure.

It is important to compare these findings amongst South African coalminers with the extensive literature on South African goldminers. A case control study of emphysema amongst autopsied goldminers showed that although a 12.7 fold increased risk of emphysema was associated with the number of years spent in high dust exposures, silicosis was not a statistically significant predictor. In this study, the number of cigarettes smoked before 1960, together with age at death were important predictors (Becklake et al, 1987). The latter study found the predominant type of emphysema to be panacinar type. These findings were somewhat different to the study by Hnizdo et al (1991), which found a much lower relationship with exposure (2.1 odds of emphysema amongst high exposed workers), a strong relationship with autopsy diagnosed silicosis and centriacinar emphysema, and that the latter form of emphysema predominated amongst goldminers. In an autopsy study investigating respiratory outcomes amongst non-smoking goldminers, Hnidzo and colleagues (1994) found only insignificant panacinar emphysema, which was not related to the silica dust exposure or presence of silicotic nodules. In addition, the degree of emphysema was not a strong predictor of lung function outcomes.

When reviewing respiratory disease post mortem profiles of black goldminers who died from unnatural causes on South African mines, prevalences of silicosis and tuberculosis was reported as 9.7% and 2.5% respectively (Murray et al, 1996). This compares with the current study on coalminers, with prevalences of silicosis and TB of 10.86% and 5.21% respectively , amongst those with exclusive coaldust exposure.

These studies amongst South African goldminers suggest that exposure to respirable mine dust results in emphysematous outcomes, with effects strongly potentiated by smoking. The exact relationship between silicosis and the development of emphysema is still unclear. In coalminers however, it has been shown that a relationship exists between coalworker’s pneumoconiosis and centriacinar emphysema. Both Leigh et al (1983) and Ruckley et al (1984) showed an association between increasing severity of pneumoconiosis amongst coalminers and emphysema score. This finding was not replicated in our study. The most probable reason for this lack of association is due to the moderate levels of CWP seen in the post mortem data (prevalence of 7.37% amongst those with exclusive coal dust exposure). It is likely that the mechanism of these two effects of coal dust exposure are independent, and that any association seen between the two may be because both are associated with exposure. The absence of an association in our data could have been due to the regression models controlling for exposure in the analysis.

A review of the PATHAUT data showed that for predominantly goldmining exposed workers over the age of 40, (n= 4302 full post mortems), a prevalence of moderate and marked emphysema of almost 26% existed in this cohort (Hnidzo et al, 1991), compared to the 14.03% of moderate or marked emphysema seen amongst the full or partial post mortems of coalworkers with exclusive coaldust exposure seen in our study. This important difference in prevalence between gold and coal miners is most likely associated with the intensive silica exposure seen in goldmining, which does not seem to be present for coal miners. Among non-smoking white goldminers (Hnidzo, 1994) the prevalence of moderate and marked emphysema is very low (1.65%), and this may suggest that the elevated prevalence amongst goldmining populations may be due to these studies being conducted on white smoking miners. Comparable gold mining studies of emphysema prevalence including black miners are not available.

6. Conclusion and Recommendations

SUMMARY OF CONCLUSIONS AND RECOMMENDATIONS

- Coaldust related diseases in South African mines are relatively low, and for certain outcomes, substantially lower than that of goldminers.
- Dust levels under current working conditions contribute to the development of respiratory disease, independently of smoking or TB.
- The effect of smoking together with exposure may have an additive effect on outcome.
- The conducting of a longitudinal cohort study would allow for a better characterisation of exposure and outcome measures, control the "healthy worker effect" and more accurately reflect the relationship between exposure and outcome.
- Research into past coaldust exposures may result in stronger exposure-effect relationships.
- More rigorous efforts at controlling dust exposure must be considered, together with the enforcement of occupational hygiene monitoring programmes currently being drafted.
- Smoking cessation programmes will allow for important positive health effects.
- Medical surveillance, with special focus on spirometry, should be improved and guidelines on removal from exposure for those with significant declines in lung function should be implemented.
- Health and safety education programmes must be conducted, emphasising the hazards of coaldust exposure and the importance of smoking cessation.

6.1 Conclusion

The parallel living sample and autopsy studies results are mutually reinforcing that dust exposures in coal mines under conditions prevailing relatively recently in South Africa are contributing to the development of respiratory disease. This is reflected in the association of exposure estimates with pneumoconiosis and, most importantly, with decrements in pulmonary function and emphysema. Moreover, these effects are seen even among non-smokers, and it appears that the contributions of smoking and dust exposure to decrements in pulmonary function are of comparable magnitude, whereas the contribution of dust exposure to development of emphysema outweighs the contribution of smoking. The evidence for a significant interaction between smoking and coal dust exposure in the development of pulmonary function decrements is modest, suggesting that effects are largely additive. The magnitude of effects seen on pulmonary function are in keeping with the range found in previous studies in international literature, offering further reassurance of the validity of the findings of the current study.

In considering the positive findings described above, it should be kept in mind that the absolute level of work-related respiratory disease is, nonetheless, relatively modest and appears substantially lower than that which has been shown in South African gold miners.

6.2 Recommendations

The findings and conclusions lead to key recommendations:

6.2.1 Research recommendations

A comprehensive longitudinal cohort study should be considered as an important development on the findings of this study. This could be a completely new cohort of workers, or a follow up of this sample as a means of further describing the extent of the "healthy worker survivor effect". Although this study found a dust related dose response effect on declines in lung function, the extent to which this effect is blunted by the apparent "healthy worker effect" seen in the study, is uncertain. Reviewing annual lung functions (conducted as part of the medical surveillance on the mines), obtaining dust exposures and job descriptions and job transfers on those still employed, and repeating lung function testing on the entire sample at the end of a five year period will allow for a better understanding of this effect on the respiratory health of coalminers.

Such prospective cohort study designs will allow for better estimates of both exposure and longitudinal lung function outcomes. It is the expectation of the researchers that such a study is likely to reveal considerably greater dust related effects on lung function declines.

Investigations into the patterns of smoking amongst underground coalminers and reasons for the apparent low prevalence and characterisation of the "healthy smoker effect" are recommended. Assessment of the latter will provide a better understanding of the effect of smoking on respiratory outcomes in coalminers specifically, and allow for the consideration of implementation of smoking cessation programmes. Although the study did not show any specific interactions between smoking and dust exposure, both these were shown to be contributors to declines in lung function, and in instances where both are present, the effect was shown to be at least additive. Research into smoking amongst miners will assist in the development of programmes of smoking cessation.

Characterisation of past exposures on the coal mines in South Africa will be an important research undertaking. One of the limitations of the current study was the inability to obtain sufficient data for periods prior to the 1990s. A research project focussed on assessing past exposures for various categories of workers, in different job descriptions and sections of the mines will provide an accurate assessment of historical exposures, unlike some of the assumptions of exposure that had to be undertaken in the current study. Such research must undertake a comprehensive review of historical dust data available on coal mines and explore the data available at the DME. This investigation will characterise the exposure trends of coalminers over different time periods. Given that this will involve assessing data collected by different sampling methods (thermal precipitators and gravimetric, CIP10 and cyclones, etc.), the project will have to determine means of standardising the exposures collected by these various means. Better exposure data could have shown a stronger exposure-effect relationship, as opposed to the results produced by the study, in which certain assumptions had to be made about exposure.

6.2.2 Medical, hygiene and policy Recommendations

Increased efforts to control exposure of coal miners to respirable dust appear warranted as, under conditions of exposure found currently in this study, clinically meaningful work-related respiratory problems can be expected to develop in a substantial fraction of miners over working lifetime. This finding strongly drives the recommendation that the legal limits for exposure to respirable dust in South African coal mines should be enforced. Given that the data levels obtained in our study – both historical and current sampling - showed that the operations were within the South African recommended standard of 2 mg/m^3, enforcement of this statutory limit seems entirely feasible in the mining operations, with a policy of gradually implementing lower levels over a period of time.

Strategies to reduce exposure must include substantially increased engineering controls, such as improved ventilation and ventilation design and improved design of continuous mining equipment. Current techniques such as dust wetting as an industry standard are important, and rigorous maintenance to ensure that such techniques are in operation at all times is vital. Engineering controls should be implemented together with work practices designed to minimise exposure – key job descriptions such as the continuous miner operator, shuttle car operator and roof bolter, should be more stringently monitored. Job rotations and other administrative controls to reduce the exposure in these high exposure categories must be considered.

Rock blasting mining operations were not the common practice at the operations on which the study was conducted. As many new mining techniques have superseded the need for blasting, and given the dust exposure dangers associated with this, policy should be developed to prevent this technique from being a continued practice on coalmines.

Further investigation of techniques to reduce the toxicity of dust, especially certain free silicate radicals, is necessary (Vallyathan et al, 1991). Laboratory tests in the use of organosilane coating of toxic dusts have shown to dramatically reduce their cellular toxicity. The value of such mechanisms needs further assessment in the South African mining industry. Although the silica content of respirable coal dust in South Africa is low, the prevalence of silicosis of 10% seen at autopsy is nevertheless a significant level, warranting intervention.

A review of the dust sampling strategies currently in use on the mines is necessary. Based on our experience and that reported in the international literature, the CIP10 samplers appear to be less appropriate than the cyclone samplers. Several samplers are currently under review in Europe to ensure that they meet the ACGIH-CEN-ISO sampling criteria. It will be imperative for the DME to give serious consideration to the proposals that may emanate from these studies. Joint co-operation between the researchers and the hygiene departments have led to at least one mining operation already using the cyclone system. We are given to understand that the DME is currently proposing draft Occupational Hygiene Standards. This review process must include the use of the "statistical population" method recommended by the DME in its previous Guidelines. The creation of "homogenous" groups for sampling does not provide an adequate characterisation of exposure of workers with specific job descriptions in specific work areas. Given that this sampling strategy was originally developed as part of a levy based system, the directives need to be revised so that the dust sampling strategies are directed toward assessing exposure for purposes of improving of workers' health. The draft Occupational Hygiene Regulations will require mines to properly investigate personal exposures thus addressing some of these issues.

The system of respiratory medical surveillance as per the Mine Health and Safety Act, including periodic standardised questionnaires, spirometry, and chest radiography should be better enforced. Although our study did not include evaluation of current medical surveillance on the mines as a stated objective, our interaction with the health services at the mines allowed the research team to cursorily review practices. It was obvious that the standard and approach to medical surveillance varied among the research mines, with some services having no access to spirometry. Clear industry guidelines or regulations under the Act need to be developed with regard to appropriate management and transfer out of dust exposure for those showing decrements in lung function. Recommendations cannot be detailed in this report. However clinical pointers will include: decline to less than the two standard deviations of predicted of FEV_1 (using the Louw equations) or in workers showing a rapidly declining trend even before this cut off is reached, in the absence of documented treatable lung pathology.

