SILICOSIS PULMONARY DYSFUNCTION AND RESPIRATORY SYMPTOMS IN SOUTH AFRICAN GOLD MINERS

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ABSTRACT

A working population of black South African gold miners on the Orange Free State goldfields was studied.

The overall prevalence of silicosis was found to be 1.4%, rising to 15% in the 51 to 55 year old age group.

Silicosis in this population is the chronic or simple variety which nevertheless accounts for significant reductions of the forced expiratory volumes and flow rates and lung diffusion. Dyspnoea is more prevalent in the men with silicosis.

Silicosis apart, exposure to mine dust and the other components of the underground environment is also associated with lung dysfunction. The changes attributable to occupational exposure are of the obstructive variety with reductions of the FEV1, MMEF and the FEV1/FVC% similar in pattern and extent to those caused by smoking.

Cough and sputum production are common and, apart from that attributable to smoking, are associated with working environments which exposed the men to the highest and the intermediate levels of dust intensity.

A limited follow-up study of the 1 197 men who participated in the main, cross-sectional study, shows that men with silicosis have a higher incidence of pulmonary tuberculosis than men without silicosis and that the incidence rises with the extent of the silicosis.

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Mr Salmon Mabena conducted every respiratory interview and performed all of the lung function tests. His mastery of language and his astonishing patience were qualities which made this study possible.

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PREFACE

The purpose of this study is to examine the influence of silicosis and the occupation of gold mining on respiratory symptoms, lung function and tuberculosis in a working population of black, migrant, South African gold miners. No previous study has examined a working population of these men.

CHAPTER 1

HISTORICAL BACKGROUND

At the time of the Roman Empire the miner was viewed as a "creature half-way between man and beast, who suffered greatly while he lived and anyway lived but a short time" [1]. Gordon, in his excellent review of the history of mining, continues with a description of the furnace-like atmosphere where in the already hot ambient temperatures, fires were used to split the rock. Men, infested with hookworm, were lashed and suffered from repeated trauma. Gordon [1] writes "I would think it miraculous if any (miners) lived long enough to develop silicosis", but with most of the mines constantly flooded and without mechanisation it is unlikely that dust was a problem.

In the 10th century a disease of miners was recognised and called "bergsucht" which Gordon believes to have encompassed an array of disorders including silicosis, mercurial or arsenical poisoning, hookworm infestation and pulmonary neoplasms. Bergsucht was then considered to be caused by demons and it was not until the 16th century that Agricola in his "De Re Metallica" attributed the high mortality of miners to the dust to which they were exposed. Agricola reported that in the mining areas there were women who had been widowed as often as seven times when their miner husbands died prematurely from 'consumption'.

The risks to the miner increased when gunpowder was introduced to the mines in 1627 and a rudimentary drilling machine was put into use in 1636.

In the 19th century mining conditions remained primitive and miners were subjected to appalling work conditions, exploitation, poverty and misery [2]. It seems, however that the contemporary concern about mining focused upon the fact that children working in the mines, who were often less than 10 years old, were not receiving any religious education and upon the moral issue that men and women were working together in near nakedness [1].

In the latter half of the 19th century the concern was with the early deaths of miners. Gordon refers to the period of 1850 to 1920 as the "siliceous holocaust".

The mines in the Transvaal Republic in southern Africa the mining industry in South Africa and farther afield. Silicosis with or without tuberculosis became a compensable disease and this applied to career miners and to the migrant black labourers who worked on the mines for short contract periods [4].

The Act required that men recruited to work on the mines must be of sound physique as established by examination by a medical practitioner [7].

In 1916, new regulations were promulgated as a result of the report of the Commission of Inquiry which had been established in 1912. The Miners' Phthisis Medical Bureau was established and has to this day, as the Medical Bureau for Occupational Diseases, continued to examine every white miner before employment and periodically thereafter [4,7]. Black men working on the mines were also to be examined but their examinations would be conducted by the mine medical officers employed by each of the mining groups [8]. At that time there were approximately 15 000 white and 175 000 black men employed by the industry.

The white miners employed for the first time after the introduction of the new conditions in 1916 were required to be of better than average physique. These men were to be known as the *new Rand miners* and their course was to be followed with interest [4].

Conditions in the mines began to improve: all new mines were required to have adequate ventilation and, there was progressive replacement of dry- with wet-drilling. By 1926, drilling with the few remaining drills which did not incorporate axial water feed was banned [4]. In 1927, Watkins-Pitchford [7], the Director of the Miners' Phthisis Medical Bureau, reported a progressive fall in the incidence of silicosis and a lengthening of time from first exposure to the development of the disease. He estimated the overall prevalence of silicosis to be 3%, with 7% of those who had worked 10 or more years having the disease. The duration of service to onset of silicosis had increased from an average 9 years in 1917 to 10.25 years in 1923.

It was noted from the excellent records which had been collected of the whole *white* working population, that within 7 years of being diagnosed as having silicosis, 54% had developed tuberculosis and half of those had died [7].

At the time of these developments in South Africa, McFarland [9] reported in 1927 that the annual mortality rate from tuberculosis in Vermont granite cutters was 1095.5 per 100 000 workers compared with a rate of 96 per 100 000 of the general, adult population. He noted that the State was considering making silicosis a compensable disease in the granite industry (fifteen years after silicosis became a compensable disease in South Africa).

Since 1912, conditions on the South African gold mines had been under the scrutiny of the Miners' Phthisis Prevention Committee which included representatives of the

State, the miners and the industry. This body and its successors played a role in the progressive improvement of the conditions in the gold mines. Dust levels had, by the mid-1930s, reached levels which are considered to be acceptable today [10]. By contrast, the situation for miners in Europe remained poor until extensive reforms in conditions of service and of dust control were introduced in the late 1950s [11] .

Although it is no longer generally associated with silicosis, tuberculosis is still highly prevalent amongst the majority of mineworkers 100 years after the start of the industry in South Africa. The surveillance of the white miners continues on the basis of excellent and far-sighted laws first introduced 75 years ago. No consistent evaluation of the 500 000 black mine workers exists. These men continue to receive compensation for silicosis and for thoracic tuberculosis but no central record exists of the exposure and health status of the men who constitute 90% of the work force on the South African gold mines.

CHAPTER 2

REVIEW OF PREVIOUS STUDIES

It is necessary to review some of the earlier work on silicosis in order to fully appreciate the modern perspective of disease associated with environmental exposures in gold mines. This review should serve to emphasise the many and substantial differences between the risks to gold miners in the early part of this century and those risks which prevail in the modern gold mine. Silicosis itself is not the same disease which afflicted our miners 60 years ago.

2.1 THE SOUTH AFRICAN ROLE IN CONTROL OF SILICOSIS

The South African role in the early control and research in the field of occupational lung disease in miners was emphasised in 1963 by Lanza who wrote "Modern research into silicosis stemming from the brilliant program maintained by the Government of the Union of South Africa emphasized the importance of silicosis and led to continued research in ... other countries". [12] In this paper Lanza makes the point that much of our knowledge on the subject could be attributed to legislation by the South

African Government which was remarkable for its time. This view is also presented by Watkins-Pitchford, one of the pioneers of silicosis research in South Africa [7]. The role of the State in silicosis and other mining-associated disorders has been widely and generally acknowledged [9,13,14,15,16].

The South African legislation not only established sets of standards for mining but resulted in the establishment and maintenance of a body of data based on a working population. The relevance of a population rather than a clinical study base is often not appreciated even today. Wright [17] in his 1949 paper writes "The physician or laboratory who receive only ill patients will think of silicosis as a universally crippling disease. A study of all silicotics in a given plant will show in contrast that most have been free of any serious complaints for many years". Thus, the South African Miners' Phthisis Bureau experience with its mandate to examine all white miners before, throughout and even after their mining careers might represent one of the first population-based studies. Watkins-Pitchford's landmark 1927 paper [7] is a striking contrast to the contemporary medical writings and even to the majority in the field of occupational health for the next 30 years. In his paper, cases of disease are presented against a denominator of 'non-cases' and he provides a perspective of degrees of disease which is not possible in the clinical case series which generally prevailed.

2.2 DETERMINANTS OF SILICOSIS

The role of free, crystalline silica in the development of silicosis has long been recognised and accepted. Some enthusiasm for sericite [16,18] enjoyed a limited vogue and Cummins, while favouring sericite, wondered about a role for silicates. He warned that because the work on the Witwatersrand was so well organised there was "perhaps a danger of applying too confidently the Johannesburg findings to allied problems elsewhere". As noted earlier, Watkins-Pitchford and Irvine [3,7] had recognised the importance of the small silica particles from their studies of lungs obtained from the autopsies which were routinely performed on men who died during or after service on the gold mines.

The importance of the intensity and the duration of exposure to silica-containing dust was also recognised by the early South African investigators. In their 1912 paper, Irvine and Watt write that black mine workers working directly at the rock face may develop silicosis within 2 years of service [6]. It was also appreciated that a measure of improved dust control was the progressive lengthening of duration of exposure before the development of disease.

The fourth factor, after particle size, duration and intensity of dust exposure, which determines the prevalence and severity of silicosis concerns the proportion of free silica as quartz in the respirable fraction of the dust [19,20]. The quartz in the Witwatersrand mines contains 90-96% free silica and the conglomerate 86% free silica according to data from Watkins-Pitchford [7]. Current data appears to indicate uncertainty as to the amount of free silica in respirable dust; Sluis-Cremer states that it is 30% [21] and Wiles 75% [22]. The threshold limit value (TLV) of respirable dust is adjusted according to the amount of free silica as quartz in the dust [23] and, in general, high quartz levels have to be compensated for by decreasing the general dust levels by increased ventilation.

There is little modern evidence to support the belief of the Miners' Phthisis Medical Commission [6] that "the risk of contracting silicosis is in inverse ratio to a man's respiratory capacity". On the contrary, the fittest men do the dustiest work [24] and are therefore more liable to develop silicosis. It is also reasonable to believe that the men who do the most physical work breathe the most and will thus have a higher than average lung dust load.

Individual susceptibility to the development of silicosis has been suggested [25]. In general, quartz loads in the lungs correlate with the degree of fibrosis [26,27] but studies from Finland have demonstrated an association of silicosis with HLA Aw19 and with haplotype AW19,B18 [28].

2.3 TYPES OF SILICOSIS

Unlike many others at the time, clear and separate identities for silicosis and tuberculosis were not questioned by Irvine, Watt or Watkins-Pitchford although Watkins-Pitchford believed that, in the majority of cases, tuberculosis played a role in the development of silicosis by interfering with the capacity of the lungs to incarcerate the dust [7].

The concept that silicosis without tuberculosis could represent different syndromes was, however, not generally recognised. Gardner [29] described some features of the different syndromes without identifying them. He referred to early silicosis as having a diffuse radiological opacification and that with continued exposure the disease became associated with a nodular opacification. These patterns are now well described [19] with acute silicosis from intense exposure presenting with severe disease within 2 to 5 years with a diffuse, ground-glass radiographic opacification which is generally less striking than that of nodular silicosis [30]. Accelerated silicosis develops after 5 to 15 years of moderately heavy silica-dust exposure and presents a nodular opacification on the chest radiograph. The nodules tend to be more evenly distributed than in chronic silicosis which develops after 20 and often 30 or 40 years of modest exposure and has predominantly upper zone nodulation [19].

The consequences of these diseases are very different. That chronic or simple silicosis is a benign condition was recognised by Watkins-Pitchford who considered it to hardly be a disease unless there was a great profusion of nodules [7]. Riddell writing in 1934 considered that silicosis without tuberculosis was "rarely associated with any ... demonstrable disability" and even advised against withdrawing men, other than the young, from further exposure [31], a view that Reid [32] repeated in 1945. Wright [17] observed "that most (silicotics) have been free of any serious complaints for many years". Lanza [12] refers to the tragedy of silicosis being tuberculosis without which it will rarely lead to death, an opinion expressed several years earlier by Hamlin [33]. In 1969, Webster stated that silicosis had not been a direct cause of death for many years [34]. In 1975, Wiles, also referring to South African gold miners, wrote, "it is now seldom a serious condition" [35] and in 1981, Becklake, referring to the disease in Canada, writes that it has little impact on health or survival [36].

By contrast, acute silicosis, which was prevalent in the South African gold mines prior to 1912 [37] and which has subsequently been described in non-mining industries [30,38,39,40], is a universally lethal disease. Those who survive the associated respiratory dysfunction invariably develop mycobacterial infection or connective tissue disorders [19].

Accelerated silicosis is an intermediate form of silicosis which shares the properties of acute silicosis at its one extreme and of chronic silicosis at the other. The longer the exposure before the disease develops the less serious are the consequences. This disorder was predicted for sandblasters by Pancoast and Pendergrass in 1926 [13] but nevertheless, that occupation resulted in an outbreak of accelerated silicosis in the 1970's [41]. Accelerated silicosis was still prevalent in Europe in the 1940s and 1950s in miners and tunnellers [11,42] and was reported in 1971 in Yugoslavia [43] and as recently as 1985 in slate pencil workers in India [44,45]. Mycobacterial infections and connective tissue disorders commonly intervene in accelerated silicosis following short periods of exposure to high intensities of dust with a high proportion of free silica. [19,41,46].

2.4 SILICOSIS AND TUBERCULOSIS

Silicosis and pulmonary tuberculosis have been so closely associated that it is difficult to establish their separate identities in the majority of published reports on disease in gold miners prior to 1940.

The first allusion to the association is said to have been Hippocrates' but is more usually credited to Georgius Agricola in the 16th century. It is certain that even until the 1930's, many workers in the field of silicosis research believed that tuberculosis was a necessary component of silicosis. Watkins-Pitchford believed that "in the very great majority" of instances, the appearance of the disease silicosis was determined by tuberculosis and not by the over-abundance of dust [7]. South Africans, Simson and Strachan were the first to clearly separate the two diseases [47].

The majority of men with silicosis eventually died of or with tuberculosis [7,13,14,29,39].

2.4.1 Silico-tuberculosis, tuberculosilicosis, silicosis and tuberculosis

The already complex relationship between tuberculosis and silicosis has been further complicated by the inconsistent definitions of disease. The distinctions drawn between silico-tuberculosis, tuberculosilicosis and silicosis with tuberculosis have been clearly but differently defined in different publications. To each has been attributed the characteristic of having consistently negative bacteriology for tuberculosis [14,48,49]. Watkins-Pitchford defined 2 types of disease [7]. The first was simple silicosis which was distinguished by a nodular fibrosis and which had little adverse effect on the health of the miner. The second variety was silicosis with tuberculosis or infective silicosis. Infective silicosis had two subdivisions, tuberculo-silicosis which was tuberculosis developing in a silicotic lung and silico-tuberculosis which was pulmonary tuberculosis with some developing silicosis. Tuberculo-silicosis was commonly seen in the white miners while silico-tuberculosis more commonly occurred in the black miner and was characterised by large, asymmetrical nodules with young connective tissue in which *Mycobacterium tuberculosis* could often be seen. Other authors have used silico-tuberculosis and tuberculo-silicosis quite differently. For example, Schepers [14] considers tuberculo-silicosis to be a florid form of tuberculosis which develops when men with a primary tuberculous complex are exposed to silica dust and silico-tuberculosis to be caused when tuberculosis is acquired after dust exposure. Silico-tuberculosis as Schepers describes the disease, has tenuous connections with tuberculosis being frequently associated with a negative tuberculin test and usually with sputum negative for *Mycobacterium tuberculosis*.

Although it was widely used, the term "miners' phthisis" was considered by Watkins-Pitchford to be ill-defined and confusing. Phthisis, meaning wasting, might, he believed, be best used to describe silicosis and tuberculosis and would thus be synonymous with infective silicosis and the other combination terms [7].

2.4.2 <u>The bacteriology of tuberculosis and silicosis</u>

It was generally accepted that the diagnosis of tuberculosis with silicosis could be extremely difficult to establish. Sputum was often not shown to contain *Mycobacterium tuberculosis* [17,48,49]. The conventional wisdom, which has obscure origins, held that the mycobacteria infecting men with silicosis were lacking in virulence and were not readily transmitted to the families of the men with both tuberculosis and silicosis. Lanza and Vane [50] attribute this view to McFarland but McFarland warns against the fallacy that tuberculosis in silicotics is not contagious [9]. Watkins-Pitchford noted the lack of transmission of tuberculosis to the families of miners but presented experimental data with guinea-pigs to show that the *Mycobacterium tuberculosis* from miners certainly did not lack virulence [7]. In another report which cited and challenged the conventional wisdom [50], it was shown that the families of men with positive bacteriology had certainly been infected and that lack of transmission was only a feature in association with negative sputum on guinea-pig culture.

The association of mycobacteria other than tuberculosis (MOTT) with silicosis was not considered to be important as recently as 1969 [51] but in 1974, MOTT were reported to have caused 50% of the mycobacterial illnesses in sandblasters with silicosis [45]. Snider [52] believes that all those with silicosis are susceptible to MOTT infection. This view was challenged by Morgan [53] who holds the opinion that the increased prevalence of MOTT infections in miners is caused by the presence of MOTT in the dust to which they are exposed. Whatever the explanation, a relationship between mining and MOTT as well as with silicosis and MOTT is now established [41,54,55] and it is possible that MOTT infections which are not transmitted from human to human [56,57] accounted for some of the earlier inconsistencies concerning the infectivity of tuberculosis suffered by miners.

2.4.3 Histology of tuberculosis with silicosis

While bacteriological proof of tuberculosis in men with silicosis was often lacking, most of the diagnoses were confirmed by histology on autopsy material. However, the criteria for the histological diagnosis of tuberculosis were not definitive [7]. The diagnosis of active tuberculosis was often based on the presence of single silicotic nodules with central necrosis with, or even without, some surrounding cellular reaction [34,47,58]. In other instances a tuberculous focus, sometimes calcified, in a hilar node was judged to be sufficient proof [37]. Sometimes the diagnosis of tuberculosis was based on the finding of an "excessive fibroid reaction" [47,48].

2.4.4 Susceptibility of gold miners to tuberculosis

The susceptibility of gold miners and others exposed to silica-dust is not a single function. Under modern mining conditions in Western countries there is now little excess risk of tuberculosis [19]. This is not true for industries, even in the Western world, where dust control is less than adequate [46]. Thus the susceptibility to tuberculosis varies with the type of silicosis. Mycobacterial infections occur in the vast majority of those with accelerated and acute silicosis even when that disease is acquired in countries where tuberculosis is uncommon [19]. The very high risks of tuberculosis in the first half of the 20th century were almost certainly a reflection of the more acute silicosis which was prevalent at that time. Acute and accelerated silicosis are not usually now encountered in the gold mining industry but even within the category of chronic silicosis, there are gradations of tuberculosis susceptibility in direct relation to the extent of the silicosis [12,59,60]. Another determinant of the prevalence of tuberculosis in men with silicosis is clearly the background prevalence of tuberculosis in the community [59,61]. With the general decline in tuberculosis in developed countries there has been a commensurate drop in the prevalence in miners in these countries. Nevertheless, the risk of pulmonary tuberculosis in those with silicosis remains higher than that in the general population[49,62,63,64].

There is no controversy concerning the increased risks of mycobacterial infection in those with silicosis but a controversy still exists about the risks in those exposed to silica-dust who do not have silicosis. Watkins-Pitchford believed that the inhalation of even a few particles of silica-dust could predispose the individual to pulmonary tuberculosis [7] . This view has been supported by those who have experimentally demonstrated the impotence of the silica-dusted lung macrophage to mycobacteria [65,66,67,68], however there is doubt about the relevance of these laboratory findings to the human situation [19,69] with the possible exception of rare instances of acute silicosis [30,38,39,70]. Nevertheless, there is a common belief that persons exposed to silica-dust who do not have silicosis are more susceptible to pulmonary tuberculosis and this view is supported by at least one study [63]. However, it is possible that this increased susceptibility is due to the fact that these exposed subjects without silicosis do, in reality, have silicosis but that it is not yet apparent on the chest radiograph [71].

It was the belief that different syndromes developed with different sequences of tuberculous infection, silica dust exposure and silicosis [7,14,29]. A 1970 report [60] in which the author was of the opinion that "exogenous superinfection" produced a more malignant form of disease in silicotic subjects than that which resulted from "endogenous re-infection", introduces yet another dimension to the association and to the sequence concept.

2.4.5 Management of tuberculosis in silicosis

Prior to 1951, it was accepted that men with both silicosis and tuberculosis would die of their disease [12,14,42,72]. Most of the early management of the problem correctly emphasised dust control and surveillance [7,73].

Later, attention focused on the use of BCG which was strongly favoured by some [49] but was considered by others to be ineffective [63] or even to cause a dangerous exacerbation of the silicosis [74].

With the introduction of effective anti-tuberculosis therapy, no dramatic results were evident [64,75].

However, many of the regimens used appeared to have been informally conceived and the early patients included many of the older miners with advanced disease including those with no objective evidence of tuberculosis. More carefully presented early treatment regimens were generally successful [76] and once rifampicin became available, the results of treatment of pulmonary tuberculosis were comparable with those in patients without silicosis [54,77,78].