A permanent job exposure profile database for each worker for his lifetime of employment needs to be developed, which captures shaft, section, job description and duration of employment within these latter categories. This system should be linked to the personal and area dust sampling collected on a routine basis at all the mines. A universal system should be developed through a SIMRAC contract, and managed by the occupational hygiene departments at each mine. This data must be transferable between mines, accompanying a worker being re-employed on new mines.

Health and safety education campaign for coal miners should be mounted which should emphasise both the hazards of exposure to respirable coal dust but also the particular importance of cessation of smoking for those with such exposures.

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8. Appendices

8.1. Biostatistical Concepts

Because this report presents a considerable amount of statistical information, a brief overview of some of the statistical concepts are defined here.

Confidence Intervals

In research studies the key objective is to determine estimates of the measures of association (for example, and odds ratio) between an exposure and a health outcome. Because this estimate may be inaccurate - due to random (chance) variation in the relationship of the measures - researchers also indicate the confidence they have in the accuracy of this point estimate. In this report, the level of confidence is usually indicated by construction of a 95% confidence interval, which can be interpreted to mean that, with 95% certainty, the true point estimate falls within this interval (i.e., only 5% of the time will the true point estimate fall outside the interval)."

Statistical Significance

In order to understand whether the value obtained from the selected population (e.g. FEV_1) is representative of the true (but unlikely to ever be known) value from the entire population, tests are conducted to determine the probability (or likelihood) of this lying within a normal distribution range (i.e. approximately where 90% or 95% of the entire population lies). These are the tests of significance – i.e. does this obtained value differ significantly from the entire population (or a comparison population). Generally, the likelihood (probability = p value) of a value lying outside a normal distribution range is referred to as statistically not significant (a non-significant p value). These cut off points are arbitrarily chosen at either 90%, 95% or any other, depending on the choice of the researcher. In this report, the convention used is the 95% cut off. For purposes of standardisation, the words "significance" or "significant" are used in this report strictly in the statistical sense.

Chi Square Tests

When attempting to show an association between two sets of categorical data [examples of categorical data: male/female; black/white; cases with TB; cases with bronchitis], such as between gender and bronchitis, the chi square test is used. These tests do not prove causation, but association.

Correlation Coefficients

The equivalent to a chi square test for continuous data (examples of continuous data: FEV_1; FVC, age, cumulative exposure), such as determining the relationship between change in FEV_1 and cumulative exposure, a correlation coefficient is obtained. Once again, this test does not show causation, but an association between the two variables.

Tests for Trend

When there is a need to determine a relationship between a categorical variable which has ordered levels, e.g. surface exposure, backbye exposure and face exposure, and a continuous variable, e.g. FEV_1 , a test can be conducted which determines whether there is a significant change in a linear manner between the two variables.

Kappa Statistic

This test is used to determine the level of agreement between two assessors for a specific outcome, e.g. two radiologists independently reviewing chest x-rays, may not agree on every x-ray, but there will be some level of overall agreement, based on the number that the both say do not have the outcome, the number that both agree has the outcome, and the numbers for which the disagree. The test used here is called the kappa test statistic.

Modelling and Regression

In trying to understand relationships between variables, it is sometimes not sufficiently useful to just compare to variables alone at one time (e.g. cumulative dust exposure and lung function), because various other variables may influence these, and while we may see an association between two variables, we cannot be certain how this relationship will be affected by other associated variables (e.g. age, height and smoking in the relationship between cumulative dust exposure and lung function). This is achieved through statistical methods, by setting up a statistical model. A model is a set of variables that the researcher believes predicts a particular outcome (e.g. age, height, smoking and dust exposure are possible predictors of the changes in lung function). These predictors are either decided through knowledge of biology (age and height causes changes in lung function) or through previous research (smoking and dust exposure causes changes in lung function). Through additional statistical testing, it can be assessed whether these predictors are appropriate or not. By including all the possible predictors (regressing) into the model, the researcher is able to state what the effect of one predictor is on the outcome in the presence of the other predictors (e.g. the lung function change for a smoker of x years, y height and 10 years dust exposure is Z, while the lung function change for a smoker of x years, q height and 20 years dust exposure is Y). This is sometimes phrased as a change in the outcome given the value of predictor 1 while predictor 2 is held constant.

The two types of regression models are the multiple linear regression and the multiple logistic regression. The former is used for continuous outcomes (FEV_1, cumulative dust exposure etc), while the latter is used for categorical (number of cases with CWP, number with emphysema) outcomes.

Parameter Coefficients

The data provided by the regression models are values for each of the predictors e.g. the lung function changes for each unit of dust exposure by the value x. This value x is referred to as the parameter coefficient, and it quantifies the amount of change in the outcome by a unit change in the predictor.

8.2 Statistical modelling of current and historic dust data

[This section is to be read in conjunction with Section 4.6.]

4.6.1 Regression model development for current exposure data

Using the current dust sampling data collected by the research team, statistical models were developed to describe the data, providing estimates of dust levels in the various categories. Because the dust concentration showed a lognormal distribution, the natural logarithm of the measured exposure was used as the dependent variable. Independent variables considered for entry into the models included mine, zone (face, backbye or surface), job description and section. The latter two variables were considered simply for comparison: it was recognised that they could not be used in a final model estimating historical exposures because this information was not generally available in the work histories taken from company records.

The following table shows the development of these models with the introduction of the different terms. Initially, simple linear regression models regressing the log of dust levels on mine, zone, job and section individually were developed. Then each of these terms were introduced into a multiple linear regression model. The data showing the fit of the models is shown in the table below.

Table 4.6.1.1 Respiratory health of South African Coalminers: models for describing exposure using dependent variable: log (dust level) (mg/m^3)

MODEL NO.	**VARIABLE**	**DF**	**SUM OF SQUARES FOR MODEL**	**P VALUE (F TEST)**	**MODEL R^2**
1	Mine	2	9.78	0.039	0.016
2	Zone	2	112.1	<0.0005	0.180
3	Job	34	196.2	<0.0005	0.316
4	Section (within Zone)	28	163.0	<0.0005	0.262
5	Mine	2	17.16	0.001	0.208
	Zone	2	119.5	<0.0005	
6	Mine	2	10.68	0.0074	0.357
	Zone	2	16.91	0.0004	
	Job	34	92.76	<0.0005	
7	Mine	2	9.78	0.011	0.407
	Zone	2	119.5	<0.0005	
	Job	24	90.37	<0.0005	
	Section	34	33.67	0.143	

Total sum of squares for each model = 621.8

Because of the absence of information from company records on specific job descriptions and actual sections worked, these terms could not be included in the final model. For this reason, the model that was finally chosen (Model no. 5 above) was described by

$$\text{Log(dust level (mg/m}^3\text{))} = \beta_0 + \beta_1 \text{ mine1} + \beta_2 \text{ mine2} + \beta_3 \text{ face} + \beta_4 \text{ backbye} + E$$

Mine was entered as two categorical variables, (mine 1 vs mine 3, mine 2 vs mine 3) as was zone (face vs surface, backbye vs surface). This provided an overall model R^2 = 0.208, with p value < 0.0001. The parameter estimates are shown as follows:

Table 4.6.1.2 Respiratory health of South African Coalminers: parameter estimates for current dust model - using dependent variable: log (dust level) (mg/m^3)

Variable	DF	Parameter Estimate	Standard Error	P value
Intercept	1	-1.23898	0.22971	<.0001
Face	1	1.74665	0.23083	<.0001
Backbye	1	0.81920	0.24320	0.0008
Mine 1	1	-0.50180	0.13350	0.0002
Mine 2	1	-0.23960	0.13414	0.0748

The above estimates are compared to the base within the category which is not shown (e.g. face vs surface, backbye vs surface; mine 1 vs mine 3, mine 2 vs mine 3).

4.6.2 Regression model development for historic data

Using the process described above for current dust data, regression models were run for the historic data as well. The variables were first considered individually within a simple linear regression model, followed by introduction into a multivariate linear regression model. The overall fit of the different models is shown. For similar reasons to those discussed above, job title and section were not considered to be useful. The model utilising mine, zone and year categories was retained.

Table 4.6.2.1 Respiratory health of South African Coalminers: models for describing exposure using dependent variable: log (dust level) (mg/m^3)

MODEL NO	VARIABLE	DF	SUM OF SQUARES FOR MODEL	P VALUE (F TEST)	MODEL R^2
1	Mine	2	514.0	<0.0001	0.054
2	Zone	2	1771	<0.0001	0.185
3	Job	239	2543	<0.0001	0.266
4	Section (within Zone)	24	849.6	<0.0001	0.111
5	Year Category	4	303.7	<0.0001	0.032
6	Mine	2	376.4	<0.0001	0.225
	Zone	2	1637	<0.0001	
7	Mine	2	269.1	<0.0001	0.312
	Zone	2	187.9	<0.0001	
	Job	239	833.0	<0.0001	
8	Mine	2	246.2	<0.0001	0.322
	Zone	2	61.91	<0.0001	
	Job	224	662.2	<0.0001	
	Section	23	105.8	0.0003	
9	Mine	2	188.9	<0.0001	0.350
	Zone	2	62.10	<0.0001	
	Job	224	664.5	<0.0001	
	Section	23	96.51	0.0007	
	Year Categories	4	213.5	<0.0001	
10	Mine	2	1584	<0.0001	0.243
	Zone	2	311.0	<0.0001	
	Year Categories	4	206.1	<0.0001	

Total sum of squares for each model = 7676

Mine and zone were entered as categorical variables, (mine 1 vs mine 3, mine 2 vs mine 3; face vs surface, backbye vs surface). The year categories were as follows: 1991 – 1993 = category 1; 1994 – 1995 = category 2; 1996 – 1997 = category 3, 1998 - 1999 = category 4 and >1999 = category 5. Following an assessment of the descriptive data, no obvious trend was seen in any specific period of time, to warrant using more specific categories. Year categories was subsequently omitted from the final model. The following model was considered to be most robust in explaining the data:

$$\text{Log (twa)} = \beta_0 + \beta_1\,\text{mine1} + \beta_2\,\text{mine2} + \beta_3\,\text{face exposure} + \beta_4\,\text{backbye exposure}$$

The overall model $R^2 = 0.243$ with a p value = 0.0001. This model generated the following parameter estimates:

Table 4.6.2.2 Respiratory health of South African Coalminers: parameter estimates for historic dust model - using dependent variable: log (dust level) (mg/m³)

Variable	Df	Parameter estimate	Standard error	P value
Intercept	1	-1.51	0.05	<0.0001
Mine 1	1	-0.30	0.05	<0.0001
Mine 2	1	0.90	0.07	<0.0001
Face	1	1.81	0.06	<0.0001
Backbye	1	0.86	0.06	<0.0001

As mentioned previously, the above estimates are compared to the base within the category which is not shown (e.g. face vs surface, backbye vs surface; mine 1 vs mine 3, mine 2 vs mine 3, etc.).

4.6.3 Regression model development for cumulative exposure

Using the regression models developed above from the investigator and historically collected data, further models to determine cumulative exposure were investigated. It was intended to employ the coefficients that were generated for the time periods from the historic data to extrapolate current exposures to past years. However, because these coefficients did not show any specific trend over the nine year period and because of variable differences between the year categories, use of this data for back extrapolation would have added little to the models. Time was thus left out of the model altogether. Use of mine and zone provided reasonably robust measures of exposure.

Because the historical data was collected with different types of samplers, it was important to consider a variable representing type of sampling device in the models. Most historical data was collected with the CIP10 sampler, whilst the current data was collected using the cyclone.

The current data and the historic data were then combined into a single dataset. The coefficients for mine, zone and sampler were generated from the regression models of this combined dataset. These coefficients were be used for providing estimates of cumulative exposure. The model that resulted from this was:

$$\text{Log(dust level (mg/m}^3\text{))} = \beta_0 + \beta_1 \text{ mine1} + \beta_2 \text{ mine2} + \beta_3 \text{ face} + \beta_4 \text{ backbye} + \beta_5 \text{ sampler} + E$$

It should be noted that as an additive model for predicting a logarithmic outcome, this regression model assumes a constant ratio between measured levels of dust using one sampler as compared to the other type of sampler. This appears intuitively to be a reasonable assumption. The model was generated had a R^2 of 21.53% and p value of <0.0001. The estimates are shown below:

Table 4.6.3.1 Respiratory health of South African Coalminers: parameter estimates for combined model - using dependent variable: log (dust level) (mg/m³)

VARIABLE	DF	PARAMETER ESTIMATE	STANDARD ERROR	P value
Intercept	1	-0.59731	0.04392	<.0001
Mine 1	1	0.23979	0.05043	<.0001
Mine 2	1	0.76346	0.06031	<.0001
Surface	1	-0.86744	0.05885	<.0001
Face	1	0.95441	0.05095	<.0001
Cyclone	1	-0.42164	0.07518	<.0001

In order to determine the dust estimates for each cell within the mine/zone matrix as generated by the above regression model, the arithmetic mean was used. Because of the lognormal distribution of the dust data, in calculating this mean, half the value of the residual variance of the model had to be incorporated.

$$\boldsymbol{c}_{ij} = \{\exp(\boldsymbol{b}_0 + \boldsymbol{b}_1 mine_1 + \boldsymbol{b}_2 mine_i + \boldsymbol{b}_3 zone_1 + \boldsymbol{b}_4 zone_2 + \boldsymbol{b}_5 sample_1 + (MSE/2)\}$$

where *x* **=** the arithmetic mean, with subscript *i* = mine and subscript *j* = zone, with $zone_1$ = surface and $zone_2$ = face, MSE = the mean square error of the regression model (the residual variance). The residual variance of the model = 1.972, residual variance/2 = 0.986. The resultant matrix is shown below:

Table 4.6.3.2 Respiratory health of South African Coalminers: cumulative dust exposure estimate mine/zone matrix (mg/m^3)

	MINE 1	**MINE 2**	**MINE 3**
SURFACE	0.788	1.329	0.619
BACKBYE	1.796	3.166	1.474
FACE	4.870	8.202	3.830

A major difficulty in estimating past exposure is the lack of any exposure data for periods prior to 1991. Although anecdotal information would suggest that respirable dust levels at face jobs were several fold higher prior to the 1990s, the lack of any quantitative (dust sampling data), or even, objective qualitative (company reports on amounts of coal mined, ventilation design and rates, etc.) data makes exposure estimation for this time period very difficult. For these reasons a sensitivity analysis was conducted: key exposure-outcome analyses were run comparing the assumption that mean face, backbye and surface exposures pre-1991 were respectively 3.5, 2.5 and 1.5 times greater than the respective mean values in the 1990s, and, in another model, 3, 1.5 and 1 times higher for periods prior to 1985, to the assumption that means were the same in both time periods (i.e., using ratios of 1, 1, and 1 times). Results for the three models were quite similar. Therefore the model assuming equal means in the two time periods was selected as the one requiring the least degree of arbitrary assumptions. To the extent that this results in added non-differential misclassification of cumulative dust exposure (CDE), there may be some bias toward the null hypothesis in study results. On the other hand, if there is, in fact, systematic underestimation of earlier exposures, this may tend to result in an overestimate of exposure-outcome "dose" response or regression slope.

8.3 Statistical modelling of the lung function data

[This section is to be read in conjunction with Section 4.10.3]

4.10.3.1 Linear regression model development

The following tables present the different linear regression models for the percent predicted values of FEV_1 and FVC, using the Louw et al predictive equations. The table shows the introduction of terms, together with the value of R^2, the overall significance of the model (F test), the β coefficients, the standard error of the coefficients and the significance of the parameter estimates. Models were run using exposure and smoking variables, the latter as two dummy variables. Revised models used pack years. Exposure was included as the cumulative dust exposure variable, CDE.

Simple linear models were first developed using percent predicted lung function outcomes (FEV_1 and FVC) measured in litres (L) regressed on cumulative dust exposure and then against pack years of smoking. Multivariate models then looked at smoking status variables (current and ex-smoker, compared to never smokers) and CDE, with new terms being added in subsequent models: current job status, diagnosed TB and an interaction term including job status and cumulative exposure. The second set of multivariate models then replaced the smoking status variables with pack years. This was followed by including both packyears and smoking status variables into a model. The final models included all these variables plus interaction terms between pack years and smoking status and cumulative exposure and job status. The models for FEV$_1$ and then FVC, are shown in the tables below, initially using smoking status, then pack years.

Table 4.10.3.1 Respiratory health of South African Coalminers: regression models for FEV$_1$ percent predicted outcomes (using Lowe et al equations)

Model	R^2 Adjusted	Intercept	β	SE (β)	P value (β)
Univariate models					
Cumulative dust exposure (CDE) (mg-years/m^3)	0.005	106.05	-0.03	0.01	0.02
Pack years	0.005	105.36	-0.21	0.09	0.02
Multivariate Model 1	0.004	105.28			
Current Smoker			-0.35	1.37	0.7
Ex-Smoker			-4.23	1.84	0.02
Multivariate Model 2	0.01	107.34			
CDE			-0.03	0.01	0.02
Current Smoker			-1.08	1.40	0.44
Ex-Smoker			-4.51	1.83	0.01
Multivariate Model 3	0.02	104.20			
CDE			-0.04	0.01	0.01
Current Smoker			-0.32	1.42	0.82
Ex-Smoker			-4.48	1.83	0.01
Current miner			4.27	1.62	0.01
Multivariate Model 4	0.06	105.15			
CDE			-0.04	0.01	0.01
Current smoker			-0.27	1.40	0.85
Ex-smoker			-3.95	1.79	0.03
Current miner			3.83	1.59	0.02
Doctor diagnosed TB			-21.23	3.49	<0.001
Multivariate Model 5	0.06	106.20			
CDE			-0.07	0.04	0.08
Current smoker			-0.28	1.40	0.84
Ex-smoker			-3.95	1.79	0.03
Current miner			2.57	2.12	0.22
Doctor diagnosed TB			-21.35	3.49	<0.001
CDE*current miner			0.04	0.04	0.37
Multivariate model 6	0.01	107.07			
CDE			-0.03	0.01	0.02
Pack years			-0.22	0.09	0.02
Multivariate Model 7	0.02	104.67			
CDE			-0.04	0.01	0.01
Pack years			-0.19	0.09	0.03
Current miner			3.64	1.59	0.02
Multivariate Model 8	0.06	105.59			
CDE			-0.04	0.01	0.01
Pack years			-0.17	0.09	0.05
Current miner			3.27	1.56	0.04
Doctor diagnosed TB			-21.36	3.49	<0.001

Model	R^2 Adjusted	Intercept	β	SE (β)	P value (β)
Multivariate Model 9	0.06	104.87			
CDE			-0.04	0.01	0.01
Current smoker			2.12	1.70	0.21
Ex-smoker			-3.02	1.83	0.10
Current miner			-3.90	1.58	0.01
Doctor diagnosed TB			-20.81	3.49	<0.001
Pack years			-0.26	0.11	0.01
Multivariate Model 10	0.06	103.89			
CDE			0.03	0.01	0.01
Current smoker			3.33	1.53	0.03
Current miner			3.92	1.58	0.01
Doctor diagnosed TB			-21.02	3.49	<0.001
Pack years			-0.30	0.10	0.01
Multivariate Model 11	0.06	104.95			
CDE			-0.04	0.01	0.01
Current smoker			1.77	1.72	0.30
Ex-smoker			-1.09	2.32	0.64
Current miner			3.85	1.58	0.02
Doctor diagnosed TB			-20.96	3.49	<0.001
Pack years			-0.81	0.42	0.06
Pack years*current smoker			0.58	0.44	0.18
Multivariate Model 14	0.06	105.68			
CDE			-0.04	0.01	0.01
Current smoker			1.96	1.44	0.24
Current miner			3.84	1.35	0.02
Doctor diagnosed TB			-21.04	3.06	<0.001
Pack years			-0.93	0.29	0.01
Pack years*Current smoker			0.71	0.30	0.04

Although all the multivariate regression models are statistically significant, the models have low R^2 (explanation of the outcome by the independent variables – the adjusted R^2 is used in the above tables to counter the effect of improved R^2 by simply adding more terms into the model), suggesting that the linear models may not be the most appropriate, or that some other factors not accounted for in the model may be influencing the outcome. (Low adjusted R^2 have been found in most other studies (Henneberger (1996)).

None of the interaction terms that were introduced showed any statistical significance. When smoking status (current and ex) was entered into the models, current smoking status failed to show any significance; however, when the continuous term, pack years was introduced simultaneously into the model, the level of significance of the current smoker term improved from a p value of 0.9 to 0.08. This effect also resulted in the drop in significance of the ex-smoker p value from 0.01 to 0.09. A history of TB diagnosed by a doctor showed the largest effect on the percent predicted value of FEV$_1$. As shown in most of the analysis above, a possible healthy worker effect seems to be evident, although this effect has been controlled for by introducing the employment status variable into the models. The regression model shows that current miners have a higher percentage predicted FEV$_1$ when compared to ex-miners. Cumulative dust exposure variable (CDE) was consistently statistically significant in all the models.