2.4.6 Silicosis and tuberculosis - summary

The difficulties in interpreting earlier data concerning tuberculosis and silicosis have not been presented to dispute the very strong associations between the two diseases, but only to emphasise the difficulty in separating, in a way which is possible today, the role played by each of the diseases in the past. It is, therefore, often not possible to make valid comparisons between either of these diseases in gold miners today with those which have been so prolifically detailed for gold miners in the first half of this century.

2.5 INDUSTRIAL BRONCHITIS

That the dust in gold mines can cause pulmonary disease other than silicosis is considered to be a recent concept [79,80,81,82,83,84]. But chronic bronchitis due to the effects of dust on the bronchi is mentioned by Gardner who quotes an unspecified and undated South African source in his 1934 paper [29], "this reaction, which has been termed a *bronchiolitis* in South Africa, is a non specific response which develops as a feature of the reaction to most types of inhaled dust". A morphological counterpart of the cough and sputum, which miners have long claimed as a work related problem [22], has been described as being a distinctive deposit of fibrous tissue, often with pigment in the walls of membranous and respiratory bronchioles and in alveolar ducts [85]. The abnormality has been termed 'mineral dust airway disease' and is ascribed to silica, iron oxide and aluminium oxide [86] and is distinct from the distortion of airways and scarring which has been described adjacent to silicotic nodules and nodes [87].

Several investigators have expressed the opinion that chronic bronchitis, whether caused by dust or by smoking, protected miners from pneumoconiosis by causing the inhaled dust to be deposited in the central airways or by improving its clearance from the lung [88,89,90]. This opinion has been challenged by several studies which showed no reduction in pneumoconiosis in miners with the symptoms of chronic bronchitis [84,91,92]. The symptoms of chronic bronchitis have generally been attributed to tobacco smoking rather than to dust exposure [19,93,94]. However, the current view supports the concept of occupational bronchitis [79] and several studies have demonstrated the presence of this syndrome in miners who do not smoke and, in smoking miners, in excess of smokers in other comparable working populations [81,82,95].

2.6 PULMONARY FUNCTION AND OCCUPATIONAL DUST EXPOSURE

Miners have frequently been noted to have dyspnoea [12] but many studies have failed to show a clear correlation between that symptom and measurable pulmonary dysfunction [96,97,98,99]. Many of the earlier studies may have been biased by the 'healthy worker effect' [100,101]. This effect would result from a self-selection by which stronger men would be found in the most physically demanding and often the most dusty work situations [24]. Zwi [99] showed that the miners doing the heaviest work with the greatest dust exposure had the best lung function. In another study with Becklake [97], they noted that there was no difference in the lung function of dust-exposed mineworkers with normal chest radiographs and railway workers. However, the data in that paper demonstrates the healthy worker effect with the younger miners having better lung function and the older miners worse lung function than the railway workers of comparable age. Thus the mineworkers showed a much greater fall of vital capacity and total lung capacity in relation to age than that seen in the railway workers, but an overall assessment failed to show any difference between these two occupational groups [97]. Even when the more severely affected men were examined [102], investigators were often unable to show an effect of dust or even of silicosis on lung function.

With more carefully designed studies, pulmonary dysfunction was increasingly noted in silica-dust exposed individuals with and without silicosis [98]. The majority of the abnormalities noted were of the obstructive variety [22,84,99]. The role of dust induced airway disease has increasingly been considered more important than pneumoconiosis as a cause of lung dysfunction in hard rock miners [90,104] and coal miners [92,105]. There are others who believe that dust-induced airway disease is less relevant. Elmes [24] has written that only in archaic conditions does dust exposure exceed cigarette smoking as a cause of significant pulmonary dysfunction. Morgan [106] who is responsible for the term 'industrial bronchitis' considered it to be a disease of the large airways and therefore less relevant than that caused by smoking as it did not cause emphysema. An opposite view is implied by

Soutar [92] who states that the airway disease induced by dust is characterised by a drop in the forced vital capacity (FVC) and not only in the forced expiratory volume in 1 second (FEV1). Kauffmann et al [107] were able to show a clear-cut drop in FEV1 in every category of smoking in subjects with occupational exposure to dust and fumes. In a *Lancet* editorial [93] it was stated that airway obstruction was uncommon in coal miners whilst bronchitic symptoms were common and largely attributable to smoking. Jacobsen [95], in response to the editorial, pointed out that both symptoms of chronic bronchitis and reduction of the FEV1 were common in non-smoking coal miners. Hurley and Soutar [108] have subsequently shown that coal mine dust exposure can lead to marked loss of FEV1.

The confusion which exists in the role of tobacco smoke, dust inhalation and pneumoconiosis in producing disturbances of lung function is further complicated by the determinant which is common to all of these factors and to lung function - age. The age of a gold miner is a package which includes his dust experience, the cigarettes he has smoked and his declining lung function [24]. In a recent paper [109] these three factors, age, tobacco smoke and dust, but not silicosis, were found to be associated with the extent of emphysema noted at necropsy in gold miners. The lack of association between the types of respiratory disease attributed to dust - chronic bronchitis, obstructive lung disease and pneumoconiosis - has been emphasised by Morgan [106]. He explained that particles with different physical characteristics are deposited in different sites and thus produce different disorders.

In reviewing the subject of dusty working environments and chronic airflow limitation, Becklake [110] has addressed the subject of another cause for the existing confusion - individual susceptibility. This need not be in the form of an acute, asthmatic response to silica dust: no acute response has been demonstrated to a bronchial challenge with silica-containing dust [111]: but in some other potentially measurable increase in airway reactivity. This additional component does not necessarily clarify the issue and adds another dimension to the subject of causality where reactivity of airways may be the cause or the effect of airway disease from dust exposure [83]. These several aspects of lung disease in association with occupational exposure will help to explain the often conflicting findings when lung function has been measured in working populations exposed to silica-containing dust [11,90,92, 105,106,112,113,114].

In summary, occupational dust exposure can cause symptoms of chronic bronchitis, chronic airflow limitation, emphysema or parenchymal disease with fibrosis, or any combination of these disorders and the disturbances of pulmonary function with which these are associated.

CHAPTER 3

THE MIGRANT LABOURER

The South African gold mines have been served by a migrant labour force of black men from rural areas of southern and central Africa. The present study was conducted on the Orange Free State gold fields where the work force consists mainly of men from Lesotho, Transkei and the Orange Free State. Other areas including Mocambique, Natal, Ciskei and Bophuthatswana contribute a small proportion of the work force.

More than 96% of the approximately 100 000 black men employed on the Orange Free State gold mines associated with the Anglo American Corporation of South Africa (AAC) are migrant workers. These men are usually poorly educated and generally illiterate. They do not have the Western obsession with time and often have no accurate knowledge of their age nor of the duration of their employment as miners. In the past, men had no identity beyond their current contract of work. They would be given new documents, a new company identity number and new medical history record for each contract. There was no official distinction between a man who had spent a life-time serving the industry and a man who was about to start his first contract. Although in 1927, Watkins-Pitchford noted that at least 95% of the current black miners had worked on the mines before, it was still common in 1979 for men to be viewed as only a period of work. Minor aberrations of health such as a single blood pressure recording of 150/95 mmHg would be grounds for rejection and men who were judged to have any degree of silicosis were compensated with nominal, difficult-to-claim sums of money, sent home and disqualified from further employment. Pulmonary tuberculosis also constituted grounds for 'repatriation' and this was usually arranged before adequate treatment had been given [115].

After 1979, the miners employed by AAC-associated gold mines were re-employed with the same company identity number. This development allowed for some continuity of employment records and even, when relevant, of medical records. In the Orange Free State AAC gold mines which are served by the Ernest Oppenheimer Hospital, health criteria for rejection were restricted to those which were necessary for the protection of the prospective employee. Men with medical conditions such as asthma, hypertension and diabetes were enrolled in a clinic programme and encouraged to continue their treatment while at home between work contracts and to return to the clinic on their return for their next work contract. This development coincided with an increased tendency for men to return to the mines which was prompted by the diminishing employment pool outside of the industry and by financial incentives offered by the industry for those who returned within a stipulated time period of 2 to 4 months.

At the time of these developments, the medical service was increasingly approached by men who had been declared to have silicosis and were thus disqualified from continuing their work as miners. Their clamour for 'leniency' with the strong implication that their repatriation was a punitive act, resulted in an unstructured investigation of silicosis in this working population. This informal study failed to show any significant pulmonary dysfunction in association with their silicosis which, in the absence of tuberculosis, appeared to be almost exclusively an uncomplicated, simple or chronic variety of that disorder. It was resolved that until a formal study could be made, men, who had been told of their disorder but wished to continue working as miners, would not be reported as silicotic unless they were planning to leave the industry, had lung dysfunction or were, on the basis of their young age, judged to be at risk of developing severe disease in the course of their potential period of future employment. It proved to be quite exceptional for a man with silicosis to elect to have compensation and repatriation or a change to a non-mining occupation. In general, the men were obsessed with continuing their work, were unaware of and unconcerned about silicosis and continued to believe that a decision to report their disease for compensation was punitive, no matter how diligently the matter was discussed with them.

At the start of the present study, the routine reporting of men with silicosis had been discontinued for approximately 5 years on the mines served by the Ernest Oppenheimer Hospital.

CHAPTER 4

OBJECTIVES AND DEFINITIONS

4.1 OBJECTIVES

The study had several objectives. The first objective was to determine the prevalence of silicosis in a working population of black miners employed in modern gold mines. The second objective was to determine the nature and extent of respiratory impairment associated with silicosis in this population. The remaining objectives relate to the longitudinal study and for the purpose of this thesis will be confined to the incidence of pulmonary tuberculosis in relation to the presence and extent of silicosis.

4.2 DEFINITIONS

For the purpose of this study, *silicosis* is defined as the presence of predominantly small rounded opacities on the chest radiograph in an individual who has been exposed to silica-containing dust [19,23 pp151]

Respiratory impairment is defined in terms of respiratory symptoms and pulmonary function [116,117].

Pulmonary tuberculosis is defined in accordance with the diagnostic criteria in use at the Ernest Oppenheimer Hospital tuberculosis facility (Appendix) [118].

CHAPTER 5

STUDY POPULATION AND DESIGN

5.1 STUDY POPULATION

The study design was such that two study populations were defined.

The first study population was the black working population of the gold mines served by the Ernest Oppenheimer Hospital. This population numbered 93 844 men at the midpoint of the sampling period. Ninety-six percent of this working population are migrant workers (chap 3, p27). During the period 1 January to 31 December 1984 the routine initial and 6-monthly periodical chest radiographs of this population were examined in the usual manner and a record was made of all of the men whose radiographs showed features compatible with silicosis. This was done on a daily basis and at the end of each day the men whose radiographs had been judged not to have features of silicosis were sampled to provide a non-silicotic control of similar age for each man who had been judged to have silicosis. The first sample of men consisted of a census (complete sample) of men from the workforce with silicosis diagnosed on the basis of their 100 mm routine chest radiographs. These men with their age-matched and chest radiograph date-matched controls then constituted the sampling frame for the second sample of this working population.

Commencing on 13 February 1984 the second sample of men was drawn for further study from the sampling frame. Men were taken from the list of the first sample and their controls in the same order in which they had been entered. Five men from the list of men thought to have silicosis were selected for every two from the list of controls. Men were taken for this second sample until 29 November 1985.

The men who had been drawn from the sampling frame and who participated in the cross-sectional study, constituted the second sample. To be eligible for participation in the cross-sectional study, a man had to have been occupationally exposed, underground in a gold mine, to have been willing to participate and able to perform forced expiratory manoeuvres and to be free of diffuse lung disease other than silicosis.

The second study population are the cohort defined by their entry into the cross-sectional study. This cohort will contribute their experience to a longitudinal study.

5.2 STUDY DESIGN

The first study examined the prevalence of silicosis in black gold miners employed on the gold mines served by the Ernest Oppenheimer Hospital.

The second study was a cross-sectional study of the same study population in which the determinant, silicosis and the outcome, respiratory impairment/disability were determined simultaneously. This association was evaluated while controlling for potential modifiers and confounders including age, smoking and exposure to mine dust.

A third study the study of the cohort which was defined by entry into the second, cross-sectional, study has a longitudinal, prospective design. Silicosis remains the determinant and the outcomes to be examined are the development of pulmonary tuberculosis and the development or progression of respiratory impairment/disability. It is also hoped that the cohort study will provide information concerning the incidence of silicosis in the non-silicotic comparison group and of the progression of silicosis in the silicotic group.

CHAPTER 6

METHODS

6.1 PREVALENCE OF SILICOSIS STUDY

The prevalence study was conducted using the routine chest radiographs which are mandated by law for all gold miners [119]. A chest radiograph is taken by The Employment Bureau of Africa (TEBA) at the start of each man's work contract. These 'initial films' of men who are to work on the mines served by the Ernest Oppenheimer Hospital are read by the medical practitioner in charge of the Anglo American Corporation (AAC) Reception Centre in Welkom. Subsequent chest radiographs are taken at the mine hostel medical stations on the sixth month after the start of the man's current work contract and six-monthly thereafter. These 'periodical films' are sent to the AAC Reception Centre to be read by the medical staff of that centre. The medical station staff do not use the routine radiograph facility other than for the routine periodical films. Radiographs required to exclude chest disease in men who present with respiratory symptoms are done by the clinical service at the Ernest Oppenheimer Hospital.

The routine chest radiographs are 100 mm films and these are all read centrally at the AAC Medical

Reception Centre. The films are read independently but previous films are available for comparison should any abnormality be noted.

During the 12 month period from 1 January 1984 to 31 December 1984, the company identity number of all men whose initial or periodical films showed features compatible with silicosis was recorded and the film packet labelled to prevent re-sampling of that man later in the sample period.

Two estimates of the number of individuals who contributed to this working population during the period of the study were made. In the first, the number of chest radiographs examined during the first 6 months of the sample period was judged to reflect the number of men as there would be no reason for any man to have had more than one radiograph during that period. As a denominator for the full sample period an estimate of the number of individuals who had been in the workforce was made by adding the number of new and returning employees during the 12 month period to the number in the workforce at the start of the period.

The use of the 100 mm chest radiograph for the diagnosis of silicosis was evaluated by comparing a set of these films read routinely by a single reader with the 125 kV full-size posterio-anterior chest radiographs from the same subjects. The full-size films were read independently by two readers using the International Labour Organisation (ILO) standard radiographs [120] and without knowledge of the reading of the miniature films. The readers were required to determine only whether the films showed features of silicosis or not.

6.2 CROSS-SECTIONAL STUDY

The company identity numbers of the men who had been identified as having silicotic changes on their routine 100 mm chest radiographs were noted together with their recorded age. Each day, from the men judged on their miniature chest radiographs to be free of silicosis, a man was chosen to match for age each man who had been identified as having silicosis.

At the end of each month the lists of company identity numbers of men with silicotic changes and their controls, in order of their dates of detection or selection, were sent to the investigator for this study.

Men were taken consecutively from the lists in a ratio of approximately five 'silicotics' to two 'controls'. Their company identity numbers were entered on envelopes with a date for the man to attend for further study and these envelopes were sent to the mine employing the man. At the mine, an almost military system operates which enables a man to be readily 'paraded' for attendance at the hospital (or for any other purpose). Mine workers are familiar with this system and are content to respond to a 'parade' which permits them to be absent from work without any loss of earnings.

The men who had been paraded then attended the Ernest Oppenheimer Hospital with their mine medical history cards sealed in the study envelope.

6.2.1 Occupational History

One of the clerks in the Ernest Oppenheimer Hospital outpatient department interviewed each man on his arrival at the hospital. Using a simple checklist (Appendix), the man was asked what year he had first worked on a gold mine, the occupation in which he had been most commonly employed and details of any time spent working on an asbestos mine. The completed questionnaire was then sent to the AAC Reception Centre for the addition of any information concerning the man's occupation on the computerised mine records.

6.2.2 Respiratory questionnaire

The man was then taken to the hospital lung function laboratory. The lung function technician, a registered nurse who is fluent in Zulu, Xhosa, Southern Sotho, Tswana and Shangaan (the languages used by the black mine workers), conducted a respiratory questionnaire

(Appendix). This questionnaire was administered, verbally, to all of the study subjects by the same interviewer.

6.2.3 Lung function tests

6.2.3.1 Equipment

All of the lung function tests were performed with the same apparatus operated by the same technician. The apparatus was a Morgan Transfertest Model A. The equipment included an 8 litre rolling seal spirometer, a flow-volume differentiator, an automatic valve box and helium and carbon monoxide gas analysers. The equipment was linked through a Medical Graphics analogue-digital converter to an Apple IIe computer with Medical Graphics operating software.

The equipment was calibrated weekly with a 4 litre syringe using air at room temperature. Electronic calibration of the system was performed daily for volume and flow signals.

BTPS factor calculations were based on an atmospheric pressure of 654 mmHg and the temperature in the lung function laboratory which was maintained with an air-conditioning unit.

6.2.3.2 Tests

All the tests were done in the morning between 09h00 and 12h00 on Mondays, Tuesdays, Thursdays and Fridays. The subjects had been asked not to smoke that morning until after the tests.

The subject had his height measured without shoes and he was weighed in indoor clothing. He was then carefully interrogated concerning his age.

The forced expiratory tests and the automated single breath diffusion study were done in accordance with the standards of the American Thoracic Society (ATS)[121 pp55-88]

Forced expiratory manoeuvres were performed with the patient seated. Attempts were continued until at least 3 of these manoeuvres were judged to be satisfactory with forced vital capacity (FVC) and forced expiratory volumes in 1 second (FEV1) within 5% of the values in at least the two best forced expiratory efforts [122] . Attempts to obtain satisfactory forced expiratory flow volume curves were not continued if a progressive reduction in the measurements was noted with successive forced expiratory manoeuvres.

Following the initial forced expiratory flow-volume curve measurements, a dose of salbutamol 200 mcg was administered by metered dose aerosol.

The subject, still seated, with a nose clip, then performed a series of single breath carbon monoxide lung diffusion (DlCO) measurements. At least 2 measurements were made with a minimum period of 4 minutes between measurements. The subject was required to produce a rapid inspiration of at least 90% of the FVC of the preceding tests, to breath hold for at least 9 seconds and to produce a satisfactory exhalation with the automatic valves set to discard the first litre and collect the second litre for analysis. The gas inhaled by the subject was analysed following each test. The results from two acceptable measurements were required not to differ by more than 5% [121]. The results of each DlCO measurement were printed out and when two satisfactory measurements had been obtained, the technician chose one test for the final report.

Following the DlCO measurements the forced expiratory flow-volume curves were measured again and recorded as the post-bronchodilator studies.

Once the lung function studies had been completed, a printed report was made which included tracings of the pre- and post-bronchodilator flow-volume and time-volume curves, the best pre- and the best post-bronchodilator FVC and FEV1 together with the other conventional flow measurements and the chosen DlCO result with its associated estimated total lung capacity. All of the results were given together with the ATS predicted values [123,124] without adjustment for the race of the subjects in accordance with the policy of the ATS at that time [125], the percentage of the predicted value and the change in the forced expiratory measurements as a percentage of the pre-bronchodilator result (Appendix).

The lung function study tracings, computer print-out and completed respiratory questionnaire were filed and stored in the lung function laboratory.

6.2.4 Chest radiograph

The subject was then taken to the hospital X-Ray Department where a full-size, postero-anterior, 125 kV chest radiograph was taken.

6.2.5 Past history of tuberculosis and/or silicosis

Finally, the man was taken to the medical outpatient department where a medical officer unsealed his study envelope and examined the enclosed medical history card. Any record of silicosis having been suspected or diagnosed or of his having had thoracic tuberculosis was noted on the study envelope. The man's visit to the hospital was recorded on his medical history card and he was then provided with transport to return to his mine.

6.2.6 Evaluation and recording

6.2.6.1 Reading of the chest radiograph

The chest radiographs were read, in batches of 50 to 100 films, by the study investigator using the technique and standard 1980 films of the ILO [120]. The films were then left, unmarked, for the second reader to read in the same room and using the same standard technique and films. When the second reader's results were available, the two readings were recorded on the computer record of the study and on each study envelope. A summary interpretation of the nodule profusion was then made using the two independent readings. The summary reading was that of the two readers if they had agreed concerning the profusion. If the two readers differed but their readings were in adjacent categories, the first reader's reading was accepted if the man's company identification number was an odd number and the second reader's if the number was even. If one category separated the two readers' readings then that intermediate category was recorded as the summary interpretation. When the two readings were separated by more than one category, a third reader was asked to read the film and the film was re-circulated to the original readers, without identifying it as a film for re-reading, by including it in the next batch of new radiographs. If the revised readings by the original readers were similar, this was used for the summary reading. If the original readers' interpretations were still dissimilar, the third reader's profusion category was used for the summary interpretation unless it differed from both of the original readings. In the event that the there was still no acceptable consensus the films were re-read by the original readers and their joint reading was taken as the summary reading. If there was still no consensus, the third reader's interpretation was taken as the summary reading.

The allocation of a subject to the silicotic or to the non-silicotic group was determined solely by the summary interpretation of the full-size chest radiograph.

6.2.6.2 Recording of lung function tests

Batches of approximately 100 lung function tests were examined by the investigator. The single-breath DlCO trace of the measurement selected by the technician was examined for smoothness and speed of the initial inspiration, comparison of the inspired volume with the FVC of the subject, good, flat breath-hold trace of adequate length and smooth, rapid expiration through the valves. Where the technician's choice was judged to be deficient an alternative trace was chosen. The forced expiratory flow-volume and time-volume curves were examined for completeness of the expiration.

The chosen DlCO, the better (pre- or post-bronchodilator) FVC, FEV1, FEV1/FVC% and maximal mid-expiratory flow rate (MMEF) and their percentage of the predicted were recorded on the computer record of the study and on the subject's study envelope. A record was also made on the computer record if there was a greater than 10% difference between the pre- and post-bronchodilator FVC, FEV1 and MMEF.

6.2.6.3 Recording of the occupational history

Finally, the occupational history questionnaire with the mine's computer record of the subject's recent mining contracts was received. The subject's occupational history was recorded on computer as the number of years from first employment on a gold mine to the date of his study or, in the few subjects who no longer worked underground, the date he last worked underground. The intensity of his silica-containing dust exposure was recorded by allocating a pre-determined grade to his stated predominant occupation. Thus machine men (drillers) and drillers assistants were rated as grade 3 intensity, winch operators, loader drivers, timber men, and members of the stope teams were recorded as grade 2 while less strenuous occupations such as locomotive drivers, and less dusty occupations such as main haulage workers, underground storemen and cage operators were rated as grade 1 intensity. Any exposure to asbestos was recorded with the duration and the time since last exposure.

6.2.6.4 Pulmonary tuberculosis

Any record of tuberculosis which had been noted on the subject's medical history card or which had been indicated by the subject on the respiratory questionnaire was noted on the computer record. All such notes were checked through the hospital records, the computer record of the Ernest Oppenheimer Hospital tuberculosis treatment programme and the reports to the Medical Bureau for Occupational Diseases (MBOD) and if confirmed, were detailed on the computer record.

6.2.6.5 Respiratory questionnaire

The information from the respiratory questionnaire was fully recorded on the computer record. Details included the subject's smoking status, details of dyspnoea including intensity and variability, cough, sputum production, a history of wheezing and a history of childhood chest illness. In addition the record noted whether the subject had smoked on the morning of the study.

6.3 LONGITUDINAL STUDY

The computerised records of the Ernest Oppenheimer Hospital tuberculosis treatment programme were regularly cross-checked with the computer record of the present study to determine the number of subjects in the present study who had developed tuberculosis. The incidence of tuberculosis was analysed by category of silicosis (0, 1, 2, and 3). The duration of follow-up was the total duration of time in person years since the date of each subject's entry to the cohort to the date of diagnosis of tuberculosis or for those who did not develop tuberculosis, to the date of analysis for this thesis, 31 July 1987.

6.4 ANALYSIS

Univariate analysis of dichotomous variables was by Chi square testing of contingency tables. Continuous variables were analysed by Student's T test when two category comparisons were made and by analysis of variance [126 pp57-82] for multiple categories.

Multivariable analysis of continuous dependent variables was done by multiple regression [126 pp183-260]. The analysis used permitted the inclusion of categorical variables. The validity of the regression equation selected for each dependent variable was confirmed by analysis of residuals. Residual analysis was done by confirming that their distribution had a 'normal' configuration and that, when plotted against the independent variable of interest, they were distributed uniformly along the zero axis [127 pp235-241]. Modification of the effect of the variable of interest by the other variables included in the model was tested using interactive variables in the model. Exclusion of variables from the model was done using a two-sided *T* test of the null hypothesis for single variables and the partial *F* test to test the null hypothesis simultaneously for several variables which did not individually reach significance [127 pp139-144]. Multivariable analysis of dichotomous dependent variables was done by logistic regression [128] with the coefficients calculated by the method of maximum likelihood [129 pp419-446].

CHAPTER

RESULTS

The study commenced on 1 January 1984 and continued until 30 November 1985. The prevalence study was completed on 31 December 1984.

7.1 PREVALENCE STUDY

7.1.1 Silicosis (numerator)

Changes compatible with silicosis were detected on 941 of the 100 880 routine 100 mm chest radiographs examined in the first, 6-month, sampling period. It was thought that the majority of men with silicosis would have been detected during this period but an additional 869 men with silicosis were detected during the next 6-month period. Thus a total of 1 810 men with silicosis were detected in the 12-month period.

7.1.2 Population (denominator)

Although the number of men in the workforce at any given point in time is known, the number of individuals who contribute to the workforce during any given period is not known.

Initially, a 6-month sample was examined to determine the prevalence of silicosis on the 100 mm routine chest radiographs. This method assumed that the majority of men would have had one chest radiograph and that no-one would have had more than one chest radiograph in this period. It thus seemed reasonable to assume that the number of men with silicosis (941) would represent the majority with that disorder and that the total number of chest radiographs (100 880) would be an accurate estimate of the number of individuals who had been included in the sample. However, it soon became apparent that the number of new cases of silicosis did not decrease after the initial sampling period and that it was thus erroneous to assume that most men were being examined by chest radiograph 6-monthly. This conclusion has been subsequently confirmed but it is also apparent that all men returning for new contracts are examined and that men who remain in the workforce are only rarely not being examined at least once in 12 months.

A 12-month sample was thus used to determine the prevalence of silicosis on the 100 mm chest radiographs. Many of the men would have been examined more than once during that period and the number of radiographs could no longer be used as the denominator. The size of the workforce at the mid-point of the 12-month sampling period was 93 844 men but the number of individuals in the study population during the period of sampling was not known. It was thus necessary to estimate the total number of men who had contributed to the workforce during that period. An approximation was used: the number of men in the workforce at the start of the sample period (87 470) was added to the number of men who joined the workforce during the sample period (45 295). The total of 132 765 is known to be an overestimate as some of the men who joined the workforce during the year had been part of the initial workforce but had left and returned within the sampling period. This overestimation of the number of individuals included in the sample affected only the denominator as the radiograph packets of the men with films showing silicosis were labelled to prevent re-sampling.

7.1.3 Prevalence of silicosis

Although the prevalence of silicosis of 136 per 10 000 gold miners (95% confidence interval (CI) 134, 138) estimated from the 12-month sample was known to have been reduced by the inflated denominator, it was greater than the 93 per 10 000 (95% CI 87,99) estimated from the 6-month sampling method.

The mean age of men with silicosis was 45.4 years with a standard deviation (SD) of 6.69 years and a median age of 45 years. An independent study conducted a year earlier found that in the general workforce the mean age was 28.7 years (SD 8.9 years)[130]. No man with silicosis was less than 26 years old. The prevalence of silicosis by age group is presented in Table 1.

TABLE 1

DISTRIBUTION OF SILICOSIS BY AGE GROUP

AGE GROUP	NO. OF CASES OF SILICOSIS	PERCENTAGE OF POPULATION IN AGE GROUP	PREVALENCE SILICOSIS/ 10 000
<26	0	48.88	0.0
26 - 30	10	17.36	4.3
31 - 35	105	13.34	59.3
36 - 40	312	9.08	258.8
41 - 45	582	5.52	794.1
46 - 50	402	3.36	901.1
51 - 55	274	1.36	1517.2
>55*	125	1.10	856.2
TOTAL	1810	100.00	136.3

The total population for this table is estimated to have been contributed to by 132 765 men which was calculated by adding to the 87 470 men in the workforce at the start of the sample period, the 45 295 new contracts issued during the sample period.

*The population age distribution data [130] does not categorise men over the age of 55 years.

7.1.4 Evaluation of 100 mm radiograph

Two hundred of the 100 mm chest radiographs used for the diagnosis of silicosis in the prevalence study were evaluated using the full-size 125 kV chest radiographs taken during the cross-sectional study as a standard. The two readers were not able to agree as to whether 15 of the full-size chest radiographs showed silicosis or not and the 100 mm films of those 15 subjects were excluded from the evaluation. Table 2 (p54) shows the results of the evaluation of the 100 mm chest radiographs. The 100 mm films were shown to be 93% sensitive and 97% specific for the diagnosis of silicosis. There was an overall agreement between the 100 mm and full-size radiographs of 95% and Cohen's kappa to determine the extent to which this agreement exceeded chance was 0.89 (where 0.0 is equivalent to no agreement beyond chance and 1.0 to perfect agreement).

(The prevalence study has been the subject of a publication [131] which is included in the Appendix.)

TABLE 2

DETECTION OF SILICOSIS BY 100mm CHEST RADIOGRAPH [131]

		LARGE FILM		
		silicosis	no silicosis	
100mm FILM	silicosis	106	2	108
	no silicosis	8	69	77
		114	71	185

Specificity 97% (69/71) x 100

Sensitivity 93% (106/114) x 100

% Agreement 95% (106 + 69)/185) x 100

Kappa 0.89 (The extent to which the agreement exceeds chance with 0 being no agreement beyond chance and 1 perfect agreement)

7.2 CROSS-SECTIONAL STUDY

A total of 1 197 men who had been exposed to silica-containing dust in a gold mine participated in the study.

7.2.1 The sample

7.2.1.1 Non-attenders

The mines were asked to parade 1 724 men to attend the study which was conducted at the Ernest Oppenheimer Hospital. Four hundred and sixty-seven men did not attend. In accordance with the request on the envelope sent to the mine (Appendix), the majority of the envelopes of the non-attenders were returned with an explanation for the non-attendance. Non-attendance was attributed to the man being on leave or having left the mine (the mine record system does not accurately distinguish these categories) in 412 cases, the request having arrived too late to arrange for the man's parade in 24 cases, the man having arrived too late to be transported to the hospital in time for the study in 15 and sundry (often irrelevant) reasons such as his having smoked or his medical history card being missing in 12. In 4 cases the envelope was not returned.

A comparison has been made between the non-attenders and the total number of men who were eligible for sampling. There was no significant difference between the mean age of the non-attenders (46.1 years, SD 7.01 years) and the total number eligible for sampling (45.4 years, SD 6.69 years) (T = 1.91, P >.05). The proportion of men who had been chosen as non-silicotic controls on the basis of their 100 mm radiographs was similar in the non-attenders to that of the total group invited to attend (chi sq df1 = 0.15, P =.30).

7.2.1.2 Exclusions

Fifty men were unable to perform the forced expiratory lung function studies and were, thus, excluded from the study. The mean age of these men (46.0 years SD 6.95) did not differ from that of the men included in the study (46.1 years, SD 6.88) (T = 0.59, P >.10). The proportion of these men who were selected as controls did not differ from the study group (chi sq df1 = 1.35, P >.20). These men were excluded after completing their occupational questionnaires; a comparison of the number of years since first exposure to silica-containing dust showed no difference between the excluded group (24.5 years, SD 9.52) and the study group (25.1 years SD 7.69) (T = 0.50, P >.10).

Ten men were excluded from the study group after completing the study when it was found that they had never worked underground in a gold mine. None of these men had been judged to have silicosis.

7.2.1.3 Repeat studies

Due to administrative errors, 15 men had been studied twice each. Their first visit studies were retained for the general analysis.

7.2.2 Missing data

Missing data from the questionnaires was supplied by sending the relevant part of the questionnaire or the specific question to the nursing personnel at the medical stations attached to each of the mine hostel complexes. The men were then called to the medical station and asked the specific question or questions. The majority of such questions related to the occupational questionnaire. For example, in 10 instances the question concerning previous exposure to asbestos had been answered in the affirmative but details of the exposure had not been sought. In 46 cases there was an apparent discrepancy between the age of the subject ascertained at the time of the lung function testing and the duration of time since the subject had first worked in a gold mine. The given answers suggested an improbably young age of first employment. In 20 cases the age or occupational history were revised by the subject but in 26 the man insisted that the data was correct although this implied that work had been started at 14 years or less in 22 men and of these 6 would have started work at 11 years of age or younger. Although the information for these 6 men seemed improbable the data was retained. In the instances where the subject provided a revised age the predicted lung function measurements were re-calculated.

Thirty-two of the study subjects had been unable to perform the single breath diffusion study. The missing data was replaced using the 'hot deck' method in which a value from a subject of similar age and radiological pattern replaced the missing value [132 p270].

7.3 DESCRIPTIVE STATISTICS

The descriptive statistics for the 1197 study subjects are presented in Tables 3 and 4 (pp61-2). The mean age of the subjects was 46.1 years (SD 6.88 years) with a range of 28 to 76 years, median and mode age 45 years. The mean height of the subjects was 166.4 cms with a range of 145 to 186 cms. The subjects had a mean duration of mine dust exposure of 25.1 years (SD 7.69 years).

7.4 DETERMINANTS OF LUNG DISORDERS

7.4.1 Age

When the 305 men of ≥49 years of age were compared with those of 49 or less years, no significant difference was found in the proportion of non-smokers, the frequency of cough nor of sputum production. There was a greater frequency of dyspnoea on more than strenuous effort in the older men but this finding was modified by silicosis and was not uniform across the categories of nodule profusion. A greater proportion of the older age group had silicosis. The predicted FEV1 increased by approximately 1.3% per 10 years of age and the predicted MMEF decreased by 0.43% per 10 years of age; both of these changes are not relevant although they reached statistical significance.

7.4.2 Occupational exposure

None of the study subjects had not been employed underground in a gold mine.

7.4.2.1 Duration of exposure

The duration of time from first exposure to dust in a gold mine to the last year of exposure ranged from 1 year to 55 years. The mean duration of exposure was 25.1 years (SD 7.69 years) with both the median and the mode duration equal to 25 years.

There were significant reductions of the FEV1, FEV1/FVC% and MMEF in those exposed for 25 years or longer compared with those exposed for less than 25 years. However the group with longer silica-containing dust exposure had smoked more and had more silicosis (Table 5, p63). A significantly larger number of those with 25 or more years underground dust exposure had suffered from pulmonary tuberculosis. There was no significant difference in the prevalence of respiratory symptoms nor of airway reactivity on the basis of duration of underground dust exposure (Table 6, p64).

7.4.2.1 Intensity of dust exposure

The intensity of the dust exposure, determined by the nature of the man's predominant occupation was rated as high (Grade 3) for 356 of the men, intermediate (Grade 2) for 690 and low (Grade 1) for 151. The men with the highest grade of dust exposure had higher FVC and slightly higher single breath diffusion for carbon monoxide (DlCO) (Table 7, p65). The higher grades of exposure were associated with an increased prevalence of dyspnoea and of sputum production (Table 8, p66).

7.4.2.3 Asbestos

Only 35 men gave a history of exposure to asbestos. The mean duration of exposure was 2.44 years with a range of 1 to 12 years and a mode of 1 year. There were no significant differences in the lung function indices nor in the frequency of respiratory symptoms in those who had been exposed to asbestos compared with those without such exposure.

TABLE 3

CONTINUOUS VARIABLES FOR THE 1197 SUBJECTS

VARIABLE	MINIMUM	MAXIMUM	MEAN	STD.DEV.
AGE (years)	28.00	76.00	46.1	6.88
HEIGHT (cms)	145.00	186.00	166.4	5.99
YEARS U/GROUND	1.00	55.00	25.1	7.69
XRAY	1	10	4.4	2.51
PACK YEARS	0.00	52.00	9.4	9.30
FVC (litres)	1.71	6.71	4.1	0.68
FVC% PREDICTED	45.00	149.00	93.6	13.50
FEV1 (litres/sec)	0.64	5.35	3.2	0.62
FEV1% PREDICTED	19.00	154.00	89.1	15.60
FEV1/FVC%	28.00	99.00	79.5	8.30
MMEF (litres/sec)	0.17	9.66	3.1	1.30
MMEF% PREDICTED	7.00	245.00	80.9	33.51
DLCOsb (ml/mmHg/min)	8.96	55.90	32.5	6.62
DlCO % PREDICTED	30.00	166.00	100.7	18.72

The FVC(forced vital capacity), FEV1 (forced expiratory volume in 1 second), MMEF (maximal mid-expiratory flow rate) and DLCOsb (single breath lung diffusion for carbon monoxide) are expressed as such and as the percentage of the measure predicted on the basis of age and height [123,124]. The FEV1/FVC% is expressed as such. PACK YEARS is a summary of the smoking history expressed as the number of years of smoking approximately 20 cigarettes per day. YRS U/GRD is the number of years since starting work underground in a gold mine. XRAY 1 to 10 reflects the extent of silicosis with 1 and 2 equivalent to the ILO [120] categories 0/0 and 0/1 and 10 as ILO 3/3.

TABLE 4

DICHOTOMOUS VARIABLES FOR ALL SUBJECTS

VARIABLE	NO. POSITIVE	PERCENTAGE
SMOKERS (CURRENT)	622	52%
EX-SMOKERS	225	19%
NON-SMOKERS	350	29%
CIGARETTE SMOKERS*	694	82%
HOME MADE CIGARETTES*	463	55%
PIPE*	461	54%
DAGGA*	58	7%
DYSPNOEA	305	25%
VARIABLE DYSPNOEA	245	20%
COUGH	916	77%
SPUTUM	747	62%
WHEEZE	272	23%
HAEMOPTYSIS	103	9%
PHTHISIS	2	0%
PULMONARY TUBERCULOSIS	61	5%
CHILD CHEST ILLNESS	381	32%
VARIABLE FVC	103	9%
VARIABLE FEV1	139	12%
VARIABLE MMEF	702	59%
ASBESTOS EXPOSURE	35	3%

Dyspnoea was judged to be present if present with walking upstairs or up hills or with any less strenuous activity. Child chest illness refers to any recalled chest illness during childhood which the subject recalled or had been told of by a parent. Variable FVC, FEV1 or MMEF refers to a change of more than 10% in the measurement before and after a dose of salbutamol by pressurised aerosol. Pulmonary tuberculosis refers to a confirmed occurrence of that disease in the past.

* Only the 622 current smokers and the 225 ex-smokers included in these categories
A history of haemoptysis was given by 7% of non smokers, 9% of smokers (current and ex-smokers) and by 10% of those with a history of tuberculosis.

TABLE 5

CONTINUOUS VARIABLES BY DURATION OF DUST EXPOSURE

LOW DUST <25 YEARS U/GROUND (544 men)
HIGH DUST >=25 YEARS U/GROUND (653 men)

VARIABLE	LOW DUST (544)		HIGH DUST (653)		T	P
	MEAN	S.D.	MEAN	S.D.		2 tail
FVC % PRED.	94.5	13.26	92.9	13.66	2.02	.0436
FEV1 % PRED.	90.5	15.17	87.0	15.86	2.81	.0051
FEV1/FVC %	80.7	8.10	78.5	8.35	4.50	.0001
MMEF % PRED.	84.6	33.63	77.8	33.53	3.51	.0005
DLCOsb % PRED	101.3	17.99	100.3	19.32	0.99	.323
XRAY	3.9	2.54	4.8	2.41	-6.38	.0001
AGE (years)	41.8	5.57	49.8	5.64	-24.56	.0001
PACK YEARS	8.2	8.06	10.3	10.12	-4.00	.0001

FVC (forced vital capacity), FEV1 (forced expiratory volume in 1 second), MMEF (maximal mid-expiratory flow rate) and DLCOsb (single breath lung diffusion for carbon monoxide) are all expressed as the percentage of the measure predicted on the basis of age and height [123,124]. The FEV1/FVC% is expressed as such. PACK YEARS is a summary of the smoking history expressed as the number of years of smoking approximately 20 cigarettes per day. XRAY is the category of round nodule profusion on the chest radiograph assessed by the standard ILO technique [120].

TABLE 6

DICHOTOMOUS VARIABLES BY DURATION OF DUST EXPOSURE

LOW DUST <25 YEARS EXPOSURE
HIGH DUST >= 25 YEARS EXPOSURE

VARIABLE	LOW DUST 544	HIGH DUST 653	CHI SQ	P
DYSPNOEA	132	173	0.78	.378
COUGH	406	510	1.99	.159
SPUTUM	337	410	0.09	.766
WHEEZE	127	145	0.22	.639
VARIABLE DYSPNOEA	111	134	0.00	.960
CHILD CHEST ILLNESS	177	204	0.23	.632
VARIABLE FEV1	63	76	0.00	.975
PULMONARY TB	19	42	5.30	.019

Dyspnoea was judged to be present if present with walking upstairs or up hills or with any less strenuous activity. Child chest illness refers to any recalled chest illness during childhood which the subject recalled or had been told of by a parent. Variable FEV1 refers to a change of more than 10% in the FEV1 measured before and after a dose of salbutamol by pressurised aerosol. Pulmonary tuberculosis refers to a confirmed occurrence of that disease in the past.

TABLE 7.