Table 4.10.3.2 Respiratory health of South African Coalminers: regression models for FVC percent predicted outcomes (using Lowe et al equations)

Model	R^2 Adjusted	Intercept	β	SE(β)	P value (β)
Cumulative dust exposure (CDE)	0.01	104.76	-0.03	0.01	0.01
Pack years	-0.001	103.31	-0.03	0.08	0.66
Multivariate Model 1	0.01	102.10			
Current Smoker			3.00	1.20	0.01
Ex-smoker			-1.66	1.60	0.30
Multivariate Model 2	0.01	103.68			
CDE			-0.02	0.01	0.04
Current smoker			2.44	1.22	0.05
Ex-smoker			-1.87	1.60	0.24
Multivariate Model 3	0.02	100.80			
CDE			-0.03	0.01	0.01
Current smoker			3.14	1.24	0.01
Ex-smoker			-1.84	1.59	0.25
Current miner			3.91	1.41	0.01
Multivariate Model 4	0.04	101.42			
CDE			-0.03	0.01	0.01
Current smoker			3.17	1.23	0.01
Ex-smoker			-1.50	1.58	0.34
Current miner			3.62	1.40	0.01
Doctor diagnosed TB			-13.89	3.08	<0.001
Multivariate model 5	0.01	104.97			
CDE			-0.02	0.01	0.01
Pack years			-0.04	0.08	0.58
Multivariate Model 6	0.01	103.06			
CDE			-0.03	0.01	0.01
Pack years			-0.03	0.08	0.74
Current miner			2.88	1.40	0.04
Multivariate Model 7	0.03	103.66			
CDE			-0.04	0.01	0.01
Pack years			-0.01	0.08	0.88
Current miner			2.63	1.38	0.06
Doctor diagnosed TB			-14.15	3.09	<0.001
Multivariate Model 8	0.05	101.21			
CDE			-0.03	0.01	0.01
Current smoker			5.01	1.50	0.01
Ex-smoker			-0.78	1.61	0.63
Current miner			3.67	1.40	0.01
Doctor diagnosed TB			-13.56	3.07	<0.001
Pack years			-0.20	0.09	0.03
Multivariate Model 9	0.05	100.95			
CDE			-0.03	0.01	0.01
Current smoker			5.32	1.35	<0.001
Current miner			3.68	1.39	0.01
Doctor diagnosed TB			-13.61	3.07	<0.001
Pack years			-0.21	0.09	0.02

Model	R^2 Adjusted	Intercept	β	SE(β)	P value (β)
Multivariate Model 10	0.04	102.34			
CDE			-0.06	0.04	0.08
Current smoker			3.16	1.39	0.01
Ex-smoker			-1.49	1.79	0.34
Current miner			2.51	2.12	0.18
Doctor diagnosed TB			-13.99	3.50	<0.001
CDE*current miner			0.03	0.04	0.37
Multivariate Model 11	0.05	101.27			
CDE			-0.03	0.01	0.01
Current smoker			4.77	1.51	0.01
Ex-smoker			0.59	2.05	0.78
Current miner			3.64	1.40	0.01
Doctor diagnosed TB			-13.66	3.08	<0.001
Pack years			-0.59	0.37	0.12
Pack years*current smoker			0.41	0.39	0.28
Multivariate Model 12	0.05	101.27			
CDE			-0.03	0.01	0.01
Current smoker			4.77	1.52	0.01
Ex-smoker			0.59	2.05	0.78
Current miner			3.64	1.40	0.01
Doctor diagnosed TB			-13.66	3.08	<0.001
Pack years			-0.17	0.10	0.07
Pack years*ex smoker			-0.41	0.39	0.28
Multivariate Model 13	0.05	101.94			
CDE			-0.05	0.04	0.17
Current smoker			4.71	1.52	0.02
Ex-smoker			0.54	2.05	0.79
Current miner			2.83	1.86	0.13
Doctor diagnosed TB			-13.74	3.09	<0.001
Pack years			-0.17	0.10	0.08
CDE*current miner			0.03	0.04	0.52
Pack years*ex smoker			-0.41	0.39	0.29
Multivariate Model 14	0.05	100.96			
CDE			-0.02	0.01	0.06
Current smoker			4.01	1.34	0.01
Current miner			3.65	1.40	0.01
Doctor diagnosed TB			-13.82	3.07	<0.001
Pack years*Ex-smoker			-0.42	0.30	0.15
Pack years*CDE			-0.01	0.01	0.15

The models of FVC showed similar patterns to those of the regression models on FEV_1, All models were strongly statistically significant, with low overall adjusted R^2. None of the interaction terms were significant. In these models, current smoker status generally showed a greater effect on lung function than ex-smoker status, but with a “protective” effect on percent predicted FVC. The packyears and smoking status variables were only significant in the model with cumulative dust exposure when included together in the model. As with the FEV_1 models, a history of TB remained strongly significant showing the greatest adverse effect on percent predicted FVC. Current job status vs ex-miner status showed a “protective” effect. Cumulative dust exposure was still consistently associated with a decline in percent predicted FVC.

4.10.3.2 Linear regression model selection and diagnostics

Model selection procedures were used to suggest appropriate models. Those models that were statistically appropriate and biologically plausible were subjected to regression diagnostics. This process allowed the selection of the most robust (i.e. that met statistical standards) linear regression models.

Three model selection procedures were used to ascertain appropriate models for percent predicted FEV_1 and FVC respectively. These procedures were adjusted R^2 (R_a^2), the Mallow's C_p and the $PRESS_P$ procedures. All the terms included in the above tables, including the interaction terms were assessed. The summary results of this analysis are presented in the following tables.

Table 4.10.3.3 Respiratory Health of South African Coalminers: summary of regression model selection statistics for percent predicted FEV_1

MODEL TERMS	R_a^2	C_p – model terms	$PRESS_p$
CDE, current smoker, current miner, previous TB, pack years pack years*current smoker (SELECTED)	0.07	1.73	217777
CDE, current smoker, current miner, previous TB, pack years, pack years*ex-smoker	0.07	1.73	217777
CDE, current smoker, current miner, previous TB, pack years*ex-smoker, pack years*current smoker	0.07	1.73	217777
CDE, current smoker, current miner, previous TB, pack years*current smoker, pack years*ex-smoker, CDE*current miner	0.06	0.86	218344
CDE, current smoker, current miner, previous TB, pack years, pack years*ex-smoker, CDE*current miner	0.06	0.86	218344
CDE, current smoker, current miner, previous TB, pack years, pack-years*current smoker, CDE*current miner	0.06	0.86	218344
CDE, current smoker, current miner, previous TB, pack years (SELECTED)	0.06	0.1	217235

Review of the above procedures showed that most models were reasonably similar in statistical terms. It was decided in terms of the research objectives that cumulative dust exposure and smoking variables should be retained in the final models. Furthermore, those models with the smallest number of terms that were statistically acceptable by the above procedures (model parsimony) would be considered. The following model met these criteria and was subjected to diagnostic assessment.

Model 1 (Multivariate Model 14 from Table 4.10.3.1)

FEV_1 % predicted = β_0 (intercept) - β_1 (cumulative dust exposure (mg-years/m^3)) + β_2 (current smoker) + β_3 (current miner) - β_4 (previously diagnosed TB) - β_5 (pack years) + β_6 (pack years x current smoker)

FEV_1 % predicted = 105.68 – 0.04*(dust level (mg/m^3) x years of exposure) + 1.96*(current smoker) + 3.84*(current miner) – 21.04*(previously diagnosed TB) – 0.93*(pack years) + 0.71*(pack years x current smoker)

A similar process was applied to determining the models for FVC:

Table 4.10.3.4. Respiratory Health of South African Coalminers: summary of regression model selection statistics for percent predicted FVC

MODEL TERMS	R_a^2	C_p – model terms	$PRESS_p$
current smoker, current miner, previous TB, pack years*CDE	0.045746	1.5	167012
CDE, current smoker, current miner, previous TB, pack years*CDE	0.045373	1.14	167345
CDE, current smoker, current miner, previous TB, pack years (SELECTED)	0.045294	1.07	167486
current smoker, current miner, previous TB, pack years*CDE, pack years*ex smoker	0.045250	1.07	167777
current smoker, current miner, previous TB, pack years*CDE CDE*current miner	0.045173	0.96	167410
CDE, current smoker, current miner, previous TB, pack years*CDE packyears*ex-smoker (SELECTED)	0.045068	0.86	168094
CDE, current smoker, current miner, previous TB, pack years, pack years*CDE	0.045068	0.86	167854

Issues such as research objectives and model parsimony were used together with the statistical model selection process detailed above to select out the following model:

Chosen Model 1 (Multivariate Model 9 from table 4.10.3.2)

FVC % predicted = β_0 (intercept) - β_1 (cumulative dust exposure (mg-years/m^3)) + β_2 (current smoker) + β_3 (current miner) - β_4 (previously diagnosed TB) - β_5 (pack years)

FVC % predicted = 100.95 – 0.03*(dust level (mg/m^3) x years of exposure) + 5.32*(current smoker) + 3.68*(current miner) – 13.61*(previously diagnosed TB) – 0.21*(pack years)

The two models chosen above for both lung function parameters respectively were then assessed for model fit. Tests looking at large externally studentised residuals, high leverage points, influence on predicted values and influence on the regression coefficients were conducted on these models. Removal of observations that met the specific cut off criteria for each of these tests resulted in minimal overall change of the β coefficients of concern in the model. In some instances, however, removal of these observations resulted in the reduction of the adjusted R^2. In the final analysis, it was decided to keep all observations in the models.

8.4 Additional analyses of radiological reading data

4.11.2 Profusion agreement

When defining normal as being less than 0/1 (i.e. 0/-; 0/0 and 0/1) and all others greater and equal to 0/1 as being positive for pneumoconiosis; the results were as follows:

Table 4.11.2.1 Respiratory health of South African Coalminers: table of agreement between readers for ≤0/1 vs >0/1

		READER 2		
		NEGATIVE	POSITIVE	TOTAL
READER 1				
NEGATIVE	N	739	96	835
	%	84.75	11.01	95.76
	Row %	88.75	11.25	
	Col %	98.06	82.05	
POSTIVE	N	16	21	36
	%	1.69	2.36	4.05
	Row %	41.67	58.33	
	Col %	1.94	17.95	
TOTAL	N	775	117	872
	%	86.58	13.42	100

The above table indicates that for 87.51% (760) of the films read the readers were in complete agreement about the degree of profusion. However, when analysed with the kappa statistic this results in 0.227 (CI = 0.135 – 0.318) – a low degree of agreement. Table 4.11.2.3 shows the level of agreement when the definition of positive pneumoconiosis is considered to be greater than 1/1. At this level, 862 (98.88%) of films are read in agreement, with the kappa statistic at 0.58 (CI = 0.34 – 0.81) indicating a high level of agreement for profusion scores.