CONTINUOUS VARIABLES BY DUST INTENSITY

VARIABLE	GRADE 1 151	GRADE 2 690	GRADE 3 356	F	P
FVC % PRED	93.1	93.0	95.0	2.61	.074
FEV1 % PRED	89.0	88.8	89.7	0.35	.706
FEV1/FVC %	79.8	79.8	78.7	1.61	.200
MMEF % PRED	81.1	81.1	80.4	0.06	.945
DLCOsb % PRED	100.9	100.0	102.3	1.95	.142
YRS U/GRD	25.1	25.0	25.3	0.14	.866
AGE (years)	47.3	46.2	45.6	2.85	.059
XRAY (1-10)	3.6	4.5	4.4	8.32	.0003
PACK YEARS	9.8	9.3	9.3	0.41	.662

FVC (forced vital capacity), FEV1 (forced expiratory volume in 1 second), MMEF (maximal mid-expiratory flow rate) and DLCOsb (single breath lung diffusion for carbon monoxide) are all expressed as the percentage of the measure predicted on the basis of age and height [123,124]. The FEV1/FVC% is expressed as such. PACK YEARS is a summary of the smoking history expressed as the number of years of smoking approximately 20 cigarettes per day. YRS U/GRD is the number of years since starting work underground in a gold mine. XRAY 1 to 10 reflects the extent of silicosis with 1 and 2 equivalent to the ILO [120] categories 0/0 and 0/1 and 10 as ILO 3/3.

TABLE 8

DICHOTOMOUS VARIABLES BY DUST INTENSITY

VARIABLE	GRADE 1 151	GRADE 2 690	GRADE 3 356	CHI SQ 2 df	P
DYSPNOEA	25	173	107	13.32	.006
COUGH	109	522	285	4.35	.114
SPUTUM	88	408	251	14.21	.001
WHEEZE	34	143	95	4.76	.093
VARIABLE DYSPNOEA	23	129	93	10.87	.004
CHILD CHEST ILLNESS	46	223	112	0.23	.892
VARIABLE FEV1	10	82	47	4.49	.101
PULMONARY TB	7	36	18	0.09	.957

Dyspnoea was judged to be present if present with walking upstairs or up hills or with any less strenuous activity. Child chest illness refers to any recalled chest illness during childhood which the subject recalled or had been told of by a parent. Variable FEV1 refers to a change of more than 10% in the FEV1 measured before and after a dose of salbutamol by pressurised aerosol. Pulmonary tuberculosis refers to a confirmed occurrence of that disease in the past.

7.4.3 Radiographic category

As no film was read as being in category 0/- nor in category 3/+, the chest radiographs were read in 10 categories of the ILO standard [120]. For the purpose of analysis the readings were recorded in categories 1 to 10 with 1 equal to the ILO category 0/0, 2 to 0/1, 3 to 1/0 up to 10 for ILO category 3/3.

A summary reading could not be made on the basis of the original two readings for 70 of the subjects. These films were read by the third reader and were reviewed independently by the two original readers. The repeat reading (unrecognised) of the original readers resolved the initial differences in 34 of the cases, the third reader's interpretation was similar to that of one of the other readers and was used as the summary reading in 23 cases and in the other 13 cases a joint reading by the original readers produced a consensus.

Assessment of the radiographic readings was performed using multiple linear regression models with the two original readings and the summary reading as the dependent factors each in two models; firstly with duration and intensity of dust exposure; and secondly with the indices of pulmonary function as the independent factors. The results differed slightly; the first reading was best predicted by the lung function studies and the summary reading best predicted by the duration and intensity of dust exposure. In view of the closeness of the models, the summary reading of the radiographs has been used in this thesis for all the analyses involving silicosis.

The consistency of the two readers was measured using Kendall's Tau-b statistic - 0.725, asymptotic standard error (ASE) 0.014 and with Spearman correlation - 0.779, ASE 0.014. Using the two 10-category readings in a linear regression model, the adjusted R squared was 0.67 and the first reader's assessment could be predicted by adding 0.9 to that of the second reader.

The first reader categorised 50% of the films as having mid-category nodule profusion (0/0, 1/1, 2/2 and 3/3) while the second reader placed 70% of the films in the mid-categories (chi sq df1 = 93, P < .0005) (Figure 1,p71).

Using the summary reading there were 340 subjects in Category 0, no silicosis, which included films read as 0/0 and 0/1. Category 1 (1/0, 1/1 and 1/2) included 432 subjects, Category 2 (2/1, 2/2 and 2/3) 376 and Category 3 (3/2 and 3/3) 49 subjects. Three men had large opacities, all three were read as Category C [120].

For the purpose of analysis by multiple regression models the 10 radiographic categories (0/0, 0/1, 1/0, ..., 3/3) were entered as a continuous variable. This manipulation permitted the use of regression models with the radiographic features as the dependent variable and also proved to be reliable when compared with the use of 3

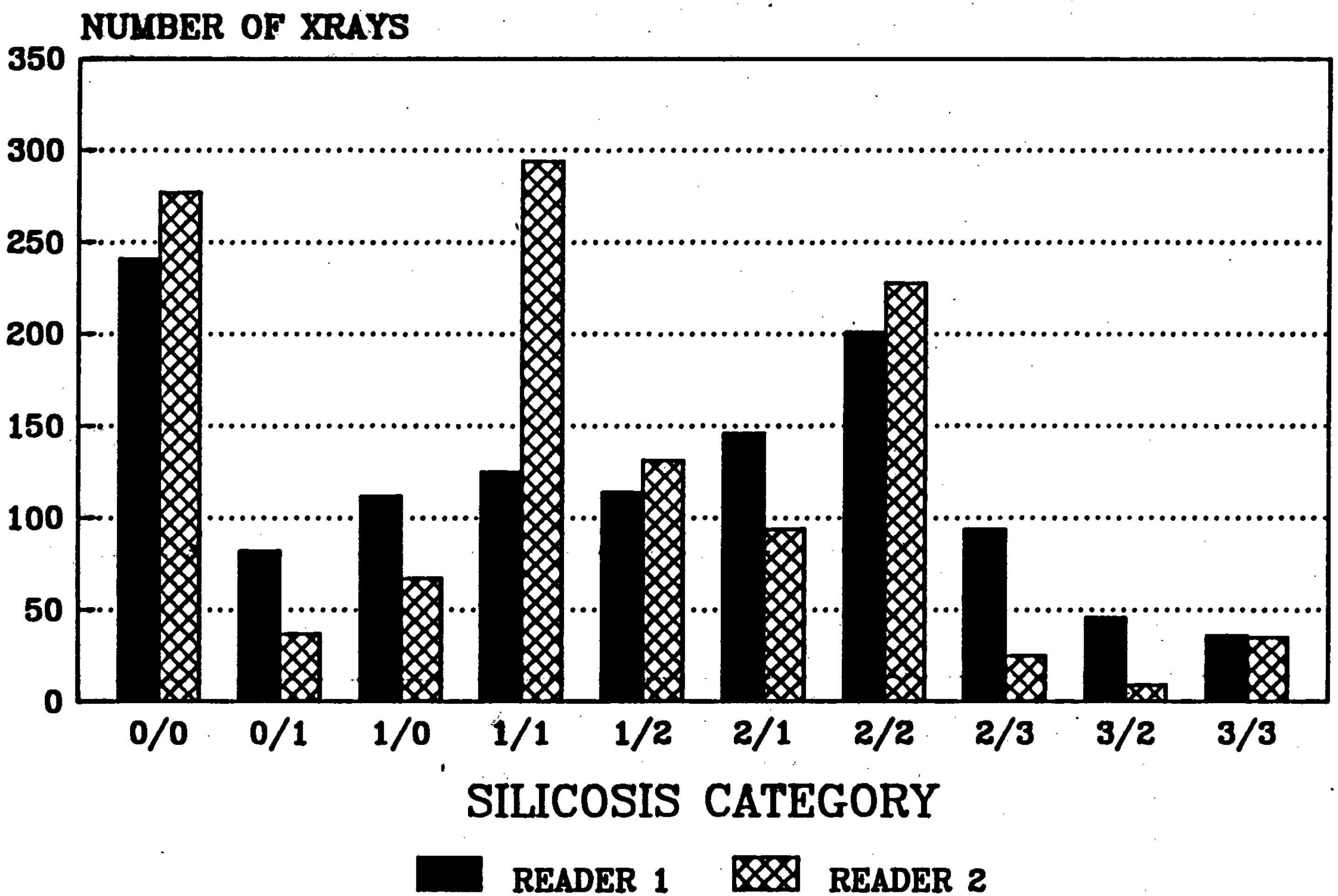
'dummy variables' when the radiographic features were entered as an independent variable.
Figures 2, 3 and 4 show that there was a good linear fit when the continuous radiographic variable was plotted against the maximal mid-expiratory flow rate (MMEF), single breath lung diffusion for carbon monoxide (DlCO) and the number of years since starting to work underground.

Table 9 (p75) shows the continuous variables compared for silicosis and no silicosis without control for other potential determinants of lung disease. All of the indices of lung function, expressed as the percentage of the predicted value corrected for age and height, were reduced in the silicotic subjects who were older and had been exposed to silica-containing dust for longer periods. The smoking history was similar in the two groups. Table 10 (p76) shows the dichotomous variables in the two groups. The frequencies of dyspnoea and of pulmonary tuberculosis were significantly greater in the silicotic group.

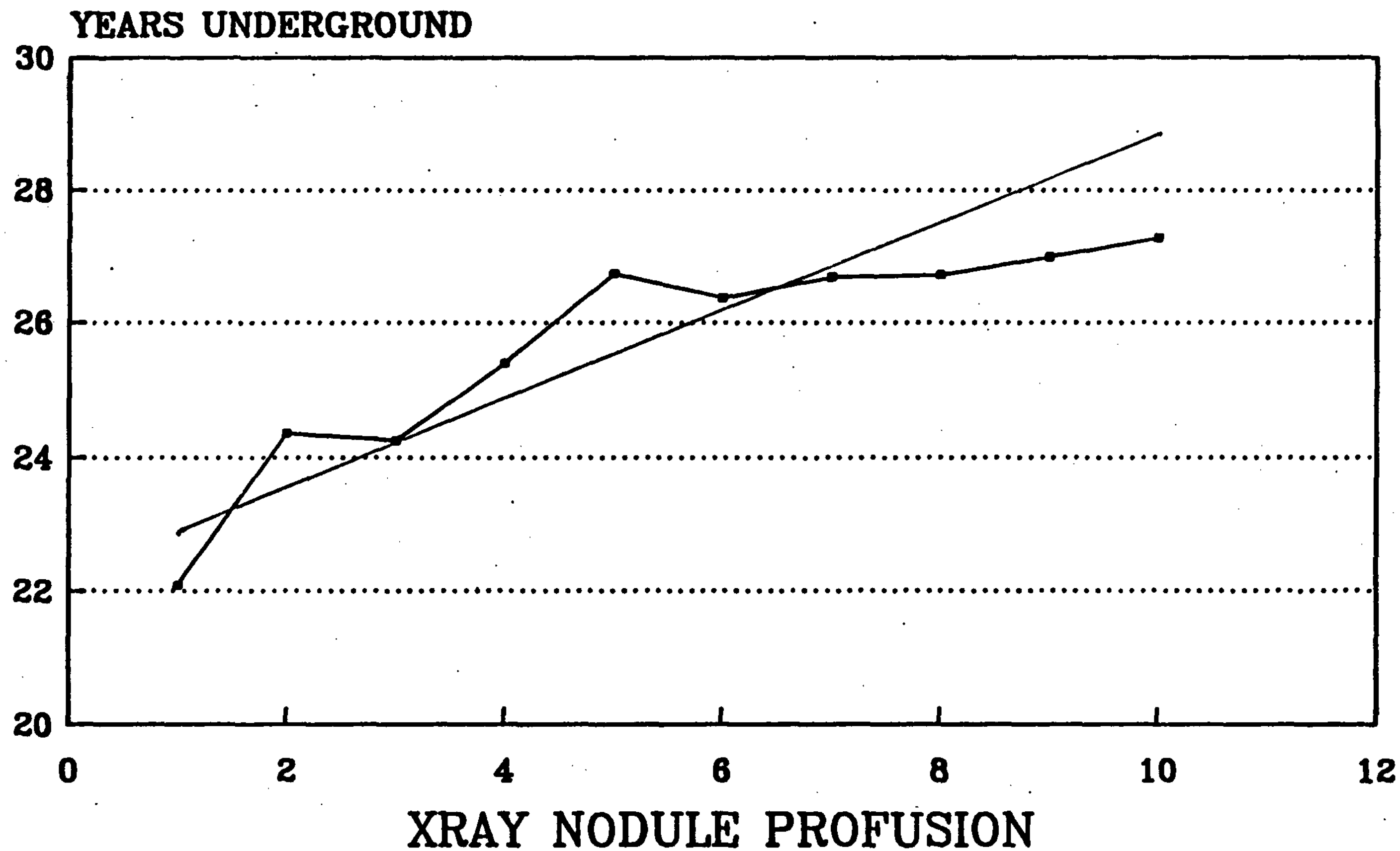
Tables 11 and 12 (pp77-78) show the continuous and Table 13 (p79) shows the dichotomous variables within the three categories of silicosis.

Analysis by multiple linear regression showed that the determinants of silicosis are duration of dust exposure and the intensity of the exposure (Table 14, p80). Exposure to Grade 1 being least likely to be associated with silicosis and exposure to Grade 2 most likely with Grade 3 (the highest intensity) being close to but slightly less predictive of silicosis than Grade 2. There was no influence direct or indirect on the prediction of silicosis by tobacco smoking nor by symptoms of cough and of sputum production. No interaction term between duration of dust exposure and other potential determinants reached significance. The relationships between silicosis, lung dysfunction, respiratory symptoms and tuberculosis will be presented in more detail in the discussion.

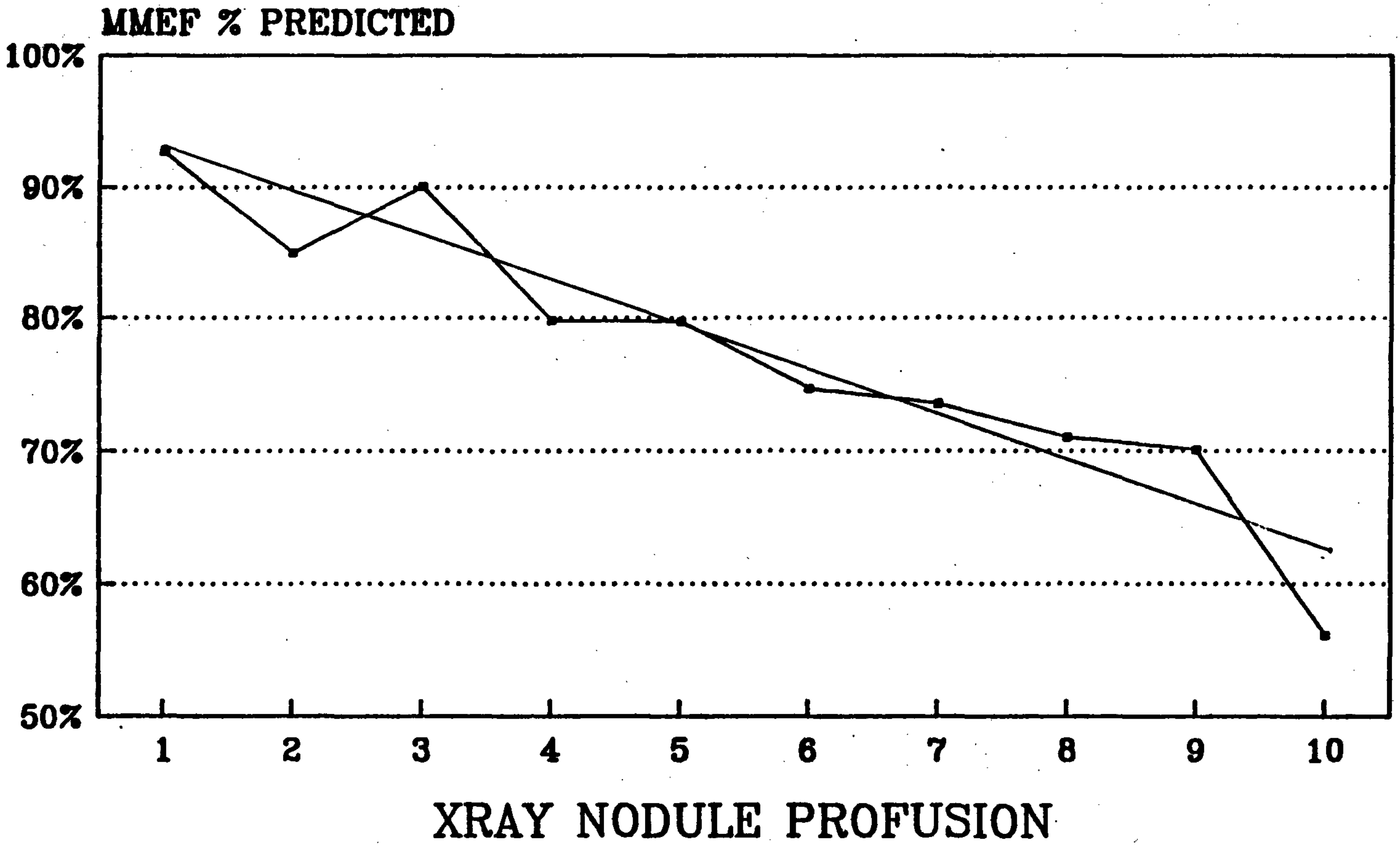
ILO NODULE PROFUSION
1ST AND 2ND READERS



XRAY NODULE PROFUSION
vs YEARS UNDERGROUND



XRAY NODULE PROFUSION
vs MMEF



XRAY NODULE PROFUSION
vs DICO % PREDICTED

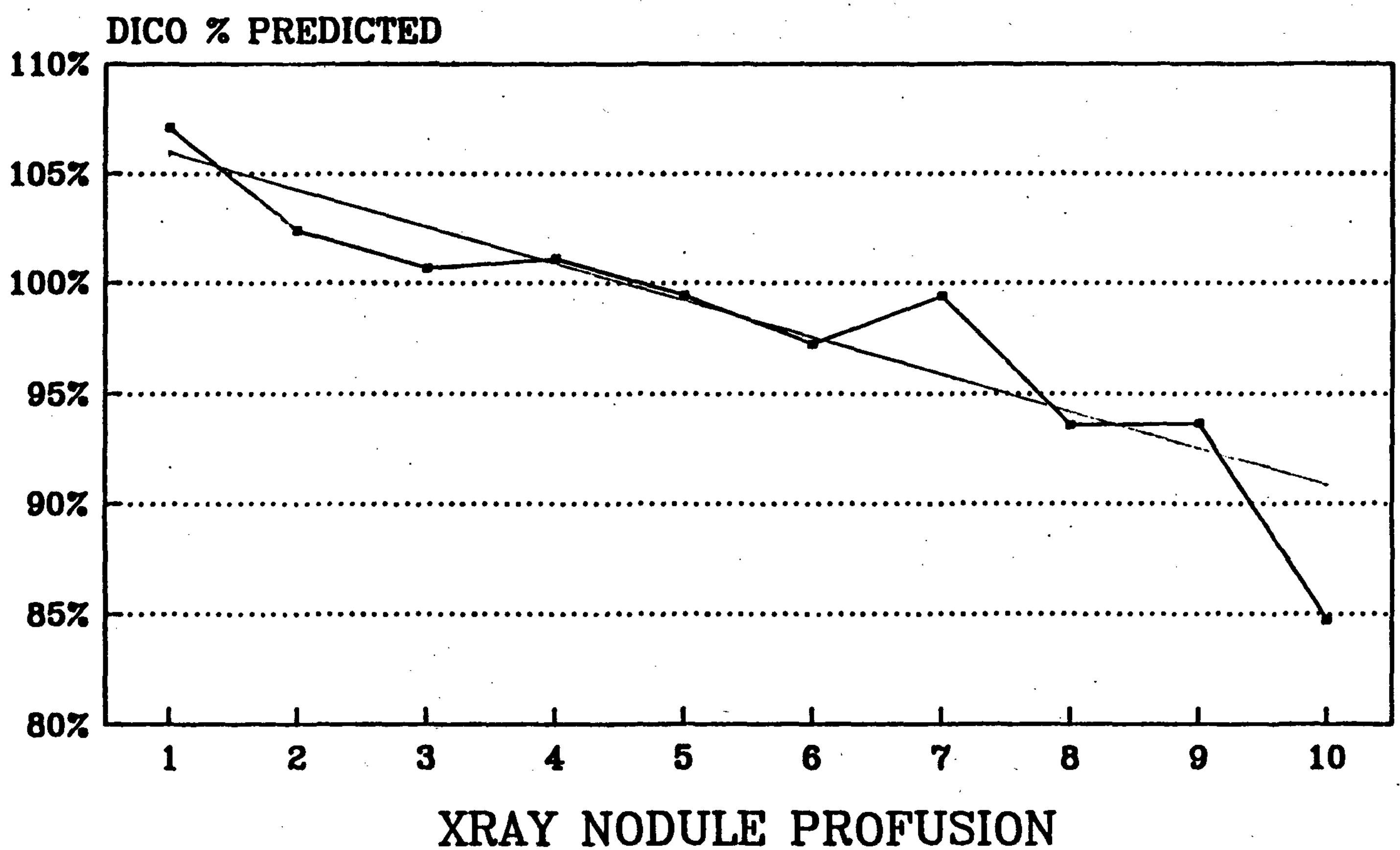


TABLE 9

CONTINUOUS VARIABLES BY SILICOSIS/NO SILICOSIS

VARIABLE	NO SILICOSIS (340) MEAN	NO SILICOSIS (340) S.D.	SILICOSIS (857) MEAN	SILICOSIS (857) S.D.	T	P 2 tail
FVC % PRED.	96.1	12.77	92.7	13.67	3.948	.0001
FEV1 % PRED.	93.7	14.56	87.3	15.62	6.593	.0001
FEV1/FVC %	81.6	7.83	78.6	8.34	5.626	.0001
MMEF % PRED.	91.2	33.81	76.9	32.52	6.789	.0001
DLCOsb % PRED	106.2	18.04	98.6	18.56	6.437	.0001
YRS U/GRD	22.6	8.30	26.2	7.18	-7.456	.0001
AGE (years)	44.7	6.75	46.7	6.85	-4.573	.0001
AGE AT START	22.1	6.18	20.5	5.09	4.589	.0001
HEIGHT (cms)	166.4	5.95	166.5	6.01	0.038	.9697
PACK YEARS	8.6	9.00	9.6	9.40	-1.570	.1166

FVC (forced vital capacity), FEV1 (forced expiratory volume in 1 second), MMEF (maximal mid-expiratory flow rate) and DLCOsb (single breath lung diffusion for carbon monoxide) are all expressed as the percentage of the measure predicted on the basis of age and height [123,124]. The FEV1/FVC % is expressed as such. PACK YEARS is a summary of the smoking history expressed as the number of years of smoking approximately 20 cigarettes per day. YRS U/GRD is the number of years since starting work underground in a gold mine. START AGE is the age that the man commenced underground work on a gold mine.

TABLE 10

DICHOTOMOUS VARIABLES BY SILICOSIS

VARIABLE	NO SILICOSIS 340	SILICOSIS 857	CHI SQ	P
SMOKERS*	188	434	0.01	.910
DYSPNOEA	59	246	16.52	.000
COUGH	248	668	3.40	.065
SPUTUM	286	541	0.67	.413
WHEEZE	66	206	2.97	.085
VARIABLE DYSPNOEA	53	192	6.95	.008
CHILD CHEST ILLNESS	102	279	0.73	.392
VARIABLE FEV1	44	95	0.82	.366
PULMONARY TB	7	54	9.06	.003

* this category includes current smokers and excludes the ex-smokers (225).
Dyspnoea was judged to be present if present with walking upstairs or up hills or with any less strenuous activity. Child chest illness refers to any recalled chest illness during childhood which the subject recalled or had been told of by a parent. Variable FEV1 refers to a change of more than 10% in the FEV1 measured before and after a dose of salbutamol by pressurised aerosol. Pulmonary tuberculosis refers to a confirmed occurrence of that disease in the past.

TABLE 11

CONTINUOUS VARIABLES BY CATEGORY 1 AND CATEGORY 2 SILICOSIS

VARIABLE	SILICOSIS CAT.1 (432) MEAN	S.D.	SILICOSIS CAT.2 (376) MEAN	S.D.	T	P 2 tail
FVC % PRED.	93.8	13.62	92.5	13.05	1.435	.1517
FEV1 % PRED.	89.4	15.45	86.1	15.04	3.105	.0021
FEV1/FVC %	79.6	7.85	77.8	8.86	3.156	.0017
MMEF % PRED.	81.5	32.72	73.4	31.83	3.558	.0004
DLCOsb % PRED	100.4	17.28	97.8	18.85	2.064	.0393
YRS U/GRD	25.6	7.45	26.6	6.92	-1.893	.0587
AGE (years)	46.6	6.97	46.8	6.83	-0.391	.6963
AGE AT START	20.9	5.62	20.2	4.54	2.126	.0338
HEIGHT (cms)	166.1	5.85	167.0	6.17	-2.066	.0339
PACK YEARS	9.9	9.14	9.0	9.42	1.434	.1518

FVC (forced vital capacity), FEV1 (forced expiratory volume in 1 second), MMEF (maximal mid-expiratory flow rate) and DLCOsb (single breath lung diffusion for carbon monoxide) are all expressed as the percentage of the measure predicted on the basis of age and height [123,124]. The FEV1/FVC % is expressed as such. PACK YEARS is a summary of the smoking history expressed as the number of years of smoking approximately 20 cigarettes per day. YRS U/GRD is the number of years since starting work underground in a gold mine. START AGE is the age that the men commenced underground work on a gold mine.

TABLE 12

CONTINUOUS VARIABLES BY CATEGORY 2 AND CATEGORY 3 SILICOSIS

VARIABLE	SILICOSIS CAT. 2 (376) MEAN	S.D.	SILICOSIS CAT. 3 (49) MEAN	S.D.	T	P 2 tail
FVC % PRED.	92.5	13.04	84.4	15.95	3.960	.0001
FEV1 % PRED.	86.1	15.04	84.4	16.98	3.729	.0002
FEV1/FVC %	77.8	8.86	77.0	7.44	0.585	.5592
MMEF % PRED.	73.4	31.83	61.8	28.52	2.437	.0152
DLCOsb % PRED	97.8	18.85	88.4	23.40	3.197	.0015
YRS U/GRD	26.6	6.92	27.2	6.63	-0.540	.5893
AGE (years)	46.8	6.83	47.0	5.93	-0.263	.7924
AGE AT START	20.2	4.54	19.9	3.68	0.437	.6623
HEIGHT (cms)	167.0	6.17	164.7	5.84	2.518	.0124
PACK YEARS	9.0	9.42	11.5	11.24	-1.698	.0903

FVC (forced vital capacity), FEV1 (forced expiratory volume in 1 second), MMEF (maximal mid-expiratory flow rate) and DLCOsb (single breath lung diffusion for carbon monoxide) are all expressed as the percentage of the measure predicted on the basis of age and height [123,124]. The FEV1/FVC % is expressed as such. PACK YEARS is a summary of the smoking history expressed as the number of years of smoking approximately 20 cigarettes per day. YRS U/GRD is the number of years since starting work underground in a gold mine. START AGE is the age that the man commenced underground work on a gold mine.

TABLE 13

DICHOTOMOUS VARIABLES BY SILICOSIS CATEGORY

VARIABLE	CATEG.1 432	CATEG.2 376	CATEG.3 49	CHI SQ 2 df	P
SMOKER	247	168	19	8.03	.018
DYSPNOEA	114	107	25	13.07	.001
COUGH	343	283	42	3.82	.148
SPUTUM	284	224	33	3.68	.159
WHEEZE	101	93	12	0.21	.901
VARIABLE DYSPNOEA	85	88	19	9.62	.008
CHILD CHEST ILLNESS	144	121	14	0.50	.780
VARIABLE FEV1	41	48	6	2.26	.323
PULMONARY TB	20	29	5	14.66	.002

Dyspnoea was judged to be present if present with walking upstairs or up hills or with any less strenuous activity. Child chest illness refers to any recalled chest illness during childhood which the subject recalled or had been told of by a parent. Variable FEV1 refers to a change of more than 10% in the FEV1 measured before and after a dose of salbutamol by pressurised aerosol. Pulmonary tuberculosis refers to a confirmed occurrence of that disease in the past.

TABLE 14

MULTIPLE LINEAR REGRESSION

DETERMINANTS OF SILICOSIS IN SILICA-DUST EXPOSED MEN

R sq 0.062 MEAN XRAY 4.39 Root MSE 2.43 P of F .0001

VARIABLE	COEFFICIENT	STD.ERROR	T	P
INTERCEPT	1.8311	0.3036	6.03	.0001
YRS U/GRD	0.0715	0.0092	7.81	.0001
DUST GRADE 2	0.9206	0.2186	4.21	.0001
DUST GRADE 3	0.7666	0.2363	3.24	.0012

YRS U/GRD is the number of years since the men first worked underground in a gold mine. Dust grade 2 is a dummy variable which is equal to 1 if the level of dust exposure was at the intermediate level - grade 2, and is otherwise equal to zero. Dust grade 3 is a dummy variable for dust exposure at the highest level - grade 3.

Silicosis in this regression model is represented by the continuous variable XRAY 1 to 10 where XRAY 1 is equivalent to ILO category 0/0 and XRAY 10 to ILO 3/3 [120].
T is the test for the significance of the contribution of that particular estimate to the regression model.
In this model, 10 years of underground exposure would add (0.0715x10) = 0.715 and work in an environment with the highest dust level, 0.7666 which would thus increase the Xray category from 1.83 to 1.83 + (0.715 + 0.766) = 3.3 or approximately ILO 1/0.
It should be noted that exposure to the intermediate level of dust is associated with more radiological changes than is exposure to the highest level (see discussion).
None of the other potential determinants included in the study made a significant contribution to the model.

7.4.4 Smoking history

There were 622 current smokers, 225 ex-smokers and 350 non-smokers amongst the study subjects. The smoking history was divided into 3 grades with those who smoked less than 5 cigarettes per day, those who smoked 5 to 15 per day and those who smoked more than 15 per day. The interviewer converted tobacco smoked as homemade cigarettes or in a pipe into cigarette equivalents [94]. The smoking history was then summarised to provide an estimate of the number of years of smoking one pack (20 cigarettes) per day. Thus one year of smoking more than 15 cigarettes per day was estimated to equal 1 pack year; 5 to 15 per day, half a pack year and less than 5, one fifth of a pack year.

The continuous variables are presented for smokers and non-smokers in Table 15 (p82) and for smokers and ex-smokers in Table 16 (p83). Significant differences of all of the predicted values of lung function except the forced expiratory volume in 1 second (FEV1) were found between the smokers and the non-smokers. There were no differences in the extent of silicosis in these two groups but a significantly greater degree of silicosis was found in ex-smokers as compared with current smokers. The dichotomous variables for smokers and non-smokers and for smokers and ex-smokers are presented in Tables 17 and 18 (pp84-85). Smokers had a greater frequency of cough, sputum production, wheeze and dyspnoea when compared with non-smokers. Ex-smokers differed from current smokers in having an increased frequency of variable dyspnoea and of airway reactivity as indicated by a change in their pre- and post-bronchodilator FEV1 of greater than 10%.

TABLE 15

CONTINUOUS VARIABLES BY SMOKER/NON-SMOKER (excluding 225 EX-SMOKERS)

VARIABLE	NON-SMOKERS (350) MEAN	NON-SMOKERS (350) S.D.	SMOKERS (622) MEAN	SMOKERS (622) S.D.	T	P 2 tail
FVC % PRED.	92.4	13.17	94.5	13.25	-2.422	.0156
FEV1 % PRED.	90.2	15.19	89.3	15.57	0.911	.3624
FEV1/FVC %	81.4	7.33	79.0	8.21	4.611	.0001
MMEF % PRED.	87.7	35.22	79.0	32.15	3.923	.0001
DLCOsb % PRED	106.5	19.21	98.5	18.10	6.546	.0001
YRS U/GRD	25.8	7.50	24.3	7.54	2.950	.0033
AGE (years)	46.5	6.85	45.5	6.50	2.250	.0244
HEIGHT (cms)	166.4	6.04	166.3	6.06	0.253	.8007
XRAY (1-10)	4.4	2.58	4.1	2.41	1.804	.0716

FVC (forced vital capacity), FEV1 (forced expiratory volume in 1 second), MMEF (maximal mid-expiratory flow rate) and DLCOsb (single breath lung diffusion for carbon monoxide) are all expressed as the percentage of the measure predicted on the basis of age and height [123,124]. The FEV1/FVC % is expressed as such. YRS U/GRD is the number of years since starting work underground in a gold mine. XRAY 1 to 10 reflects the extent of silicosis with 1 and 2 equivalent to the ILO [120] categories 0/0 and 0/1 and 10 as ILO 3/3.

TABLE 16

CONTINUOUS VARIABLES BY SMOKER/EX-SMOKERS (excluding 350 NON-SMOKERS)

VARIABLE	EX-SMOKERS (225) MEAN	S.D.	SMOKERS (622) MEAN	S.D.	T	P 2 tail
FVC % PRED.	93.1	14.51	94.5	13.25	1.410	.1590
FEV1 % PRED.	87.0	16.15	89.3	15.57	1.860	.0630
FEV1/FVC %	78.0	9.40	79.0	8.21	1.516	.1300
MMEF % PRED.	75.8	32.97	79 0	32.15	1.270	.2300
DLCOsb % PRED	98.0	17.72	98.5	18.10	0.298	.7657
YRS U/GRD	26.5	8.12	24.3	7.54	3.688	.0002
AGE (years)	47.4	7.70	45.5	6.50	-3.662	.0003
HEIGHT (cms)	166.7	5.72	166.3	6.06	-0.751	.4528
XRAY (1-10)	5.1	2.53	4.1	2.41	-5.050	.0001
PACK YEARS	16.0	11.10	23.9	9.29	10.240	.0001

FVC (forced vital capacity), FEV1 (forced expiratory volume in 1 second), MMEF (maximal mid-expiratory flow rate) and DLCOsb (single breath lung diffusion for carbon monoxide) are all expressed as the percentage of the measure predicted on the basis of age and height [123,124]. The FEV1/FVC % is expressed as such. PACK YEARS is a summary of the smoking history expressed as the number of years of smoking approximately 20 cigarettes per day. YRS U/GRD is the number of years since starting work underground in a gold mine. XRAY 1 to 10 reflects the extent of silicosis with 1 and 2 equivalent to the ILO [120] categories 0/0 and 0/1 and 10 as ILO 3/3.

TABLE 17

DICHOTOMOUS VARIABLES BY SMOKERS AND NON-SMOKERS

VARIABLE	NON-SMOKER 350	SMOKER 622	CHI SQ	P
DYSPNOEA	71	165	4.74	.029
COUGH	210	527	74.70	.000
SPUTUM	156	446	69.94	.000
WHEEZE	50	155	15.22	.000
VARIABLE DYSPNOEA	56	126	2.67	.102
CHILD CHEST ILLNESS	107	198	0.16	.684
VARIABLE FEV1	39	64	0.17	.678
PULMONARY TB	11	32	2.12	.145

Dyspnoea was judged to be present if present with walking upstairs or up hills or with any less strenuous activity. Child chest illness refers to any recalled chest illness during childhood which the subject recalled or had been told of by a parent. Variable FEV1 refers to a change of more than 10% in the FEV1 measured before and after a dose of salbutamol by pressurised aerosol. Pulmonary tuberculosis refers to a confirmed occurrence of that disease in the past.

TABLE 18

DICHOTOMOUS VARIABLES BY SMOKERS AND EX-SMOKERS

VARIABLE	EX-SMOKER 225	SMOKER 622	CHI SQ	P
DYSPNOEA	69	165	1.42	.234
COUGH	179	527	3.18	.074
SPUTUM	145	446	4.13	.042
WHEEZE	67	155	2.02	.156
VARIABLE DYSPNOEA	63	126	5.71	.017
CHILD CHEST ILLNESS	76	198	0.29	.593
VARIABLE FEV1	36	64	5.18	.023
PULMONARY TB	18	32	2.43	.119

Dyspnoea was judged to be present if present with walking upstairs or up hills or with any less strenuous activity. Child chest illness refers to any recalled chest illness during childhood which the subject recalled or had been told of by a parent. Variable FEV1 refers to a change of more than 10% in the FEV1 measured before and after a dose of salbutamol by pressurised aerosol. Pulmonary tuberculosis refers to a confirmed occurrence of that disease in the past.

7.4.5 Childhood chest illness

Thirty-two percent (381) of the men stated that they had suffered from a childhood chest illness which they recalled or had been told of by a parent. Table 19 (p87) shows the continuous variables of those with a history of childhood chest illness compared with those without such a history. The group with a positive history of childhood illness were slightly, although statistically significantly, shorter than those without such a history. The comparison of dichotomous variables between the two groups shows that those with the history of childhood disease had an increased frequency of dyspnoea, variable dyspnoea, cough and wheeze (Table 19, p87).

7.4.6 Awareness of disease

No subject indicated that he was aware of having silicosis and the interviewer found that the subjects had no knowledge of the disorder. The word, "phthisis" was known to some of the men it was either taken to mean tuberculosis or some other unspecified disease of unknown origin. There is no word in the languages used by this working population nor in the *lingua franca* of the mining industry, "fanagalo", for silicosis.

TABLE 19

CONTINUOUS VARIABLES BY HISTORY OF CHILDHOOD CHEST ILLNESS

VARIABLE	NO CHILDHOOD ILLNESS (816)		CHILDHOOD ILLNESS (381)		T	P
	MEAN	S.D.	MEAN	S.D.		2 tail
FVC % PRED.	93.2	13.31	94.7	13.85	-1.790	.0734
FEV1 % PRED.	88.8	15.66	89.7	15.47	-0.908	.3640
FEV1/FVC %	79.6	8.38	79.2	8.13	0.720	.4700
MMEF % PRED.	81.5	34.29	79.6	31.78	0.910	.3600
DLCOsb % PRED	100.9	19.01	100.3	18.11	0.513	.6083
YRS U/GRD	25.2	7.96	24.9	7.08	0.627	.5306
AGE (years)	46.1	6.90	46.2	6.85	0.110	.9124
HEIGHT (cms)	166.8	5.99	165.6	5.91	3.377	.0008
XRAY (1-10)	4.4	2.53	4.4	2.47	0.009	.9927
PACK YEARS	9.2	9.18	9.8	9.54	-1.092	.2752

FVC (forced vital capacity), FEV1 (forced expiratory volume in 1 second), MMEF (maximal mid-expiratory flow rate) and DLCOsb (single breath lung diffusion for carbon monoxide) are all expressed as the percentage of the measure predicted on the basis of age and height [123,124]. The FEV1/FVC % is expressed as such. PACK YEARS is a summary of the smoking history expressed as the number of years of smoking approximately 20 cigarettes per day. YRS U/GRD is the number of years since starting work underground in a gold mine. XRAY 1 to 10 reflects the extent of silicosis with 1 and 2 equivalent to the ILO [120] categories 0/0 and 0/1 and 10 as ILO 3/3.

TABLE 20

DICHOTOMOUS VARIABLES BY HISTORY OF CHILDHOOD CHEST ILLNESS

VARIABLE	NO CHILDHOOD CHEST ILLNESS 816	CHILDHOOD CHEST ILLNESS 381	CHI SQ	P
DYSPNOEA	182	123	13.62	.000
COUGH	600	316	12.80	.000
SPUTUM	496	251	2.87	.090
WHEEZE	172	100	3.95	.047
VARIABLE DYSPNOEA	140	105	17.27	.000
VARIABLE FEV1	94	45	0.02	.883
PULMONARY TB	39	22	0.53	.466

Dyspnoea was judged to be present if present with walking upstairs or up hills or with any less strenuous activity.
Variable FEV1 refers to a change of more than 10% in the FEV1 measured before and after a dose of salbutamol by pressurised aerosol.
Pulmonary tuberculosis refers to a confirmed occurrence of that disease in the past.

7.5 RESPIRATORY SYMPTOMS

7.5.1 Dyspnoea

A subject was judged to have dyspnoea if he acknowledged any difficulty or discomfort with breathing other than with heavy work or with running. A total of 305 men stated that they had dyspnoea on walking up stairs or up hills or with lesser exertion. Table 21 (p90) shows the analysis by logistic regression of independent variables which were associated with a history of dyspnoea. The degree of silicosis was the strongest determinant of dyspnoea and this symptom was also contributed to by the intensity of dust exposure. The number of years of underground work did not contribute to this symptom.

7.5.2 Cough

A man was judged to have a cough on the basis of his answer to the simple question "do you cough". The majority of the men (916) stated that they coughed and 629 men reported that they coughed on most days. Analysis by logistic regression showed that smoking was the only significant determinant of this symptom (Table 22, p91) however 60% of the 350 men who had never smoked also gave a history of coughing and it is possible that the occupational dust exposure contrast was insufficient to establish that relationship.

TABLE 21

ASSOCIATIONS WITH DYSPNOEA ANALYSED BY LOGISTIC REGRESSION

305 SUBJECTS WITH DYSPNOEA   892 SUBJECTS WITHOUT DYSPNOEA

VARIABLE	COEFFICIENT	STD ERROR	O.R. (CONTRAST)	P
YEARS U/GRD	-0.2642	.0128	0.00 (25:10)	.0391
DUST GRADE 2	0.4754	.2419	1.61	.0054
DUST GRADE 3	0.7835	.2543	2.19 (1:0)	
XRAY (1 - 10)	0.1340	.0282	3.34 (10:1)	.0000
PACK YEARS	0.02178	.00718	1.69 (24:0)	.0025
AGE (YEARS)	0.04182	.01419	2.31 (55:35)	.0033
CONSTANT	-3.6975	.5571		

The coefficients were estimated by the method of maximum likelihood.
Yrs U/GRD refers to the number of years since the man first worked underground in a gold mine.
Dust Grade refers to the intensity of dust to which the men has been exposed in his predominant underground occupation. The coefficient of Dust Grade 2 indicates the additional Odds (expressed as the natural log) for being dyspnoeic associated with exposure to DUST GRADE 2 as compared with that of being exposed to DUST GRADE 1. DUST GRADE 3 is the additional Odds for dyspnoea for exposure to grade 3 dust intensity compared with that of DUST GRADE 1.
XRAY (1 - 10) refers to the extent of silicosis with 1 equal to ILO 0/0 and 10 to ILO 3/3 [120].
O.R.(Odds Ratio) is the odds that a subject will have dyspnoea. If the O.R. is 1 that variable has no influence; O.R.>1 indicates an excess chance and O.R.<1 a decreased chance of dyspnoea induced by increasing values of the variable.
The CONTRAST refers to the values of that variable being compared: thus a smoker of 24 pack years is being compared with a non-smoker. The O.R. of 1.69 indicates that the smoker has a 69% greater chance of being dyspnoeic than the non-smoker, given that the other variables are the same.