Table 4.11.2.3 Respiratory health of South African Coalminers: table of agreement between readers for ≤1/1 vs > 1/1

		READER 2		
		NEGATIVE	POSITIVE	TOTAL
READER 1				
NEGATIVE	N	855	8	863
	%	98.05	0.92	98.97
	Row %	99.09	0.91	
	Col %	99.77	53.33	
POSTIVE	N	2	7	9
	%	0.23	0.80	1.03
	Row %	22.22	77.78	
	Col %	0.23	46.67	
TOTAL	N	857	15	872
	%	98.28	1.72	100

Further analysis was conducted on the actual differences in terms of the ILO scale between the two readers. Considering the movement from one ILO category to the next as being a half point change (e.g. 0/0 to 0/1 = ½ point difference; 1/1 to 1/2 = ½ point difference; 1/1 to 2/1 = 2 x ½ point difference), half point differences were calculated between the readings of each reader. Table 4.11.2.4 shows these findings.

Table 4.11.2.4 Respiratory health of South African Coalminers: Half point differences between the two readers

Half Point Difference	Frequency (%) (n = 872) (n (%))
0	629 (72.13)
1	168 (19.26)
2	71 (8.14)
3	17 (1.91)
4	3 (0.34)
5	1 (0.11)

The readers were identical in 629 (72.13%) cases, and in a further 168 (19.26%) the readers were only a half point different from each other using the ILO classification. Thus only 92 (10.35%) were read with two or more half point differences. For the more extreme readings (more than three or more than four half points), the discrepancies were reasonably close. For those read with four or more half point differences, three were read as 0/0 by one and 1/2 by the other, one was read as 2/2 by one and 0/1 by the other. The 17 with three half point differences were, in 14 cases read as 0/0 by one reader and as 1/1 by the other, the remaining three cases were 1/1 and 0/0 respectively.

4.11.3. Relationship of profusion score with Cumulative Dust Exposure

Because of the different definitions of pneumoconiosis using the profusion score (0/1; 1/0 or 1/1), and because the above analyses employ the definition 1/1, it was decided to further examine whether important differences existed between the readers for the various cumulative dust exposure levels. This was done by transforming the profusion reading into a continuous variable, and comparing the means for each reader in each CDE group. The profusion score was determined as follows:

if profusion = 0/0 then profusion score=1;
if profusion = 0/1 then profusion score=2;
if profusion = 1/0 then profusion score=3;
if profusion = 1/1 then profusion score=4;
if profusion = 1/2 then profusion score=5;
if profusion = 2/1 then profusion score=6;
if profusion = 2/2 then profusion score=7;
if profusion = 2/3 then profusion score=8;
if profusion = 3/2 then profusion score=9;
if profusion = 3/3 then profusion score=10;

Profusion scales that were not read for any films by either reader (0/- and 3/+) have not been included in the scoring. This was then analysed by looking at the mean value of profusion score for each cumulative dust exposure category stratified by reader and by current job status.

Table 4.11.3.7. Respiratory health of South African Coalminers: means of profusion scores in each cumulative dust exposure category for each reader

	CUMULATIVE DUST EXPOSURE CATEGORIES								
READER	Low 0.62–19.39 mg-years/m^3 mean score SD Range n			Medium 19.40-72.01 mg-years/m^3 mean score SD Range n			High 72.0-258.7 mg-years/m^3 mean score SD Range n		
	All	Current	Ex	All	Current	Ex	All	Current	Ex
Reader 1	1.12 0.42 1-4 284	1.07 0.28 1-3 176	1.19 0.56 1-3 108	1.17 0.48 1-4 303	1.17 0.49 1-4 229	1.19 0.49 1-3 76	1.32 1.04 1-8 303	1.31 1.00 1-8 292	1.43 1.50 1-7 14
Reader 2	1.29 0.70 1-7 286	1.19 0.48 1-3 176	1.47 0.93 1-7 108	1.30 0.71 1-5 305	1.29 0.74 1-5 229	1.30 0.60 1-3 76	1.80 1.28 1-10 305	1.78 1.25 1-10 291	2.21 1.81 1-7 14
Mean differences between readers - p value	0.01	0.001	0.06	0.01	0.03	0.23	0.01	0.001	0.23

Tests for differences between mean profusion score were statistically significantly different in the different exposure categories for each reader respectively (for all categories, p value <0.001). For both readers an increase in profusion score is seen with increasing exposure. Profusion scores were significantly correlated with exposure groups: Moderately significant correlation of profusion score with increasing exposure was seen in the assessments conducted by reader 2: (r^2 = 0 .25, 0.27 and 0.14 for all, current and ex-miner groups respectively, all p values <0.02). Assessments of Reader 1 showed significant correlation of score with exposure in the "all miners" and "current miner" categories (r^2= 0.12 and 0.13 respectively). The level of significance remained when the data was stratified by employment status. There were no statistical differences in mean scores in the ex-miner group.

8.5 Additional analyses of the pathological data

4.12.1 Levels of agreement in the pilot study

Table 4.12.1.2 shows the number of diagnoses by each reviewing pathologist (n=28).

Table 4.12.1.2 Respiratory health of South African Coalminers: number of diagnoses by each reviewer and PATHAUT

Disease	Reviewer 1	Reviewer 2	Reviewer 3	PATHAUT
Bronchitis	13	19	20	14
Macules	18	21	20	8
Nodules	7	11	11	9
Silicosis	7	11	7	10
Tuberculosis	5	5	5	4
Lung cancer	3	5	4	4
Pneumoconiosis (any)	26	26	26	18

The kappas for the three reviewing pathologists for different categories of disease as well as for each reviewing pathologist and PATHAUT (shown as a range for the 3 pathologists) are shown in Table 4.12.1.3. A kappa 0.2 indicates poor agreement, >0.2-0.4 fair agreement, >0.4-0.6 moderate agreement, >0.6-0.8 good agreement and >0.8-1 very good agreement.

Table 4.12.1.3. Respiratory health of South African Coalminers: Kappa scores for the reviewers

	Reviewer 1 vs 2	Reviewer 1 vs 3	Reviewer 2 vs 3	PATHAUT (range)
Bronchitis	0.5	0.4	0.7	0.0-1.0
Macules	0.7	0.9	0.9	0.2-0.3
Nodules	0.5	0.7	0.7	0.6-0.8
Macules and/or nodules	0.8	0.8	0.7	0.3
Silicosis	0.5	0.6	0.5	0.6
Tuberculosis	0.8	0.8	0.8	0.6-0.8
Lung cancer	0.6	0.7	0.9	0.7-0.9
Pneumoconiosis (any)	1.0	1.0	1.0	0.2

The above tables show that for 'any' pneumoconiosis the reviewing pathologists were in complete agreement, with excellent agreement with PATHAUT for higher grades of pneumoconiosis. PATHAUT pathologists called minor/trivial grades of pneumoconiosis negative. This reflects the compensation aspect of PATHAUT. Kappas for the three reviewing pathologists were good to excellent for nodules of coal workers' pneumoconiosis, and good for silicosis. The scores for the reviewing pathologists were fair to moderate for bronchitis. This reflected the different diagnostic criteria of the three reviewing pathologists.

The second review was conducted on 31 cases of pure coal mine dust exposure using the same criteria as per first review. Agreement between the consensus of the reviewing pathologists and the PATHAUT diagnosis is shown in Table 4.12.1.4.

Table 4.12.1.4 Respiratory health of South African Coalminers: agreement between reviewers for pneumoconiosis

	Pneumoconiosis		
	Present	**Trivial**	**Absent**
PATHAUT pathologists	19	0	12
Reviewing pathologists	19	12	0

The kappas for the three reviewing pathologists for different categories of disease as well as for each reviewing pathologist and PATHAUT (shown as a range for the three pathologists) are shown in Table 4.12.1.5.

Table 4.12.1.5. Respiratory health of South African Coalminers: kappa scores for reviewers for various disease outcomes

	Reviewer 1 vs 2	**Reviewer 1 vs 3**	**Reviewer 2 vs 3**	**PATHAUT (range)**
Bronchitis	0.3	0.3	0.3	-0.01-0.1
Macules	0.2	0.2	1.0	0.07-1.0
Nodules	0.5	0.7	0.7	0.5-0.8
Macules and/or nodules	1.0	1.0	1.0	0.1
Silicosis	0.6	0.9	0.5	0.5-0.9
Tuberculosis	1.0	1.0	1.0	1.0
Lung cancer	0.7	0.7	1.0	0.7-1.0
Pneumoconiosis (any)	1.0	1.0	1.0	0.1-0.2

As per the previous review, for the category “any” pneumoconiosis the reviewing pathologists were in complete agreement. There was excellent agreement with PATHAUT for higher grades of pneumoconiosis. Macules and nodules are difficult to differentiate. On PATHAUT they are combined into one category. For this combined category, there was complete agreement between the reviewing pathologists. The poor kappas with PATHAUT reflect the different criteria for minor trivial disease.

4.12.6 Logistic regression for pathological data

In order to control for all the covariates of interest within the PATHAUT dataset, logistic regression models were run for the various pathological outcomes. The exposure covariates of interest were the categories of years working in coal, categories of smoking status and race. Dummy variables were created for each of the categories and introduced into the logistic regression model. Years working in coal was introduced as a continuous variable in the models; however it showed no greater influence in the models when compared to the use of the dummy variables for dust exposures. Logistic regression models were run for the subset of cases with only coal exposure AND on whom history on years of exposure to coaldust was available (n=3167).

The following procedure was conducted for the outcomes of TB, silicosis, coalworkers’ pneumoconiosis, emphysema and cancer:

The first step was to introduce the two dummy variables for the exposure categories (medium and high compared to low), followed by the introduction of the two dummy variables for the smoking categories (ex and current compared to never smoker) and then the introduction of the race variable (black miner compared to white). Each of the models were tested for all the cases in the dataset, and subsequently only for those with exclusive coal exposure. For each model, analysis was run with and without the age variable. Only the final model, including all the variables is reported in table 4.12.6.1. Each term introduced into the model is shown with its log of the β coefficient (in a logistic regression model, this is interpretable as the odds ratio) and 95% confidence interval of this log value.

As mentioned previously, a significant percentage of the cases did not have smoking histories. As a result the above described models were refined to run without any smoking variable and subsequently only cases with smoking history. The former models were problematic in that the overwhelming majority of cases without smoking history (n=2442, 77.11%) were black miners (n=2382, 97.54%). This meant the models excluding no smoking history had to exclude the race variable. Outcomes which were seen almost exclusively in black miners also were excluded (TB and Coal Workers' Pneumoconiosis, CWP). Therefore the following procedure was adopted: For outcomes of TB and CWP, the models (n= 3167) were run excluding all smoking variables but including race. For outcomes of cancer the models (n=768) were run excluding race and those without information on smoking history. For silicosis and emphysema, because the numbers of black and white workers were equally large, both models were run. The results of the logistic regression models are shown in the main body of the text, section 4.12.6.