The analysis shows that men who have worked longer underground are less likely to be dyspnoeic. This could represent a 'survivor' effect or an error induced by multicolinearity due to dependence between the variables age, years underground and pack years.

TABLE 22

ASSOCIATIONS WITH COUGH ANALYSED BY LOGISTIC REGRESSION

916 SUBJECTS WITH COUGH   281 SUBJECTS WITHOUT COUGH

VARIABLE	COEFFICIENT	STD. ERROR	O.R. (CONTRAST)	P
PACK YEARS	0.07008	.00928	5.38 (24:0)	.0000
CONSTANT	0.6334	.0919		

The coefficients were calculated by the maximum likelihood method and represent the natural logarithm of the odds ratio for that variable.
Pack Years refers to the equivalent of smoking one pack - 20 cigarettes - per day for one year. Thus a man who smoked 5 cigarettes each day for 10 years is recorded as having 2.5 pack years.
O.R.(Odds Ratio) is the odds that a subject will have a cough. If the O.R. is 1 that variable has no influence; O.R.>1 indicates an excess chance and O.R.<1 a decreased chance of a cough induced by increasing values of the variable.
The CONTRAST refers to the values of that variable being compared: thus a smoker of 24 pack years is being compared with a non-smoker. The O.R. of 5.38 indicates that the smoker has a 538% greater chance of having a cough than the non-smoker.

Other variables entered did not reach significance including YEARS worked UNDERGROUND, XRAY features of silicosis, GRADE of dust exposure, AGE and evidence of airway reactivity (FEV1 >10% different between before and after salbutamol measurement).

7.5.3 Sputum

Sputum production was judged to be present if the man responded positively to the question "do you produce sputum". Altogether 747 men stated that they produced sputum, 507 of them produced sputum on most days and 240 only occasionally. Analysis by logistic regression showed sputum production to be related to smoking and to the intensity of occupational dust exposure (Table 23, p93).

7.5.4 Wheezing and variable dyspnoea

A total of 272 of the men said that they had noted wheezing. Those who had noted wheezing were likely to have other respiratory symptoms including dyspnoea, variable dyspnoea, cough and sputum production (Table 24, p94). There was, however, no association between the history of wheezing and a measure of airway reactivity - a change of FEV1 of more than 10% after a bronchodilator (chi sq 0.184, P = 0.668). Of the potential determinants, analysis by logistic regression showed that tobacco smoking and to a lesser extent, the radiological features of silicosis were associated with a history of wheezing (Table 25, p95). On the other hand, the associated symptom, variability of dyspnoea was found to be related to the extent of the radiological features of silicosis and the intensity of dust exposure (Table 26, p96).

TABLE 23

ASSOCIATIONS WITH SPUTUM PRODUCTION ANALYSED BY LOGISTIC REGRESSION

747 MEN PRODUCED SPUTUM 450 MEN DID NOT PRODUCE SPUTUM

VARIABLE	COEFFICIENT	STD. ERROR	O.R. (CONTRAST)	P
PACK YEARS	0.0545	.00735	3.70 (24:0)	.0000
DUST GRADE 2	0.06297	.1877	1.06	.0007
DUST GRADE 3	0.58359	.2074	1.79 (1:0)	
CONSTANT	-.1694	.1814		

The coefficients were estimated by the method of maximum likelihood.
Dust Grade refers to the intensity of dust to which the man has been exposed in his predominant underground occupation. The coefficient of Dust Grade 2 indicates the additional Odds (expressed as the natural log) for producing sputum associated with exposure to DUST GRADE 2 as compared with that of being exposed to DUST GRADE 1. DUST GRADE 3 is the additional Odds for producing sputum for exposure to grade 3 dust intensity compared with that of DUST GRADE 1.
O.R.(Odds Ratio) is the odds that a subject will produce sputum. If the O.R. is 1 that variable has no influence; O.R.>1 indicates an excess chance and O.R.<1 a decreased chance of sputum production induced by increasing values of the variable.
The CONTRAST refers to the values of that variable being compared: thus a smoker of 24 pack years is being compared with a non-smoker. The O.R. of 3.7 indicates that the smoker has a 370% greater chance of producing sputum than the non-smoker, given that the other variables are the same.

Other variables entered did not reach significance including YEARS worked UNDERGROUND and XRAY features of silicosis

TABLE 24

ASSOCIATIONS WITH VARIABILITY OF DYSPNOEA ANALYSED BY LOGISTIC REGRESSION

245 MEN WITH VARIABLE DYSPNOEA   952 MEN WITHOUT VARIABLE DYSPNOEA

VARIABLE	COEFFICIENT	STD. ERROR	O.R. (CONTRAST)	P
DUST GRADE 2	0.1503	.2492	1.16	.0063
DUST GRADE 3	0.60163	.2587	1.83 (1:0)	
XRAY (1 - 10)	0.1105	.02920	2.70 (10:1)	.0002
CONSTANT	-2.1459	.2578		

The coefficients were estimated by the method of maximum likelihood.
Dust Grade refers to the intensity of dust to which the man has been exposed in his predominant underground occupation. The coefficient of Dust Grade 2 indicates the additional Odds (expressed as the natural log) for having variable dyspnoea associated with exposure to DUST GRADE 2 as compared with that of being exposed to DUST GRADE 1. DUST GRADE 3 is the additional Odds for variable dyspnoea for exposure to grade 3 dust intensity compared with that of DUST GRADE 1.
XRAY (1 - 10) refers to the extent of silicosis with 1 equal to ILO 0/0 and 10 to ILO 3/3 [120].
O.R.(Odds Ratio) is the odds that a subject will have variable dyspnoea. If the O.R. is 1 that variable has no influence; O.R.>1 indicates an excess chance and O.R.<1 a decreased chance of variable dyspnoea induced by increasing values of the variable.
The CONTRAST refers to the values of that variable being compared: thus a man with a chest radiograph showing 3/3 nodule profusion is being compared with a man with 0/0 nodule profusion. The O.R. of 2.7 indicates that the man with 3/3 silicosis has a 270% greater chance of having variable dyspnoea than the man with a 0/0 radiograph, given that the other variables are the same.

Other variables entered which failed to reach significance included YEARS worked UNDERGROUND, PACK YEARS smoked and airway reactivity as indicated by a difference of more than 10% in the pre-and post-salbutamol measurements of the FEV1.

TABLE 25

ASSOCIATIONS WITH WHEEZE ANALYSED BY LOGISTIC REGRESSION

272 MEN COMPLAINED OF WHEEZING   925 MEN DID NOT WHEEZE

VARIABLE	COEFFICIENT	STD. ERROR	O.R. (CONTRAST)	P
PACK YEARS	0.029765	.007159	2.04 (24:0)	.0000
XRAY (1 - 10)	0.054193	.02773	1.63 (10:1)	.0509
CONSTANT	-1.7659	.1034		

The coefficients were estimated by the method of maximum likelihood.
XRAY (1 - 10) refers to the extent of silicosis with 1 equal to ILO 0/0 and 10 to ILO 3/3 [120].
O.R.(Odds Ratio) is the odds that a subject will have a wheeze. If the O.R. is 1 that variable has no influence; O.R.>1 indicates an excess chance and O.R.<1 a decreased chance of wheezing induced by increasing values of the variable.
The CONTRAST refers to the values of that variable being compared: thus a man with a chest radiograph showing 3/3 nodule profusion is being compared with a man with 0/0 nodule profusion. The O.R. of 2.7 indicates that the man with 3/3 silicosis has a 163% greater chance of wheezing than the man with a 0/0 radiograph, given that the other variables are the same.

Although the coefficient/standard error value (Z) for XRAY did not reach significance at the 5% level, this variable was shown to be of significance by the maximum likelihood Chi square analysis.
Other variables entered which failed to reach significance included YEARS worked UNDERGROUND and airway reactivity as indicated by a difference of more than 10% in the pre-and post-salbutamol measurements of the FEV1.

TABLE 26

ASSOCIATIONS OF OTHER SYMPTOMS WITH WHEEZING BY LOGISTIC REGRESSION

VARIABLE	COEFFICIENT	STD. ERROR	O.R.	P
COUGH	0.9628	.302	2.62	.0017
SPUTUM	0.61477	.213	1.85	.0045
VARIABLE DYSPNOEA	0.72349	.207	2.06	.0006
DYSPNOEA	0.91634	.1979	2.50	.0000
CONSTANT	-2.9744	.2516		

This analysis shows that there is an association between all of the symptoms enquired after and wheezing.
O.R. (Odds Ratio) indicates the odds that wheezing will be present for each of the variables. The variables are all dichotomous and the O.R. for cough of 2.62 indicates that compared with subjects with no cough, subjects with a cough will have a 262% greater chance of wheezing.

7.6 PULMONARY FUNCTION TESTS

7.6.1 Forced vital capacity (FVC)

The mean FVC expressed as the percentage of the predicted value based on age and height [123] was 93.6% (SD 13.50%). The FVC was highest for those in the dustiest occupations. When analysed by multiple linear regression, the strongest determinant of the FVC was the presence and extent of silicosis on the chest radiograph (Table 27, p99). Evidence of airway reactivity from a greater than 10% change in FEV1 after salbutamol was associated with a small but significant reduction of the best of the pre- and post-bronchodilator FVC.

7.6.2 Forced expiratory volume in 1 second (FEV1)

The mean FEV1, also expressed as the percentage of the predicted value based on height and age [123], was 89.1% (SD 15.60%) (Table 28, p100). The FEV1 was significantly reduced with increasing radiological categories of silicosis, with longer periods of work underground and with tobacco smoking. This last factor is noted to be significant although no significant difference was found when the mean predicted FEV1 in smokers was compared with that in non-smokers using a Student's T test. The best FEV1 was significantly reduced in those who displayed increased airway reactivity indicated by a greater than 10% change in the FEV1 after salbutamol inhalation. There was an improvement in the actual FEV1 in relation to the predicted FEV1 with increasing age.

7.6.3 FEV1/FVC %

The mean FEV1/FVC% which is expressed as such and not as a percentage of the predicted value was 79.5% (SD 8.30%). There was a reduction in the FEV1/FVC% with an increase in profusion of nodules on the chest radiograph, with increasing duration of occupational dust exposure, with tobacco smoke and with airway reactivity (>10% change in FEV1 after salbutamol) (Table 29, p101).

7.6.4 Maximal-mid-expiratory flow rate (MMEF)

The mean MMEF expressed as the percentage of the predicted value for age and height [123] was 80.9% (SD 33.51%) (Table 30, p102). The MMEF was decreased in association with the radiological profusion of nodules, the duration of silica-containing dust exposure, number of pack years equivalent of tobacco smoking and with evidence of airway reactivity. There was a small and probably insignificant increase of the MMEF in relation to the predicted value with increasing age of the subject.

TABLE 27

MULTIPLE LINEAR REGRESSION

DETERMINANTS OF THE FORCED VITAL CAPACITY IN DUST EXPOSED MEN WITH AND WITHOUT SILICOSIS

R sq 0.039 MEAN FVC 93.63 % pred Root MSE 13.26 P of F .0001

VARIABLE	COEFFICIENT	STD.ERROR	T	P
INTERCEPT	97.3877	0.8207	118.66	.0001
XRAY (1 - 10)	-0.9219	0.1528	-6.03	.0001
DUST GRADE 3	2.0364	0.8387	2.43	.0153
REACTIVE AIRWAYS	-2.7140	1.1966	-2.27	.0235

The XRAY represents the ILO category of silicosis with XRAY 1 equivalent to ILO category 0/0 and XRAY 10 to ILO 3/3 [120].
Dust grade 3 is a dummy variable which is equal to 1 if the level of dust exposure was at the highest level - grade 3, and is otherwise equal to zero.
Reactive airways is a dummy variable which is equal to 1 if the pre-and post-salbutamol FEV1 measurements varied by more than 10% and is otherwise equal to zero.
T is the test for the significance of the contribution of that particular estimate to the regression model.

It is noted that exposure to the highest level of dust is associated with a greater vital capacity (see discussion).
Using the regression model, a man with a chest radiograph showing a nodular opacification equivalent to ILO silicosis category 2/2 [120] which is represented by XRAY 7, will have a forced vital capacity expressed as a percentage of the predicted which is (0.9219 x (7-1)) = 5.5% less than that of an otherwise similar man with XRAY 1 (ILO 0/0).

TABLE 28

MULTIPLE LINEAR REGRESSION

DETERMINANTS OF THE FORCED EXPIRATORY VOLUME IN 1 SECOND IN MEN WITH AND WITHOUT SILICOSIS

R sq 0.089 MEAN FEV1 89.12 % pred Root MSE 14.92 P of F .0001

VARIABLE	COEFFICIENT	STD.ERROR	T	P
INTERCEPT	94.3366	3.1561	29.89	.0001
XRAY (1 - 10)	-1.5001	0.1764	-8.50	.0001
YRS U/GRD	-0.2134	0.0829	-2.57	.0102
AGE (years)	0.1897	0.0920	2.06	.0395
PACK YEARS	-0.1596	0.04712	-3.39	.0007
REACTIVE AIRWAYS	-4.7000	1.3467	-3.49	.0005

The XRAY represents the ILO category of silicosis with XRAY 1 equivalent to ILO category 0/0 and XRAY 10 to ILO 3/3 [120].
YRS U/GRD represents the number of years since the man first worked underground in a gold mine.
Reactive airways is a dummy variable which is equal to 1 if the pre-and post-salbutamol FEV1 measurements varied by more than 10% and is otherwise equal to zero.
T is the test for the significance of the contribution of that particular estimate to the regression model.

It should be noted that age had a positive effect indicating that the estimate of the predicted FEV1 increases with increasing age (see discussion).
Smoking, expressed as pack years - the equivalent of smoking 20 cigarettes per day for a year - has a significant negative influence on the FEV1 which was not apparent smoking was used as a dichotomous variable (see Table 15,p82). Using the model, the predicted FEV1 would be 4% less for a man who has smoked 20 pack years compared with a similar man who has never smoked.

TABLE 29

MULTIPLE LINEAR REGRESSION

DETERMINANTS OF THE FEV1/FVC % IN DUST EXPOSED MEN WITH AND WITHOUT SILICOSIS

R sq 0.096 MEAN FEV/FVC 79.48 % Root MSE 7.90 P of F .0001

VARIABLE	COEFFICIENT	STD.ERROR	T	P
INTERCEPT	86.9447	0.8368	103.90	.0001
XRAY (1 - 10)	-0.5534	0.0933	-5.93	.0001
YRS U/GRD	-0.1332	0.0306	-4.35	.0001
PACK YEARS	-0.1433	0.0247	-5.80	.0001
REACTIVE AIRWAYS	-2.9986	0.7130	-4.21	.0001

The XRAY represents the ILO category of silicosis with XRAY 1 equivalent to ILO category 0/0 and XRAY 10 to ILO 3/3 [120].
YRS U/GRD is the number of years since the men first worked underground in a gold mine.
Reactive airways is a dummy variable which is equal to 1 if the pre-and post-salbutamol FEV1 measurements varied by more than 10% and is otherwise equal to zero.
T is the test for the significance of the contribution of that particular estimate to the regression model.

TABLE 30

MULTIPLE LINEAR REGRESSION

DETERMINANTS OF THE MAXIMAL MID-EXPIRATORY FLOW RATE IN DUST EXPOSED MEN WITH AND WITHOUT SILICOSIS

R sq 0.097 MEAN MMEF 80.93 % pred Root MSE 31.91 P of F .0001

VARIABLE	COEFFICIENT	STD.ERROR	T	P
INTERCEPT	98.6738	6.7512	14.62	.0001
XRAY (1 - 10)	-2.9464	0.3774	-7.81	.0001
YRS U/GRD	-0.6063	0.1773	-3.42	.0006
PACK YEARS	-0.5143	0.1008	-5.10	.0001
REACTIVE AIRWAYS	-7.9275	2.8808	-2.75	.0060
AGE (years)	0.3499	0.1969	1.78	.0758

The XRAY represents the ILO category of silicosis with XRAY 1 equivalent to ILO category 0/0 and XRAY 10 to ILO 3/3 [120].
YRS U/GRD is the number of years since the men first worked underground in a gold mine.
Reactive airways is a dummy variable which is equal to 1 if the pre-and post-salbutamol FEV1 measurements varied by more than 10% and is otherwise equal to zero.
T is the test for the significance of the contribution of that particular estimate to the regression model.

Although the coefficient for age was not significant removal of this variable increased the root mean square error.

7.6.5 Single breath carbon monoxide lung diffusion (DlCO)

The mean DlCO expressed as the percentage of the predicted based on the height and age of the subject [124] was 100.7% (SD18.72). The DlCO was progressively reduced with increasing radiological nodule profusion and with exposure to tobacco smoke (Table 31, p104).

Of the 612 smokers, 215 stated that they had smoked during the morning prior to the test. There was no significant difference in the mean predicted DlCO in those that had smoked (98.2%) and the 397 smokers who stated that they had not smoked (98.8%) (T = 0.39, P = .69).

7.6.6 Response to bronchodilator

Following inhalation of salbutamol 200 mcg, the FVC changed by more than 10% in 103 subjects, the FEV1 in 139 subjects and the MMEF in 702 subjects. The change in FEV1 was taken to represent a specific test of airway reactivity and subjects with and without this response were compared. The two groups differed in all the components of the forced expiratory flow volume curve but not in DlCO, age, duration of underground work nor category of silicosis (Table 32, p105). There were no differences in the two groups with regard to respiratory symptoms nor to a history of chest illness in childhood (Table 33, p106).

TABLE 31

MULTIPLE LINEAR REGRESSION

DETERMINANTS OF THE SINGLE BREATH LUNG DIFFUSION FOR CARBON MONOXIDE IN DUST EXPOSED MEN WITH AND WITHOUT SILICOSIS

R sq 0.082 MEAN DLCO 100.74 % pred Root MSE 17.96 P of F .0001

VARIABLE	COEFFICIENT	STD.ERROR	T	P
INTERCEPT	110.3974	1.2049	91.62	.0001
XRAY (1 - 10)	-1.6169	0.2071	-7.81	.0001
PACK YEARS	-0.3464	0.0559	-6.20	.0001
DUST GRADE 3	2.2596	1.1358	1.99	.0469

The XRAY represents the ILO category of silicosis with XRAY 1 equivalent to ILO category 0/0 and XRAY 10 to ILO 3/3 [120].
Dust grade 3 is a dummy variable which is equal to 1 if the level of dust exposure was at the highest level - grade 3, and is otherwise equal to zero.
Reactive airways is a dummy variable which is equal to 1 if the pre-and post-salbutamol FEV1 measurements varied by more than 10% and is otherwise equal to zero.
T is the test for the significance of the contribution of that particular estimate to the regression model.

Exposure to the highest intensity of dust is noted to have a positive influence on the DLCOsb (see discussion).

TABLE 32

CONTINUOUS VARIABLES BY AIRWAY REACTIVITY

VARIABLE	NORMAL REACTIVITY (1058) MEAN	S.D.	HYPERREACTIVE (139) MEAN	S.D.	T	P 2 tail
FVC % PRED.	93.9	13.43	91.3	13.84	2.16	.0312
FEV1 % PRED.	89.7	15.24	84.9	17.60	3.39	.0007
FEV1/FVC %	79.6	8.74	76.9	11.89	3.30	.0010
MMEF % PRED.	81.8	33.02	73.9	36.34	2.63	.0087
DlCO % PRED	100.6	18.65	102.2	19.25	-0.99	.3242
YRS U/GRD	25.1	7.67	25.0	7 85	0.22	.8290
AGE (years)	46.2	6.82	45.6	7.32	0.95	.3448
XRAY (1-10)	4.4	2.50	4.4	2.62	-0.01	.9933
PACK YEARS	9.4	9.37	9.1	8.78	0.28	.7725

FVC (forced vital capacity), FEV1 (forced expiratory volume in 1 second), MMEF (maximal mid-expiratory flow rate) and DLCOsb (single breath lung diffusion for carbon monoxide) are all expressed as the percentage of the measure predicted on the basis of age and height [123,124]. The FEV1/FVC % is expressed as such. PACK YEARS is a summary of the smoking history expressed as the number of years of smoking approximately 20 cigarettes per day. YRS U/GRD is the number of years since starting work underground in a gold mine. XRAY 1 to 10 reflects the extent of silicosis with 1 and 2 equivalent to the ILO [120] categories 0/0 and 0/1 and 10 as ILO 3/3.