4.12.7 Emphysema amongst those with full or partial post-mortems

All assessments (cardiorespiratory organs only, partial and full post-mortems) conducted by the pathologists for the PATHAUT system, are graded for emphysema (absent, insignificant, moderate or marked). Because of tissue damage, when only cardiorespiratory organs are submitted for assessment, the grading of emphysema is not accurate and, in most instances, likely to be underestimated. In the latter cases, no typing of the emphysema is done. It was considered important to review those cases in which inflation of the lungs was done. This subsetting results in the exclusion of most of the cases on the database. The figure 14.12.2.1 shows the loss of cases available for analysis when subsetting of the data occurs.

Further analysis was conducted on cases in which full or partial post-mortems were conducted on those with exclusive coal exposure (n=456). Of these, 170 (37.28%) had no emphysema, 222 (48.68%) were considered insignificant, 60 (13.16%) moderate, and four (0.88%) marked grades of emphysema. Analysis for association and trend with increasing years of exposure were conducted on those on whom years of coaldust exposure was available (n=100). This latter subset consisted of 96 white and four black miners. Smoking history was absent in 15 cases. There were 21 cases (21%) with moderate and marked emphysema, all of which presented in white miners of the higher exposure groups.

Table 4.12.7.1 Respiratory health of South African Coalminers: emphysema outcomes vs categories of years of exposure to coal for exclusively coal exposed (n (% of years of coal exposure))

	YEARS OF COAL EXPOSURE CATEGORIES					
OUTCOME (n (% of total cases) n = 100	0.1 – 2.5 years (n= 4) (n (%)	2.6 - 7 years (n=5) (n (%)	7.1 – 15.9 years (n=20) (n (%)	16 - 55 Years (n=70) (n (%))	FISHER TEST P VALUE	TREND TEST P VALUE
Significant Emphysema (21 (21%))	0 (0.00)	0 (0.00)	5 (25.00)	16 (22.86)	0.72	0.35

No statistically association (p value 0.72) or trend (p value=0.35) between exposure and emphysema outcome (insignificant and absent vs moderate and marked) was seen. No significant findings were seen with smoking either.

Table 4.12.7.2 Respiratory health of South African Coalminers: emphysema outcomes vs smoking status

OUTCOME (n (% of total cases) n = 85	NEVER SMOKER (n (% of category) n=11	EX SMOKER (n (% of category) n=22	CURRENT SMOKER (n (% of category) n=58	FISHER TEST P VALUE
Significant Emphysema (20 (23.53)	2 (18.18)	4 (18.18)	14 24.14	0.80

Logistic regression on this subset (n=100) showed no statistical significance of emphysema outcomes for exposure (odds ratio point estimates reaching infinity, and confidence intervals extending from -infinity to +infinity, when compared to low exposure). Smoking terms were also not statistically significant, with odds of 1.42 (confidence interval: 0.26 – 7.62) comparing smokers to never smokers and odds of 0.97 (confidence intervals: 0.15-6.54) comparing ex-smokers to never smokers. None of these logistic regression models had a statistically significant fit (p >0.20). These findings are probably strongly influenced by the small sample size. Because of these results, further bivariate analysis was conducted, by dichotomising the exposure and smoking variables. Exposure variables were categorised as low and medium low vs medium high and high, while smoking was categorised as current and ex-smoker vs never smoker. Using this, smoking status adjusted analysis was conducted for significant emphysema outcomes against exposure. Mantel Haenszel smoking adjusted odds for emphysema outcome was 1.6 times greater in the high exposure group as compared to the low exposed groups. However, this result was not statistically significant, with confidence intervals of 0.42 – 6.12. This was expected, with many of the cells in the strata having values of 0.

8.6 Tables illustrated with graphs/figures in the main body of report

Table 4.3.1.1 Respiratory health of South African Coalminers: mean number of years worked in defined exposure category

		Employment Status	
Exposure Category	**All miners (years (SD))**	**Current miner (years (SD))**	**Ex-miner (years (SD))**
Surface	5.38 (8.38)	5.60 (8.48)	4.72 (8.05)
Backbye	2.22 (4.29)	1.97 (4.06)	2.98 (4.87)*
Coalface	8.28 (9.01)	9.83 (9.31)	3.44 (5.82)*

* = p < 0.005

Table 4.4.1.1 Respiratory health of South African Coalminers: geometric mean time weighted averages of respirable coal dust for the different sampling cycles in the different exposure zones in each mine

Cycle	**Mine 1 Mean (mg/m^3) SD n**			**Mine 2 Mean (mg/m^3) SD N**			**Mine 3 Mean (mg/m^3) SD n**		
	Face	**B/bye**	**Surface**	**Face**	**B/bye**	**Surface**	**Face**	**B/bye**	**Surface**
Round 1	0.63 3.60 34	0.26 2.20 12	0.35 3.60 2	1.11 1.68 26	0.29 3.19 17	0.04 3.13 2	1.77 3.09 30	1.60 2.03 15	1.23 3.56 5
Round 2	0.99 2.64 37	0.29 2.19 8	0.06 1.12 2	1.09 2.59 29	0.39 3.50 15	-	1.97 1.73 26	0.35 4.57 15	0.07 4.85 5
Round 3	1.24 2.80 31	1.49 1.97 10	0.63 2.48 4	1.75 1.84 28	1.70 1.95 15	0.29 2.41 4	2.01 2.03 27	0.20 2.27 11	0.03 1
Overall	0.91 3.39 102	0.48* 2.97 30	0.31 3.52 8	1.28 2.11 63	0.56* 3.71 47	0.15 3.56 6	1.90 2.23 73	0.52* 4.06 41	0.24 7.69 11

* = statistically significant differences between backbye and face, p<0.05.

Table 4.5.1.2 Respiratory health of South African Coalminers: geometric means of dust levels in mg/m^3 by mine and year

	DUST LEVELS IN EACH MINE					
	MINE 1		**MINE 2**		**MINE 3**	
	n	**(mg/m^3) (SD)**	**n**	**(mg/m^3) (SD)**	**n**	**(mg/m^3) (SD)**
1991					132	0.23 (4.87)
1992					157	0.44 (4.73)
1993	140	0.99 (4.67)			210	0.39 (5.20)
1994	220	1.07 (4.57)			166	0.61 (6.23)
1995	268	1.64 (3.72)			173	0.62 (5.75)
1996	265	1.08 (5.28)	108	1.31 (3.62)	265	0.61 (6.24)
1997	272	1.04 (4.72)	128	1.15 (3.04)	293	0.68 (5.11)
1998	262	0.43 (3.89)	163	1.08 (3.68)	61	0.38 (5.48)
1999	58	0.39 (3.89)	173	1.70 (2.48)		
2000			124	1.40 (3.50)		

Table 4.9.1.1 Respiratory health of South African Coalminers: respiratory symptoms as reported positive by current and ex-miners

		Employment Status	
Symptom	All miners (n (%)) (n=896)	Current miner (n (%)) (n=684)	Ex-miner (n (%)) (n=212)
Frequent cough	205 (22.28)	64 (9.04)	141 (63.51)*
Cough on most days for 3 months each year	162 (17.61)	38 (5.31)	124 (55.86)*
Phlegm on most days for 3 months each year	173 (18.82)	61 (8.61)	112 (50.8)*
Cough and phlegm for 3 weeks or more each year	104 (11.30)	53 (7.46)	51 (22.97)*
Severe breathlessness (breathless when dressing)	92 (10.00)	22 (3.01)	70 (31.53)*
Wheezing on most days and nights	134 (14.57)	45 (6.31)	89 (40.09)*
Using medication for wheezing	47 (5.11)	13 (1.72)	34 (15.32)*

Current miner n = 697; Ex-miner n = 222

Percentages shown are of employment status, and not total study participants

* = significant difference, $p < 0.0001$

Table 4.9.1.2 Respiratory health of South African Coalminers: respiratory symptoms as reported positive by underground and surface miners.

		Exposure Status	
Symptom	All miners (n (%)) (n=896)	Under-ground (n (%)) (n=674)	Surface (n (%)) (n=222)
Frequent cough	205 (22.28)	154 (22.85)	51 (20.73)
Cough on most days for 3 months each year	162 (17.61)	123 (18.25)	39 (15.85)
Phlegm on most days for 3 months each year	173 (18.82)	141 (20.95)	32 (13.01)*
Cough and phlegm for 3 weeks or more each year	104 (11.30)	81 (12.02)	23 (9.35)
Severe breathlessness (breathless when dressing)	92 (10.00)	70 (10.39)	22 (8.94)
Wheezing on most days and nights	134 (14.57)	104 (11.30)	30 (12.20)
Using medication for wheezing	47 (5.11)	34 (5.04)	13 (5.28)

Table 4.9.2.1 Respiratory health of South African Coalminers: association and trends for categorical outcomes vs categories of cumulative dust exposure (number (% within exposure category))

	CUMULATIVE DUST EXPOSURE CATEGORIES				
Response (n=896 (% of total respondents)	Low 0.62 – 20.10 mg years /$m^{3.}$ N = 298 (n (%))	Medium 20.11-72.77 mg years /$m^{3.}$ N = 298 (n (%))	High 72.78-258.70 mg years /$m^{3.}$ N = 300 (n (%))	Chi square p-value	Trend test p value
Usual Cough (205 (22.28))	92 (30.77)	74 (23.57)	39 (12.70)	<0.0001	<0.0001
Cough for 3 months per year (162 (17.61))	75 (25.08)	59 (18.79)	28 (9.12)	<0.0001	<0.0001
Usual wheeze (134 (14.57))	64 (21.40)	54 (17.20)	16 (5.21)	< 0.0001	<0.0001
Usual phlegm (173 (18.82))	69 (23.08)	63 (20.13)	41 (13.36)	0.007	0.001
Breathless when walking (111 (12.07)	49 (16.39)	40 (12.74)	22 (7.17)	0.002	0.0002
Breathless when dressing (92 (10))	43 (14.38)	31 (9.87)	18 (5.86)	0.002	0.0004
History of TB (27 (2.93))	8 (2.68)	8 (2.68)	11 (3.58)	0.71	0.22

Table 4.9.2.2 Respiratory health of South African Coalminers: Association and Trends for Categorical outcomes vs categories of cumulative dust exposure (number (% within exposure category)) – excluding ex-miners