TABLE 33

DICHOTOMOUS VARIABLES BY AIRWAY REACTIVITY

VARIABLE	NORMAL REACTIVITY 1058	HYPER-REACTIVE 139	CHI SQ	P
DYSPNOEA	265	40	0.90	.343
COUGH	810	33	0.00	.937
SPUTUM	651	96	2.97	.085
WHEEZE	232	40	3.28	.070
VARIABLE DYSPNOEA	215	35	1.79	.181
DYSPNOEA AT NIGHT	59	10	0.21	.659
CHILD CHEST ILLNESS	336	45	0.02	.883
PULMONARY TB	55	6	0.20	.657

Dyspnoea was judged to be present if present with walking upstairs or up hills or with any less strenuous activity.
Child chest illness refers to any recalled chest illness during childhood which the subject recalled or had been told of by a parent.
Pulmonary tuberculosis refers to a confirmed occurrence of that disease in the past.

7.6.7 Lung function by day of week

A total of 296 of the 1197 subjects had performed their lung function tests on a Monday and had, thus not been exposed to mine dust for at least 45 hours prior to the test compared with an average of 18 hours since exposure for those tested on the other weekdays. There was no significant difference in the lung function tests between the Monday and other days groups. There was a tendency for the Monday group to have more reactive airways indicated by a change in FEV1 between pre- and post-bronchodilator measurements of more than 10% (chi sq df1 = 4.05, P = .044).

7.7 EFFECT MODIFICATION

In the general linear models for each of the measurements of lung function, no interaction variable involving the main determinant and the other potential determinants reached significance. There was, thus, no evidence of effect modification on or by tobacco smoking, duration of dust exposure, intensity of dust exposure and silicosis.

7.8 RESPIRATORY IMPAIRMENT

Using the American Thoracic Society definition of respiratory impairment [116], 43 men had moderate impairment on the basis of FVC, FEV1 or DlCO being less than 60% of predicted and 7 men had severe impairment on the basis of FVC being less than 51% or FEV1 or DlCO being less than 41%. Moderate or severe impairment correlated with dyspnoea greater than grade 1 (chi sq df1 = 40.8, P <.001) and there was significantly greater smoking history (P =.01), duration of dust exposure (P = .003) and, particularly, grade of silicosis (P = .0001) in those with moderate or severe impairment. There were no significant differences between the ages of those with and those without impairment.

7.9 PREDICTED LUNG FUNCTION

The regression equations used for the predicted lung function tests in this study were compared with a set of regression equations derived from the study population. The members of the study population used for this analysis were the 218 subjects who had never smoked and who had no silicosis or silicosis with a nodule profusion less than 2/1 [120]. The results are presented in Table 34 (p109) and show a close relationship between the American Thoracic

Society (ATS) predicted values which are used throughout this thesis [123,124] and the values in this subset of the study population.

TABLE 34
REGRESSION EQUATIONS FOR LUNG FUNCTION

	REGRESSION EQUATION						PREDICTED	% DIFFERENC
FVC								
ATS	0.06H	-	0.0214A	-	4.650		4.38 litre	
EOH	0.056H	-	0.0236A	-	4.179		4.05 litre	- 7.5%
FEV1								
ATS	0.0414H	-	0.0244A	-	2.190		3.57 litre	
EOH	0.0401H	-	0.0266A	-	2.150		3.30 litre	- 7.6%
MMEF								
ATS	0.0204H	-	0.038A	+	2.133		3.78 litres/sec	
EOH	0.0214H	-	0.0499A	+	2.242		3.50 litres/sec	- 7.4%
DlCO								
ATS	0.41H	-	0.21A	-	26.31		32.24 ml/min/mmHg	
EOH	0.37H	-	0.30A	-	12.58		35.16 ml/min/mmHg	9.1%

A = age in years H = height in cms

ATS - American Thoracic Society [123,124]
EOH - Ernest Oppenheimer Hospital - present study regression equations derived from subjects who have never smoked and who have less than ILO category 2/1 nodule profusion [120] on their chest radiographs.

The calculated values are based on a man of the study mean height (166.42 cms) and mean age (46.12 years)

7.10 PULMONARY TUBERCULOSIS

A history of pulmonary tuberculosis in the past (lifetime prevalence) was obtained and confirmed for 61 of the subjects in the study. The lifetime prevalence of pulmonary tuberculosis was 2.1% in those without silicosis, 4.6% in those with category 1 silicotic nodule profusion, 7.7% in category 2 and 10.2% in category 3 silicosis. The difference between these prevalences is significant (chi sq df3 = 14.65, P = .002). After controlling for silicosis and for age there is evidence of a small but significant contribution by duration of silica-containing dust exposure to the probability of developing pulmonary tuberculosis.

The men who had had pulmonary tuberculosis prior to their study had significant reductions of FEV1, FEV1/FVC%, MMEF and DlCO. They were not significantly older but had worked for longer underground and had smoked more than those who had not had tuberculosis (Table 35, p111). The 70 men who developed tuberculosis after entry to the cohort had no significant reduction of their lung function, tested before they developed tuberculosis, compared with those who did not have and did not develop tuberculosis. The men who had had tuberculosis complained more of cough than those with no past history of tuberculosis but could not otherwise be distinguished by their symptoms (Table 36, p112).

TABLE 35

CONTINUOUS VARIABLES BY HISTORY OF PULMONARY TUBERCULOSIS

VARIABLE	NO TUBERCULOSIS (1136) MEAN	S.D.	TUBERCULOSIS (61) MEAN	S.D.	T	P 2 tail
FVC % PRED.	93.8	13.29	91.0	16.79	1.566	.1177
FEV1 % PRED.	89.4	15.32	83.8	19.48	2.725	.0065
FEV1/FVC %	79.5	9.13	76.1	9.91	2.773	.0056
MMEF % PRED.	81.5	33.14	69.43	38.32	2.759	.0059
DLCOsb % PRED	101.2	18.5	91.5	20.47	3.998	.0001
YRS U/GRD	25.0	7.69	28.1	7.40	-3.077	.0021
AGE (years)	46.1	7.04	47.6	6.90	-1.579	.1146
HEIGHT (cms)	166.5	6.00	166.1	5.94	0.491	.6238
XRAY (1-10)	4.31	2.50	5.7	2.39	-4.188	.0001
PACK YEARS	9.22	9.28	12.0	9.32	-2.316	.0207

FVC (forced vital capacity), FEV1 (forced expiratory volume in 1 second), MMEF (maximal mid-expiratory flow rate) and DLCOsb (single breath lung diffusion for carbon monoxide) are all expressed as the percentage of the measure predicted on the basis of age and height [123,124]. The FEV1/FVC % is expressed as such. PACK YEARS is a summary of the smoking history expressed as the number of years of smoking approximately 20 cigarettes per day. YRS U/GRD is the number of years since starting work underground in a gold mine. XRAY 1 to 10 reflects the extent of silicosis with 1 and 2 equivalent to the ILO [120] categories 0/0 and 0/1 and 10 as ILO 3/3.

TABLE 36

DICHOTOMOUS VARIABLES BY PULMONARY TUBERCULOSIS

VARIABLE	NO PTB 1136	PAST PTB 61	CHI SQ	P
DYSPNOEA	283	22	3.79	.052
COUGH	861	55	6.66	.010
SPUTUM	703	44	2.59	.107
WHEEZE	253	19	2.60	.107
VARIABLE DYSPNOEA	231	14	0.19	.667
CHILD CHEST ILLNESS	359	22	0.53	.466
VARIABLE FEV1	133	6	0.20	.657

Dyspnoea was judged to be present if present with walking upstairs or up hills or with any less strenuous activity.
Child chest illness refers to any recalled chest illness during childhood which the subject recalled or had been told of by a parent.
Variable FEV1 refers to a change of more than 10% in the FEV1 measured before and after a dose of salbutamol by pressurised aerosol.

TABLE 37

ASSOCIATIONS WITH PULMONARY TUBERCULOSIS ANALYSED BY LOGISTIC REGRESSION

VARIABLE	COEFFICIENT	STD ERROR	O.R. (CONTRAST)	P
YRS U/GRD	0.030467	.01317	1.58(25:15)	.0198
XRAY (1 - 10)	0.22348	.04099	7.47(10:1)	.0000
CONSTANT	-4.0756	.4087		

The coefficients were estimated by the method of maximum likelihood. Yrs U/GRD refers to the number of years since the man first worked underground in a gold mine. XRAY (1 - 10) refers to the extent of silicosis with 1 equal to ILO 0/0 and 10 to ILO 3/3 [120].

7.11 SUMMARY OF CROSS-SECTIONAL STUDY RESULTS

7.11.1 Silicosis

Multivariable analysis shows that silicosis as defined by the presence of regular nodular opacification on the chest radiograph is associated with dyspnoea, a reduction of the FVC, FEV1, FEV1/FVC%, MMEF and DlCO. Silicosis is associated with an increase in the lifetime prevalence of pulmonary tuberculosis which increases with an increase in the extent of silicosis (Table 37, p112).

The independent determinants of silicosis include the duration and intensity of silica-containing dust exposure.

7.11.2 Duration of silica-containing dust exposure

Duration of silica-containing dust exposure determines the extent of silicosis and is also associated with reductions of FEV1, FEV1/FVC% and MMEF. There is no association between respiratory symptoms and duration of dust exposure. After controlling for silicosis, as defined, there is a direct relationship between the occurrence of pulmonary tuberculosis and the duration of silica-containing dust exposure (Table 37, p112).

7.11.3 Intensity of dust exposure

The intensity of dust exposure is directly related to the frequency of cough, sputum production and dyspnoea.

Silicosis is more strongly associated with the intermediate intensity level of dust exposure than with the highest level. The levels of FVC and D1CO are higher in men who are exposed to the highest intensity of silica-containing dust.

7.12 COHORT (LONGITUDINAL) STUDY

The cohort of 1 197 men formed by inclusion in the cross-sectional study had contributed 2961.1 person years of experience on 31 July 1987. Five men had died; one with cirrhosis of the liver; one in a motor accident; one in a mine mud rush; one from a stab wound in the heart; and one man who had no respiratory impairment and had category 2 silicosis died of an unknown cause, while at home.

None of the subjects has yet been recalled for follow-up lung function studies.

7.12.1 Pulmonary tuberculosis

There had been a total of 70 incident cases of pulmonary tuberculosis since the dates on which the subjects had entered the cohort. The overall incidence of pulmonary tuberculosis was 2.36 per 100 person-years of follow-up. The incidence density ratio for tuberculosis in men with silicosis compared with men without is 7.4 ($P < .001$) and within the silicotic group the incidence density increases with increasing nodule profusion. The incidence of tuberculosis by category of silicosis is presented in Table 38 (p115).

TABLE 38

INCIDENCE OF PULMONARY TUBERCULOSIS IN RELATION TO SILICOSIS

CATEGORY OF SILICOSIS (no. in category)	INCIDENT CASES OF PTB	CASES/100 PERSON YEARS SINCE ENTRY	ESTIMATED 5 YEAR RISK OF PTB
0 (340)	7	0.77	3.8%
1 (432)	21	2.03	9.7%
2 (376)	29	3.20	14.8%
3 (49)	13	11.85	44.7%
TOTAL (1197)	70	2.36	11.1%

TABLE 39

SUMMARY OF RESULTS

DETERMINANTS

OUTCOMES	SILICOSIS	YEARS U/GROUND	DUST INTENSITY	SMOKING
DYSPNOEA	x		x	x
COUGH				x
SPUTUM			x	x
WHEEZE	x			x
TUBERCULOSIS	x	x		
FVC%	x			
FEV1%	x	x		x
FEV1/FVC	x	x		x
MMEF	x	x		x
DLCO	x			x
SILICOSIS		x	x	

The outcomes with relation to the lung function measurements FVC, FEV1, FEV1/FVC, MMEF and DlCO indicate that those measurements are reduced by the determinant. All of the other outcomes are increased by the determinant.

CHAPTER 8

DISCUSSION

8.1 GENERAL

This study of black, migrant South African gold miners has examined the prevalence and relevance of silicosis in this population. No previous study has examined the health of a working population of these men in relation to their occupational exposure.

The prevalence of silicosis was found to be 136 cases per 10 000 of the black working population rising to a peak of 1 518 cases per 10 000 gold miners in the 51 to 55 year age group.

After controlling for the effects of mine dust exposure, smoking and age, a clear association was found between silicosis and dyspnoea, silicosis and reductions of the DlCO, FVC, FEV1, FEV1/FVC% and MMEF, and between silicosis and pulmonary tuberculosis.

Although the study was not designed to examine the effects of mine dust exposure other than silicosis, the data presented show a reduction of FEV1, FEV1/FVC% and MMEF with an increase in the duration of dust exposure after controlling for the effects of silicosis, age and smoking. There was no association between respiratory symptoms and the duration of dust exposure, but the intensity of dust exposure was directly associated with the frequency of sputum production and dyspnoea.

8.2 PREVALENCE OF SILICOSIS

8.2.1 General

The estimation of the prevalence of silicosis in a working population of black, migrant gold miners, was made while establishing a sampling frame for the cross-sectional study which forms the major part of this thesis. No previous evaluation of the 100 mm chest radiograph has been made to determine the appropriateness of this routine method for the detection of silicosis (and tuberculosis) in South African gold miners. In this study the prevalence of silicosis has been estimated and the sensitivity and specificity of the 100 mm chest radiograph has been examined using the full-size, 125 kV postero-anterior chest radiograph as the criterion of validity.

8.2.1 Limitations of the study

The major limitation of the study to determine the prevalence of silicosis was the lack of knowledge of the number of non-silicotic men who contributed to the workforce during the period of the study. This subject has been discussed in section 7.1.2 p49. The method used to estimate the number of men who contributed to the workforce during the sampling period is known to have overestimated the denominator and resulted in an underestimate of the prevalence of silicosis in the population. The extent of this underestimate is not known but if one were to assume a stable workforce with no exchange of individuals, the denominator would be the number of men in the working population at the mid-point of the study period and the prevalence of silicosis would be 193 cases per 10 000 men. In fact, 800 to 1000 men leave the mines each week and their places are taken by others and the mid-point workforce is clearly an underestimate of the number of subjects in the denominator and thus overestimates the prevalence of silicosis. It would thus be reasonable to assume that the true prevalence of silicosis lies between the 136 and 193 cases per 10 000 men.

8.2.3 Conclusion

The prevalence of silicosis in this working population has been estimated to be 136 per 10 000 men and is not likely to exceed 193 per 10 000 men. In the 51 to 55 year old age group the prevalence of silicosis is approximately 1500 per 10 000 (table 1, p52).

The use of the 100 mm chest radiograph appears to have been validated for the detection of silicosis. The sensitivity of 93% is not excessively low for a slowly progressive disorder where repeated evaluations are routinely made and early diagnosis is not essential.

CROSS-SECTIONAL STUDY

8.3 LIMITATIONS OF THE STUDY

8.3.1 General

The cross-sectional study was a prevalence study in that it examined the prevailing determinant and outcome status of those who were currently working. Such a study is not sensitive to different patterns of disease and will underestimate the acute forms of a disorder if they lead to early retirement or death and overestimate the more benign and chronic disorder which does not lead to disability [133]. There is, however, no evidence to suggest the existence of an acute form of silicosis in this population [34] and a prevalence study may be appropriate in this instance.

The cross-sectional design by which the determinant and the outcome are examined simultaneously has also introduced limitations which are characteristic of such a design. In cross-sectional studies the changes attributable to exposure or other determinants are estimated by studying different individuals with different determinant experience rather than by making serial measurements of the same individuals over time. The cohort effect is a special problem of cross-sectional studies [134,135] and is caused by the differences between cohorts born at different calendar time. Thus a man born in 1937 will not necessarily be the same at 60 years of age as a man of 60 who was born in 1927. Glindmeyer et al [134] have shown a cohort effect which amounts to 44 ml or more increase in the FEV1 per decade; thus a 50 year old man in 1987 should have an FEV1 which is 44 ml more than that which a 50 year old man had in 1977. Nevertheless, the cross-sectional design has been widely employed [81,103,113,136] and may have some advantage over longitudinal studies especially when these involve measurements such as lung function tests which may be very difficult to control for intra-subject variability and lack of precision of measurement [14,135].

The general quality of the data was adversely influenced by a complete lack of specific funding for the study. No additional staff were made available and those involved in the study did their part while continuing with their normal, full-time occupations.

A further, general defect which will be addressed more specifically elsewhere was the lack of personal, health and occupational data for this working population which had generally been considered to be too transient to warrant relevant record keeping.

8.3.2 The comparison group

The comparison group was formed following the entry to the cross-sectional study on the basis of the summary reading of the full-size chest radiograph but the group was designed at the time of the prevalence study when each case of silicosis was matched by age with a man without silicosis. This design created a group with an age distribution which was similar to that of the men with silicosis. The selection of this comparison group optimised the estimate of the effect of silicosis by providing a good contrast of that determinant and comparability for age and the associated determinants of lung dysfunction, duration of occupational exposure, and smoking. It should be noted that there was no further attempt to match the men with silicosis to the men without silicosis in the sample created for the cross-sectional study and that direct matching for dust exposure was not made at any stage of the study.

It would have been more interesting to have had a second comparison group to create a contrast in the exposure to mine dust. This contrast would have permitted the development of a more stable regression analysis of the effect of mine dust on lung function. This was not possible for two reasons. Firstly, if a group of the younger and thus less exposed miners had been used the cohort effect would have caused a lack of comparability of features other than the difference in dust exposure. This lack of comparability is particularly evident in developing countries [137]. In this working population change with calendar time has been shown in a study which demonstrated the greater height of the younger miners [130]. Secondly, the use of a comparison group from another industry would also not have produced comparable subjects: the salaries in the gold mining industry are higher than those paid to labourers in other industries. As a result, the stronger, healthier men seek and retain work as miners and those physically less well endowed tend to move to other industries. Thus, as is often the case in studies of occupational exposure, lack of exposure is seldom found in an otherwise comparable group [138 pp31-32].

8.3.3 Quality of data

8.3.3.1 Age

Age is one of the more fundamental attributes in any study of this nature. In the population of the present study, knowledge of age is not a general attribute. The age data used in the prevalence study was based on the estimate of each man's age which is made by one of the several clerks employed by the AAC Reception Centre. In the cross-sectional study, the age data was obtained by careful interview of each subject by one individual. The interviewer found that while the majority of men had no idea of their age many did know their year of birth. In some instances this anomaly had caused confusion in that a some of the men did not understand that their age changed each year. In cases where neither the age nor the year of birth were known, the interviewer estimated the man's age using his appearance, information about the age or status of his children or his recollection of major events. Occasionally, the man's age was apparent from his name when names such as Kaiser or Adolph were known to have been popular at a certain time.

Although the age data lacks the accuracy which would be expected in a similar study in a developed country, there is no reason to believe that the estimation of age was biased by knowledge of the man's status in the study; the study design ensured that the man's status with regard to silicosis remained unknown until the study data had been collected.

8.3.3.2 Smoking history

Tobacco smoking habits often vary in this study population according to the man's working status. Cigarette smoking is common during periods of employment but cigarette consumption may fall to very low levels or be replaced with pipe smoking when the man is away from the mine at his home. The one interviewer attempted to obtain an estimate of average consumption from each subject but it is possible that the answer obtained was biased by the subject's most recent consumption pattern. As with the information concerning age, there is no reason to believe that the information concerning tobacco consumption was biased by the man's silicosis status.

8.3.3.3 Respiratory symptoms

The questionnaire concerning respiratory symptoms was conducted by one interviewer for all of the subjects. The questionnaire was designed with the assistance of the interviewer; an experienced pulmonary technician and a registered nurse. The questionnaire did not conform with any of the standard respiratory questionnaires. Its design was dictated by knowledge of the study population, the vocabulary of their several home languages and their beliefs and understanding of symptoms. The questionnaire was printed in English but was conducted in the subject's language by the interviewer. The unstructured nature of the questions asked and the use of several different dialects and languages might have resulted in some inconsistency. However, as noted before, the interviewer had no means of knowing whether the subject would be allocated to the comparison group or to the silicotic group and it is unlikely that the outcome of the interview could have been biased by the subject's determinant status.

The questionnaire included a question about 'phthisis', a word which was believed to be associated with occupational lung disease by the black gold miner. In asking this question it became apparent that no subject was aware of silicosis as a disorder and that there was no word or phrase for any occupational lung disease (other than pulmonary tuberculosis) in any of the languages used by the subjects nor in the lingua franca of the mines, 'Fanagalo'. Therefore, it seems reasonable to assume that the answers to the questionnaire were not biased by the subject's awareness of his silicosis status.

8.3.3.4 Occupational data

There are no accurate data of duration and intensity of exposure for the migrant black gold miner. Men work on the mines for the duration of their contract and then return home for varied periods before returning to work a new contract. The occupational questionnaires were conducted by any one of the several clerks employed in the outpatient department of the Ernest Oppenheimer Hospital. It was felt to be inappropriate to have the occupational questionnaire conducted by the same interviewer who conducted all the respiratory questionnaires as this might have introduced some bias in the respiratory interview. Because no specific clerk could be made available by the hospital authorities for the occupational interview, the questionnaire was constructed for simplicity and for lack of ambiguity.