	CUMULATIVE DUST EXPOSURE CATEGORIES				
Response (n=684 (% of total respondents)	Low 0.62 – 20.10 mg years /$m^{3.}$ N = 179 (n (%))	Medium 20.11-72.77 mg years /$m^{3.}$ N = 218 (n (%))	High 72.78-258.70 mg years /$m^{3.}$ N = 287 (n (%))	Chi square p-value	Trend test p value
Usual Cough (63 (9.04))	16 (9.09)	19 (8.30)	28 (9.59)	0.88	0.36
Cough for 3 months per year (37 (5.31))	6 (3.41)	12 (5.24)	19 (6.51)	0.35	0.08
Usual wheeze (44 (6.31))	11 (6.25)	21 (9.17)	12 (4.11)	0.06	0.05
Usual phlegm (60 (8.61))	8 (4.55)	22 (9.61)	30 (10.27)	0.04	0.04
Breathless when walking (28 (4.02))	9 (5.11)	6 (2.62)	13 (4.45)	0.40	0.43
Breathless when dressing (21 (3.01))	8 (4.55)	3 (1.31)	10 (3.42)	0.47	0.14
History of TB (18 (2.58))	2 (1.14)	5 (2.18)	11 (3.77)	0.20	0.04

Table 4.9.2.3 Respiratory health of South African Coalminers: association and trends for categorical outcomes vs categories of cumulative dust exposure (number (% within exposure category)) –ex-miners only

	CUMULATIVE DUST EXPOSURE CATEGORIES				
Response (n=212 (% of total respondents)	Low 0.62 – 20.10 mg years /$m^{3.}$ N = 119 (n (%))	Medium 20.11-72.77 mg years /$m^{3.}$ N = 80 (n (%))	High 72.78-258.70 mg years /$m^{3.}$ N = 13 (n (%))	Chi square p-value	Trend test p value
Usual Cough (142 (62.68))	76 (61.79)	55 (64.71)	11 (73.33)	0.66	0.18
Cough for 3 months per year (125 (56.05))	69 (56.10)	47 (55.29)	9 (60.00)	0.94	0.41
Usual wheeze (90 (40.36))	53 (43.09)	33 (38.82)	4 (26.67)	0.44	0.10
Usual phlegm (113 (50.09))	61 (49.59)	41 (48.81)	11 (73.33)	0.20	0.07
Breathless when walking (83 (37.22)	40 (32.52)	34 (40.00)	9 (60.00)	0.09	0.01
Breathless when dressing (71 (31.84))	35 (28.46)	28 (32.94)	8 (53.33)	0.14	0.03
History of TB (9 (4.04))	6 (4.88)	3 (3.53)	0 (0.00)	0.63	0.17

Table 4.9.3.1 Respiratory health of South African Coalminers: association and trends for categorical outcomes vs categories of smoking status (number (% within response))

Response (n=896)	**Smoker n=397**	**Ex smoker n=147**	**Never smoker n=352**	**Chi Square p value**
Usual Cough (205 (22.28))	126 (31.66)	31 (21.09)	48 (12.80)	< 0.0001
Cough for 3 months per year (162 (17.61))	102 (25.63)	24 (16.33)	36 (9.60)	<0.0001
Usual wheeze (134 (14.57))	91 (22.86)	18 (12.24)	25 (6.67)	<0.0001
Usual phlegm (173 (18.82))	105 (26.45))	29 (19.73)	39 (10.40)	<0.0001
Breathless when walking (111 (12.07))	67 (16.83)	18 (12.24)	26 (6.93)	<0.0001
Breathless when dressing (92 (10))	60 (15.08)	12 (8.16))	20 (5.33)	<0.0001
History of TB (27 (2.93))	12 (3.02)	7 (4.76)	8 (2.13)	0.23

Table 4.9.4.1 Respiratory health of South African Coalminers: association and trends for categories of packyears (entire dataset)

	CATEGORIES OF PACKYEARS						
RESPONSE (n (% of total respondents)) (n=896)	No Smoking (n=352) (n (%))	Low (n=180) (n (%))	Medium (n=182) (n (%))	High (n=182) (n (%))	CHI SQUARE P-VALUE	TREND TEST P VALUE	TREND EXCLUD-ING NO PACK YEAR
Usual Cough (205 (22.31))	48 (12.80)	42 (23.33)	53 (29.12)	62 (34.07)	0.0001	0.0001	0.01
Cough for 3 months per year (162 (17.61))	36 (9.60)	33 (18.33)	44 (24.18)	49 (26.92)	0.0001	0.0001	0.03
Usual wheeze (134 (14.58))	25 (6.67)	29 (16.11)	35 (19.23)	45 (24.73)	0.0001	0.0001	0.02
Usual phlegm (173 (18.85))	39 (10.41)	36 (20.11)	43 (23.63)	55 (30.22)	0.0001	0.0001	0.01
Breathless when walking (111 (12.08))	26 (6.93)	25 (13.89)	31 (17.03)	29 (15.93)	0.0008	0.001	0.33
Breathless when dressing (92 (10.01))	20 (5.33)	18 (10.00)	29 (15.93)	25 (13.74)	0.0003	0.0004	0.21
History of TB (27 (2.94))	8 (2.13)	7 (3.89)	5 (2.75)	7 (3.85)	0.57	0.18	0.46

Midpoints of pack year categories used for trend tests (low = 1.6 pack years; medium = 5.3 pack years and high = 12 pack years)

Table 4.10.1.1 Respiratory health of South African Coalminers: lung function means for categories of cumulative dust exposure for the full dataset

	CUMULATIVE DUST EXPOSURE CATEGORIES		
	Low 0.62 – 20.10 mg/m$^{3\cdot}$years n = 278 (mean (SD))	Medium 20.11-72.77 mg/m$^{3\cdot}$years n = 285 (mean (SD))	High 72.78-258.70 mg/m$^{3\cdot}$years n = 294 (mean (SD))
FEV$_1$ (L (SD))	3.41 (0.75)	3.47 (0.72)	3.23 (0.64)
FEV$_1$ % Predicted (% (SD)	103.67 (18.80)	107.50 (18.59)	102.16 (17.27)
FVC (L (SD))	4.16 (0.83)	4.29 (0.76)	4.00 (0.71)
FVC % predicted (% (SD))	102.22 (16.71)	106.53 (15.54)	100.76 (15.38)
Ratio (% (SD))	81.43 (7.75)	80.37 (8.73)	79.68 (7.58)

Table 4.10.1.3 Respiratory health of South African Coalminers: actual lung function means and % predicted for categories of cumulative dust exposure stratified by employment status

	Employment Status					
	Current Miner (n = 670)			Ex Miner (n=187)		
	CDE Categories			CDE Categories		
	Low 0.62 – 20.10 mg-years/m^3 n = 174 (mean (SD))	Medium 20.11-72.77 mg-years/m^3 n = 214 (mean (SD))	High 72.78-258.70 mg-years/m^3 n = 282 (mean (SD))	Low 0.62 – 20.10 mg-years/m^3 n = 104 (mean (SD))	Medium 20.10-72.77 mg-years/m^3 n = 72 (mean (SD))	High 72.78-258.70 mg-years/m^3 n = 11 (mean (SD))
FEV$_1$ (L (SD))	3.39 (0.76)	3.57 (0.65)	3.25 (0.63)	3.44 (0.75)	3.19 (0.86)	2.89 (0.83)
FEV$_1$ % predicted (% (SD))	103.97 (18.63)	109.19 (17.06)	102.44 (17.03)	103.19 (19.18)	102.51 (21.86)	95.52 (21.96)
FVC (L (SD))	4.13 (0.86)	4.36 (0.70)	4.03 (0.69)	4.20 (0.79)	4.03 (0.89)	3.54 (0.91)
FVC % predicted (% (SD))	102.29 (16.92)	107.66 (14.88)	101.10 (15.07)	102.11 (16.45)	103.18 (17.03)	92.82 (20.64)
Ratio (% predicted)	81.71 (7.23)	81.27 (7.25)	79.71 (7.45)	80.97 (8.57)	77.72 (11.76)	79.00 (10.66)

Table 4.10.1.4 Respiratory health of South African Coalminers: lung function percent predicted FEV$_1$ and FVC stratified on exposure

	EXPOSURE STATUS	
	Underground (n=649)	Surface (n=208)
FEV$_1$ % Predicted (% (SD)	105.14 (17.98)	102.21 (19.29)*
FVC % predicted (% (SD))	104.14 (15.61)	100.09 (17.01)*

Table 4.10.2.1 Respiratory health of South African Coalminers: smoking status vs lung function outcomes (mean (standard deviation))

	SMOKER n=379	**EX-SMOKER n=141**	**NON SMOKER n=337**
FEV$_1$ (L (SD))	3.41 (0.72)	3.21 (0.75)	3.39 (0.67)
FEV$_1$ % predicted (SD)	104.92 (18.13)	101.05 (21.07)	105.28 (17.20)
FVC (L (SD))	4.23 (0.76)	4.00	4.11 (0.76)
FVC % predicted (SD)	105.10 (15.41)	100.44 (18.41)	102.10 (15.46)

Table 4.11.3.1 Respiratory health of South African Coalminers: association and trends for radiological outcomes vs categories of cumulative dust exposure (number (% within exposure group)) – reader 1

	CUMULATIVE DUST EXPOSURE CATEGORIES				
Response (n=872 (% of all films)	Low 0.62 – 20.10 mg years /m$^{3.}$ N = 283 (n (%))	Medium 20.11-72.77 mg years /m$^{3.}$ N = 290 (n (%))	High 72.78-258.70 mg years /m$^{3.}$ N = 299 (n (%))	Chi square p-value	Trend test p value
Radiological evidence of TB (33 (3.71))	11 (3.87)	11 (3.63)	11 (3.63)	0.98	0.44
Pneumoconiosis (17 (1.91))	2 (0.70)	2 (0.66)	13 (4.29)	<0.0007	<0.0001

Table 4.11.3.2. Respiratory health of South African Coalminers: Association and Trends for radiological outcomes vs categories of cumulative dust exposure (number (% within exposure group)) – Reader 2

	CUMULATIVE DUST EXPOSURE CATEGORIES				
Response (n=872 (% of all films)	Low 0.62 – 20.10 mg years /m$^{3.}$ N = 283 (n (%))	Medium 20.11-72.77 mg years /m$^{3.}$ N = 290 (n (%))	High 72.78-258.70 mg years /m$^{3.}$ N = 299 (n (%))	Chi square p-value	Trend test p value
Radiological evidence of TB (49 (5.57))	22 (7.69)	14 (4.59)	13 (4.26)	0.13	0.06
Pneumoconiosis (38 (4.12))	3 (1.03)	7 (2.23)	28 (9.12)	<0.001	<0.001
Radiological evidence of emphysema (217 (24.22))	66 (23.08)	74 (22.26)	77 (25.25)	0.83	0.28

Table 4.11.3.3 Respiratory health of South African Coalminers: association and trends for radiological outcomes vs categories of cumulative dust exposure (number (% within exposure group)) – current miners only - reader 1

	CUMULATIVE DUST EXPOSURE CATEGORIES				
Response (n=684 (% of all films)	Low 0.62 – 20.10 mg years /m$^{3.}$ N = 179 (n (%))	Medium 20.11-72.77 mg years /m$^{3.}$ N = 218 (n (%))	High 72.78-258.70 mg years /m$^{3.}$ N = 287 (n (%))	Chi square p-value	Trend test p value
Radiological evidence of TB (24 (3.46))	5 (2.84)	9 (3.96)	10 (1.44)	0.83	0.45
Pneumoconiosis (14 (2.02))	0 (0.00)	2 (0.88)	12 (4.14)	0.002*	0.0003

*** Fishers Exact test, because cells have values < 5.**

Table 4.11.3.4 Respiratory health of South African Coalminers: association and trends for radiological outcomes vs categories of cumulative dust exposure (number (% within exposure group)) – current miners only - reader 2

	CUMULATIVE DUST EXPOSURE CATEGORIES				
Response (n=684 (% of all films)	Low 0.62 – 20.10 mg/m$^{3.}$years N = 179 (n (%))	Medium 20.11-72.77 mg/m$^{3.}$years N = 218 (n (%))	High 72.02-258.70 mg/m$^{3.}$years N = 287 (n (%))	Chi square p-value	Trend test p value
Radiological evidence of TB (42 (6.03))	17 (9.66)	12 (5.24)	13 (4.47)	0.06	0.03
Pneumoconiosis (32 (4.59))	0 (0.00)	7 (3.06)	25 (8.56)	<0.001	<0.001
Radiological evidence of emphysema (168 (24.14))	41 (23.40)	54 (23.58)	73 (25.09)	0.88	0.31

Table 4.11.3.5 Respiratory health of South African Coalminers: association and trends for radiological outcomes vs categories of cumulative dust exposure (number (% within exposure group)) – ex miners only - reader 1

	CUMULATIVE DUST EXPOSURE CATEGORIES				
Response (n= 188 (% of all films)	Low 0.62 – 20.10 mg/m$^{3.}$years N = 104 (n (%))	Medium 20.11-72.77 mg/m$^{3.}$years N = 72 (n (%))	High 72.02-258.70 mg/m$^{3.}$years N = 12 (n (%))	Chi square p-value	Trend test p value
Radiological evidence of TB (9 (4.57))	6 (5.56)	2 (2.63)	1 (7.69)	0.37*	0.50
Pneumoconiosis (3 (1.52))	2 (1.85)	0 (0.00)	1 (7.69)	0.16*	0.14

Table 4.11.3.6 Respiratory health of South African Coalminers: association and trends for radiological outcomes vs categories of cumulative dust exposure (number (% within exposure group)) – ex miners only - reader 2

	CUMULATIVE DUST EXPOSURE CATEGORIES				
Response (n= 188 (% of all films)	Low 0.62 – 20.10 mg/m$^{3.}$years n = 104 (n (%))	Medium 20.11-72.77 mg/m$^{3.}$years n = 72 (n (%))	High 72.02-258.70 mg/m$^{3.}$years n = 12 (n (%))	Fisher's test p-value	Trend test p value
Radiological evidence of TB (7 (3.54))	5 (4.63)	2 (2.63)	0 (0.00)	0.15*	0.16
Pneumoconiosis (6 (2.69))	3 (2.44)	0 (0.00)	3 (20.00)	<0.0001	<0.001
Radiological evidence of emphysema (48 (24.24))	24 (22.22)	20 (26.32)	4 (28.57)	0.76	0.25

Table 4.11.4.1 Respiratory health of South African Coalminers: means of lung function outcomes vs pneumoconiosis status for each reader

	Reader 1			**Reader 2**		
	Profusion ≥ 1/1 (n=17) mean (SD)	Profusion < 1/1 (n=840) mean (SD)	T test P value	Profusion ≥ 1/1 (n=36) mean (SD)	Profusion < 1/1 (n=821) mean (SD)	T test P value
% Predicted FEV_1	94.52 (15.81)	104.63 (18.33)	0.02	101.73 (16.98)	104.55 (18.39)	0.44
% Predicted FVC	82.55 (9.58)	90.08 (13.97)	0.03	86.56 (11.51)	90.08 (14.02)	0.19

Table 4.12.3.1 Respiratory health of South African Coalminers: autopsy outcomes vs categories of years of exposure to coal for full dataset (coal and mixed dust exposure) (n (% of years of coal exposure)

	YEARS OF COAL EXPOSURE CATEGORIES					
Outcome (n (% of total cases) N = 5713	0.1 – 1.6 years (n=1457) (n (%)	1.7 - 5 years (n=1487) (n (%)	5.1 – 13 years (n=1379) (n (%)	13.1 - 55 years (n=1390) (n (%)	Chi square p value	Trend test p value
TB (290 (5.08%)	74 (5.08)	82 (5.51)	75 (5.44)	59 (4.24)	0.40	0.09
CWP (298 (5.32)	13 (0.89)	26 (1.75)	79 (5.73)	181 (13.02)	<0.0001	<0.001
Silicosis (1228 (21.45)	374 (25.67)	285 (19.17)	259 (18.78)	310 (22.30)	0.0001	0.19
Emphysema (2119 (37.17)	443 (30.40)	400 (26.90)	475 (34.45)	801 (57.63)	<0.0001	<0.001
Cancer (184 (3.23))	39 (2.68)	35 (2.35)	36 (2.61)	74 (5.32)	<0.0001	0.001
Mesothelioma (10 (0.18))	1 (0.07)	4 (0.27)	1 (0.07)	4 (0.29)	0.34*	0.17

* Fisher's exact test used because cells less than 5 contained in 4x2 table.

Table 4.12.3.3 Respiratory health of South African Coalminers: autopsy outcomes vs categories of years of exposure to coal for exclusively coal exposed (n (% of years of coal exposure)

	YEARS OF COAL EXPOSURE CATEGORIES					
OUTCOME (n (% of total cases) n = 3166	0.1 – 2.5 years (n= 786) (n (%)	2.6 - 7 years (n=783) (n (%)	7.1 – 15.9 years (n=801) (n (%)	16 - 55 Years (n=795) (n (%))	CHI SQUARE P VALUE	TREND TEST P VALUE
TB (165 (5.21))	45 (5.73)	40 (5.11)	43 (5.37)	37 (4.65)	0.81	0.20
CWP (230 (7.37))	16 (2.04)	19 (2.43)	71 (8.86)	124 (15.60)	<0.0001	<0.0001
Silicosis (344 (10.86))	44 (5.60)	62 (7.92)	97 (12.11)	141 (17.74)	<0.0001	<0.0001
Emphysema (982 (31.33))	98 (12.47)	124 (15.84)	273 (34.08)	487 (61.26)	<0.0001	<0.0001
Emphysema (moderate and marked vs insignificant and absent) (204 (6.45))	6 (0.76)	20 (2.55)	51 (6.37)	127 (15.97)	<0.0001	<0.0001
Cancer (70 (2.24))	2 (0.25)	4 (0.51)	24 (3.00)	40 (5.03)	<0.0001	<0.0001
Mesothelioma (5 (0.16)	0 (0.00)	1 (0.13)	1 (0.12)	3 (0.38)	0.33*	0.03

Table 4.12.3.5 Respiratory health of South African Coalminers: means years of exposure for different grades of emphysema.

EMPHYSEMA GRADE (n = 3167 (%))	Mean	SD
Absent (2220 (70.10))	7.85	8.74
Insignificant (700 (22.10))	16.87	12.96
Moderate (228 (7.20))	21.84	12.80
Marked (19 0.(60))	25.82	12.17

Table 4.12.4.1 Respiratory health of South African Coalminers: autopsy outcomes vs smoking status

OUTCOME (n (% of total cases) n = 2411	NEVER SMOKER (n (% of outcome) n=272	EX SMOKER (n (% of outcome) n=628	CURRENT SMOKER (n (% of outcome) n=1511	CHI SQUARE P VALUE
TB (60 (2.49))	12 (4.41)	21 (3.34)	27 (1.79)	0.014
Silicosis (762 (31.61)))	96 (35.29)	266 (42.36)	400 (26.47)	<0.0001
CWP (76 (3.15))	7 (2.57)	25 (3.98)	44 (2.91)	0.37
Emphysema (1324 (54.91))	92 (33.82)	384 (61.15)	848 (56.12)	<0.0001
Significant Emphysema (421 (17.46))	13 (4.78)	137 (21.82)	271 (17.94)	<0.0001
Cancer (129 (5.35))	4 (1.47)	35 (5.57)	90 (5.96)	0.01

Table 4.12.5.1 Respiratory health of South African Coalminers: differences in pathological outcomes between race groups (full dataset)

OUTCOME (n=7739) (n (% of total)	BLACK (N=5132) (% of outcome)	WHITE (N=2607) (% of outcome)	Chi Square p value	Relative Risk (95% Conf Intervals)
TB (410 (5.30))	348 (6.78)	62 (2.38)	<0.0001	2.85 (2.19-3.72)
Silicosis (1421 (18.36))	623 (12.14)	798 (30.61)	<0.0001	0.4 (0.36-0.43)
CWP (419 (5.41))	344 (6.70)	75 (2.88)	<0.0001	2.33 (1.92-2.98)
Emphysema (2613 (33.76)	1191 (23.21)	1422 (54.55)	<0.0001	0.43 (0.40-0.45)
Significant Emphysema (598 (7.73))	146 (2.84)	452 (17.34)	<0.0001	0.16 (0.14-0.20)
Cancer (206 (2.66))	67 (1.31)	139 (5.33)	<0.0001	0.24 (0.18-0.32)

Table 4.12.5.2 Respiratory health of South African Coalminers: differences in pathological outcomes between race groups (coal exposure only)

OUTCOME (n=5060) (n (% of total)	BLACK (N=4149) (% of outcome)	WHITE (N=911) (% of outcome)	Chi Square p value	Relative Risk (95% Conf Intervals)
TB (279 (5.51))	270 (6.51)	9 (0.99)	<0.0001	6.59 (3.40 – 12.74)
Silicosis (518 (10.24))	404 (9.74)	114 (12.51)	0.01	0.78 (0.64 – 0.94)
CWP (350 (6.92))	301 (7.25)	49 (5.38)	0.04	1.35 (1.00 – 1.81)
Emphysema (1428 (28.22))	977 (23.55)	451 (49.51)	<0.0001	0.47 (0.43 – 0.52)
Significant Emphysema (263 (5.50))	122 (2.94)	141 (15.98)	<0.0001	0.19 (0.15 - 0.24)
Cancer (92 (1.82))	53 (1.28)	39 (4.28)	<0.0001	0.30 (0.20 – 0.45)