Each man was asked to indicate the year in which he had first been employed underground on a gold mine and the occupation in which he had been predominantly employed. If he no longer worked underground, the date when he last worked underground was also recorded. The interviews were conducted by clerks who not only did not know the subject's silicosis status but also, in general, had no knowledge of the purpose of the interview.

The duration of exposure used in this study reflects the total time elapsed between the man's first and his last underground gold mine work contract. This figure thus includes periods spent at home between contracts and is not a precise measure of the actual total period of mine dust exposure. The possibility that a systematic difference in time spent away from the mine between work contracts exists between the men with and the men without silicosis has been investigated. Regression analysis of the duration of dust exposure shows a correlation between that determinant and several indices of lung function and between the duration of exposure and the category of silicosis. Thus it seems that this index of duration of exposure, although imprecise, is valid.

The surrogate for intensity of exposure was the nature of the man's predominant occupation. This has also been examined and appears to be validated by its correlation with dyspnoea, variable dyspnoea and sputum production, and to some extent with silicosis. This aspect will be discussed in more detail in section 8.5.5.1, p149.

8.3.4 Validity of data

8.3.4.1 Internal Validity

Internal validity exists when the inferences of a study reflect the status of the study subjects without bias. To have internal validity a study must be without selection bias, information bias and confounding [139 pp82-89]. The method of selection of subjects from the study population was based on the pre-existing, routine radiological screening facility with no element of self-referral nor self-selection. The assessment of the subject's outcome status, his pulmonary function and his respiratory symptoms was made without knowledge of his determinant status thus preventing any diagnostic bias [140]. The assessment of the determinants of interest, silicosis and duration and intensity of dust exposure, were made without knowledge of the subject's outcome status thus avoiding information bias. The lack of awareness by the subjects for their determinant status with regard to silicosis (7.4.6, p83) ensured that there was no recall bias in the main issue. There is a suggestion that recall bias might have operated in relation to the question concerning childhood chest illness which had an association with dyspnoea, cough and variable dyspnoea (Table 19, p87). Confounding is said to occur where there is lack of comparability between the two groups with regard to a determinant of the outcome [138 p321]. In this study, all of the recognised determinants of the outcome, pulmonary dysfunction and respiratory disability, have been included in the study data and controlled for in the analysis.

Thus the study does appear to conform with conventional standards for internal validity.

8.3.4.2 External validity

External validity requires that the subjects studied are an unbiased sample of the study population. The formation of the study frame, by selecting all subjects with silicosis in the process of the routine radiological surveillance and matching those subjects with age and date-of-radiograph non-silicotic controls, created a sample of the working population with the same age distribution as the census (complete sample) of the men with silicosis. That sampling frame was then sampled in order of date of miniature radiograph but with a designed ratio of probable silicotics to probable non-silicotics. The sample which entered the cross-sectional study is likely to be representative of the older age working population in all respects other than in the distribution of silicotic to non-silicotic subjects. External validity or the generalisability of the study findings to the study population may be satisfied when there is no sampling bias and when there is internal validity [141 pp12-13]. Ultimately, when these criteria for external validity are satisfied, generalisability becomes a matter of judgement [139 pp95-96] and there appears to be no reason why the findings of this study should not apply to the general working population of black, migrant gold miners.

8.3.5 Reliability of data

The several weaknesses of the study were mainly due to the nature of the study population and the lack of formal demographic and occupational exposure data. While the study design appears to have minimised any systematic error and the findings appear to be valid there must be some doubt about the precision of the measurements of the determinants and the outcome. The measurement of the main determinant, silicosis, appears to have been reliable although no formal study was made to test the intra-reader agreement, the tests of inter-reader agreement including Cohen's kappa and Kendall's tau-b indicated that the measurement of silicosis was reliable (7.4.3, p67). The tendency, noted in the present study, for the readers to emphasise the mid-categories of nodule profusion is a recognised phenomenon [142] and is due to a large extent to the guidelines of the ILO for the reading of their standard radiographs [120]. The two readers differed in the extent to which they favoured the mid-categories. The summary reading distribution of 60% in the mid-categories is similar to that reported for other studies [142]. Obesity and poor film quality have been identified as major sources of inconsistent radiograph reading [143]. In the present study, very few of the subjects were obese [130] and the radiographs were taken in a modern hospital facility by professional radiographers and were of good quality. There was a good linear association between the summary radiograph readings and the degree of pulmonary dysfunction which would appear to validate the readings [144].

The measurements of lung function were conducted throughout with close attention to the ATS guidelines [121,122]. All of the tests were performed on the same apparatus and by the same technician. The apparatus used has not been validated in a formal study and there can be no absolute certainty concerning the accuracy of the equipment or of the associated computer software, however, any inaccuracy should be equally distributed across the determinant contrast and would not be expected to be a source of bias.

The precision of the measurement of respiratory symptoms cannot be assessed as a non-standard questionnaire was used and repeatability was not examined. A similar constraint must apply to the results of the occupational questionnaire.

Thus the major weakness of the study relates to the lack of precision of some of the data. This appears to be comparable in the index and comparison groups. It can thus be concluded that the study inferences are not biased but that the strength of any association may have been underestimated as a result of the imprecision of the data [132 pp285-307].

8.4 COMPARABILITY OF THE SUBJECTS

The presumption in a cross-sectional study which compares the exposed with the non-exposed or populations with specific and defined differences is that the groups compared are similar in all respects other than the aspect of interest. It has been noted that this presumption has prevented the use of comparison groups from other industries or even from different age cohorts in the same industry. The subject of comparability extends beyond the obvious and factors such as the healthy worker effect [101] and the sick worker effect [106] can create differences in groups within an industry. Similar constraints apply when comparing smokers with non-smokers; is it reasonable to assume that they are comparable in all respects other than their smoking habits? Can one assume that the older men even in the tight age cohort of this study are similar in all respects other than age to the younger men in the study or do they have the characteristics of survivors or those of sick men sheltering in a familiar occupation?

8.4.1 <u>Healthy worker effect</u>

The healthy worker effect was first described and named by McMichael [101] who noted that the mortality rate of men who were actively employed was less than that of the general population. Rothman [139 p84] states that the effect "derives from a screening process, perhaps largely self-selection, that allows relatively healthy people to become or remain workers, whereas those who remain unemployed, retired, disabled, or otherwise out of the active worker population are as a group less healthy". Whilst the healthy worker effect appears now to be quite obvious, it was not accounted for in the design and analysis of studies of occupational exposure prior to 1974. In another way, the healthy worker effect was used when in 1916 the "New Rand Miner" was introduced on the Witwatersrand gold mines. The introduction of exceptionally fit young men was based on an observation - possibly the first of the healthy worker effect - that the more physically fit men appeared to suffer less from the effects of mine dust exposure [6]. The assumption made was that these physically fit men were less susceptible whilst in truth it is probable that they had more reserve and could better tolerate progressive respiratory impairment.

In the present context the healthy worker effect will be extended to examine lung function rather than mortality. The effect results in a systematic underestimation of the consequences of occupational exposure as measured by cross-sectional studies. Thus men entering and staying in an industry with high physical demands will have better than average lung function and even after years of exposure to a substance harmful to the lung, might have had their lung function reduced only to the average normal range. Simultaneous measurement of exposure and lung function will then result in the conclusion that the exposure has not affected lung function when the predicted values used are general population-based. On the other hand, longitudinal studies where the subject provides his own baseline, would show a more rapid than average loss of function [107].

Workers in different industries are often compared to determine the effects of an exposure which is confined to one of the industries. It cannot, however, be presumed that workers in different industries are comparable in all aspects apart from the exposure of interest. The fallacy can be shown by examining the study of Zwi and Becklake in which the lung function of gold miners without silicosis was compared with that of railway workers [97]. In that study, no significant difference was found between the lung function of the two groups and the authors concluded that, in the absence of silicosis, the occupation of gold mining could not be shown to have an adverse effect on lung function. However review of the data they presented, with knowledge of the healthy worker effect, shows that the gold miners had higher baseline lung function and a more rapid decline than the railway workers. Similarly, Sluis-Cremer [145] concluded that black gold miners had no significant decline in their lung function as a result of 10 or more years of occupational exposure. In his study, the comparison group of black employees of a medical institution were probably mainly messengers and cleaners and thus not comparable with the men engaged in heavy physical activity in the gold mines.

Modern epidemiologic studies are designed to take account of the healthy worker effect but the process of self-selection can also operate within an industry. In the present study there is evidence that the healthier men work in the dustiest occupations; the men exposed to the highest intensity of dust, the drillers and their assistants [6,26,146] had levels of FVC and DlCO which were significantly higher than those of men in less dusty occupations. This distribution has also been referred to by Elmes who states that the fittest men do the heaviest and the dustiest work [24].

The healthy worker effect is more complex than had been previously appreciated. It may not be a constant factor and has, in some instances, been shown to apply only in the first years after men start an occupation [100]. The extent of the effect may vary according to outside influences including the general economic climate. Thus, with generally poor employment opportunities, the healthier workers leave industries because their employability is good. At the same time, workers with respiratory symptoms who might normally leave a dusty industry, stay in their jobs for fear of becoming unemployed. This trend can result in a sick worker effect [106]. There is reason to believe that the current South African situation, with a high unemployment rate amongst the black population and the relatively good salaries paid by the gold mining industry, has caused a sharp reduction in the employment of new recruits through retention of older and possibly disabled men within the industry. Thus both the sick worker and the healthy worker effects may be operating together.

8.4.2 Age

The age distribution of the study sample is narrow and any lack of comparability on the basis of age should be minimal. Nevertheless, as mentioned above, the older men may be especially healthy and have thus retained their positions in the industry or they may be disabled and remain in the industry for fear of not finding employment elsewhere. In other words, they may not be strictly comparable with the younger men in the study sample. There is evidence of a survivor population or healthy worker effect in the older age group, who have greater FEV1 and MMEF measurements in relation to the predicted value, when one would have expected lower measurements given the direct relationship between age and the extent of dust exposure. When these indices of lung function are examined by multiple regression with age controlled for the duration of dust exposure and for silicosis and smoking, the greater FEV1 and MMEF persist. However, these results must be interpreted with caution as the analysis is not strictly valid given the lack of the required independence between age, duration of dust exposure and smoking. On the other hand, evidence for increased disability in the older age group is apparent in an increase frequency of dyspnoea in that group. However, this increase in dyspnoea is not uniform across the categories of silicosis. When analysed by logistic regression, there is a significant increase in dyspnoea with age when controlled for silicosis, dust exposure and smoking, but the lack of independence between these determinants might also invalidate this analysis. On balance, it would appear that there are elements of both a survivor effect and of a sick worker effect in the older age group of the study sample but that the influence of each is small.

8.4.3 Tobacco smoking

Recent studies have shown that there may be a 'healthy smoker effect' [147,148]. This effect appears to be a self-selection of those with lesser lung function to be non-smokers. As with the healthy worker effect, this self-selection might have resulted in a systematic underestimate of the effects of smoking where non-smokers are used to provide predicted values for the indices of lung function [147]. The present study suggests that the healthy smoker effect operates in this population. When compared with non-smokers, smokers and ex-smokers had higher levels of FVC which was significant for smokers. The non-smokers had been exposed to mine dust for longer and they were older than the smokers but neither of these determinants was noted to influence the FVC (the forced vital capacity expressed as the percentage of the predicted value for the age and height of the subject [123]). The observed differences between the smokers and non-smokers are significant, if small, and they might indicate that the smokers, prior to their tobacco smoke exposure, had generally higher indices of lung function.

Comparisons between the men who were smoking at the time of the study and those who no longer smoked but had smoked in the past, showed differences which would be expected from the greater tobacco smoke exposure of the current smokers. However, the ex-smokers differed in another respect; they had a greater frequency of increased airway reactivity as measured by a change of more than 10% between the pre- and post-bronchodilator FEV1. It cannot be determined from this study whether the increase in airway reactivity determined that the subject stopped smoking or whether it was caused by his having stopped smoking. A tendency for smokers to have increased airway reactivity has been demonstrated [149] and it is probable that those with the greatest reactivity are the ones most likely to be symptomatic and to stop smoking. This feature does, however, suggest that the ex-smoker might differ at least in degree from the current smoker. The ex-smokers were older than the smokers, had been exposed to mine dust for longer and had more silicosis but had smoked, on average, 30% fewer pack years.

It is unlikely that the lack of comparability of these groups has had a significant effect on the main association of the present study but it is possible that it has caused an underestimate of the effect of smoking on lung function in the study sample.

8.4.4 Childhood chest illness and airway reactivity

In the context of comparability of populations, there is no evidence to suggest that the subjects in the present study with a history of a chest illness in childhood represent a subset of the study sample. Increased airway reactivity has a complex relationship with childhood chest illness [150], and with responses to tobacco smoking [149] and to occupational exposure [110]. In the present study, no association could be demonstrated between airway reactivity and a history of childhood chest illness.

Increased airway reactivity may be associated with occupational exposure to dust or gases [110], but it is not certain whether it is caused by such exposure, or whether it is an intrinsic characteristic of the subject. Subjects with increased airway reactivity were evenly distributed across the determinants of interest, dust exposure and silicosis, and are thus unlikely to lead to bias in determining the main associations in the present study.

8.5 POTENTIAL DETERMINANTS OF RESPIRATORY DISORDER

The present study addresses the subject of respiratory disorder by examining lung function and respiratory symptoms including dyspnoea and the symptoms of chronic bronchitis. The factors which influence respiratory status include age, tobacco smoking, airway reactivity, and occupational exposures and diseases. Apart from the determinants of interest in this study, silicosis and mine dust exposure, the other determinants were included because of their potential to modify or confound the main determinant/outcome relationship. Because these additional determinants have not previously been examined in this population, their individual contributions to respiratory status have been studied.

8.5.1 Age

In the age group included in the present study, lung function measurements progressively change with ageing. The influence of age on lung function has been controlled by using a predicted value for each measurement which is specific for the subject's age [123,124]. Thus, a normal man of 35 years will have an FVC which is approximately 100% of predicted as will a normal man of 50 years. There is no evidence of an additional age dependent deterioration of lung function in this population once adjustment has been made for the age-related factors such as pack years of cigarette smoking and duration of dust exposure. With regard to respiratory symptoms, there was no increase in bronchitic symptoms which could be attributed to age and, after controlling for silicosis, a small increase in dyspnoea.

8.5.2 Airway reactivity

It has been suggested that airway reactivity may be a factor which determines the extent to which a subject responds to bronchial irritants including tobacco smoke [149,151,152] and occupational dust exposure [107,110]. In the present study there is evidence that airway reactivity, measured by a change in FEV1 in excess of 10% between the best pre- and post-bronchodilator measurements, is associated with a reduction of the subject's best FEV1, FEV1/FVC%, MMEF and FVC after controlling for all of the other potential determinants. The increased bronchial reactivity has no association with respiratory symptoms; and respiratory symptoms including wheezing have been shown to be poor predictors of airway reactivity [153].

It is not possible with the design of the present study to determine whether the increased reactivity of airways was caused by exposure [110] or preceded it. Other reports have indicated that increasing reactivity of the airways might be one of the signs of occupational disease [154,155]. Poor reproducibility of the forced expiratory manoeuvre may be caused by reactive airways and is associated with a reduction in the indices of flow and volume [154,155]. The ATS requirements for performing lung function tests [122] would usually exclude such subjects from further study. In the present study, subjects who showed a progressive fall in their flow and volume measurements were not excluded; their best expiratory flow-volume effort was accepted. Such poor reproducibility has been related to increased reactivity and to increased response to bronchodilators [156]. Increased responsiveness to bronchodilators - the criterion for hyper-reactivity of the bronchi in the present study - has been shown to be comparable with the standard, methacholine response test of airway reactivity [156].

8.5.3 Childhood chest illness

It has been suggested that there is an association between childhood chest illness and adult obstructive lung disease [157]. In other studies, increased bronchial reactivity has been postulated as the link between childhood chest illness and the susceptibility of the adult to bronchial disease [150,158,159]. If such an association, either a direct one or one via bronchial hyper-reactivity, does exist it might be expected to influence the reaction of bronchi to mine dust. In the present study, 32% of the subjects gave a history of a childhood chest illness. These men did not have an increased frequency of airway reactivity nor any excess in the pulmonary function changes associated with exposure to mine dust. They did complain more often of dyspnoea, cough and wheeze; and these symptoms could have resulted in a biased response: subjects with symptoms being more likely to recall a childhood illness. An increase in respiratory symptoms, with occupational exposure to silica, of subjects who had chest illnesses in childhood has been previously reported [160].

8.5.4 Tobacco smoking

In the present study, 52% of the subjects were current smokers, 19% were ex-smokers and 29% had never smoked. Cigarettes were, or had been, smoked by 82% of the smokers and ex-smokers. The smokers and ex-smokers had significant reductions of MMEF, FEV1/FVC% and D1CO compared with those who had never smoked. The smokers and, to a non-significant extent, the ex-smokers had higher FVC than those who had never smoked. The ex-smokers had a small excess of airway hyper-reactivity when compared with either the current smokers or those who had never smoked. The current smokers did not, but the ex-smokers did, have a significant reduction of FEV1 when the means were compared with those who had never smoked. In this last respect, the present study differs from many others [81,161,162] in having failed to demonstrate a significant mean reduction in FEV1 in those who have smoked when compared with those who have never smoked. Fletcher and Peto [163] have pointed out that prevalence studies often underestimate the effect of smoking based on the FEV1, because of the generally small effect on the non-susceptible smokers who constitute the great majority. A study from Tucson [164] presents findings similar to those of the present study with the FEV1 of smokers showing a non-significant reduction when compared with that of non-smokers. It is possible that this reflects the "healthy smoker effect", given that the smokers in that study also had a significantly higher FVC than those who had never smoked. In the present study, it is possible that the smoking histories have been exaggerated: smoking, especially of bought cigarettes (as opposed to the homemade variety), is a symbol of status in this population and this attitude may have caused an exaggeration of the smoking history; although the smoking data is similar to that of other studies in South African black men [165,166]. These men do not smoke at work as the Orange Free State gold mines are declared "fiery mines"; they also smoke far less when at home between contracts and it is possible that their answer to the questionnaire represented their peak rather than their average consumption. It has been said [167] that a fall of the FEV1 is clearly evident only after the consumption of 20 pack years and the average consumption by smokers and ex-smokers in the present study sample was just above that being 22 pack years. The actual loss of FEV1 in relation to smoking has been calculated in several studies. In one, the changes in FEV1 were said to be apparent at every age in smokers compared with non-smokers and the data presented shows a 7.3% mean reduction in FEV1 in smokers of approximately 20 pack years [161]. In another study [162] it was calculated that 10.8 ml of FEV1 were lost per pack year of smoking. In the present study the mean loss of FEV1 in the current and ex-smokers was estimated to be 2.4

ml per pack year with an average of 22 pack years smoked and in the Tucson study [164] the average loss of FEV1 was 4.0 ml and the average smoked was 45 pack years. Elmes [24] and Morgan [168] have emphasised the role of smoking over occupational dust exposure as a cause of morbidity in workers in dusty occupations. Morgan places the influence of dust at approximately one quarter to one third of that of smoking and notes, too, that susceptible smokers die leaving a survival population, who are less susceptible to smoke, at work on the mines.

A study of slate workers in Wales [113] shows a complex relationship between pneumoconiosis and smoking; men with pneumoconiosis suffer a loss of FEV1 which is not comparable across the categories of smoking, being greatest in non-smokers. In the present cross-sectional study it is possible that a similar effect has confounded the relationship between FEV1 loss and exposure to tobacco smoke. A more complex relationship between occupation lung disease and smoking is supported in the present study by the significant association between a falling FEV1 and smoking, when assessed by multiple regression while controlling for silicosis, duration of dust exposure, age and airway hyper-reactivity. Using the regression equation, for a man of the study average, 46 years of age and 166 cms height, the FEV1 loss can be calculated to be 5 ml per pack year which is similar to the loss of FEV1 in the Tucson study [164]; but substantially different from the 2ml loss per pack year calculated from the crude mean FEV1 for the different smoking categories.

This detailed assessment of the loss of FEV1 in relation to smoking is presented to highlight some of the features of the cross-sectional study; the importance of the concept of non-comparability of populations in contrasting exposure categories, and the indispensable role of multiple regression analyses in unravelling the contributions of several potential determinants of a disorder.

Smoking, whether current or in the past, was associated with an increased frequency of cough, sputum production and wheeze, while the ex-smokers were dyspnoeic significantly more than those who had never smoked.

No relation could be shown between smoking and the extent of silicosis but ex-smokers had more silicosis than current smokers and non-smokers.

8.5.5 Dust exposure

Throughout this thesis references are made to mine dust. Dust should be taken to refer to all of the substances which are contained in the mine atmosphere. The earlier concern with the mining environment has led to an emphasis of silica-containing dust as the occupational exposure of importance. However, other elements in the mine may be of as much relevance as dust, as Irvine and Watt noted in their 1912 paper [6]. Nitrous fumes from explosives are known to cause lung disease which is usually acute but which may be chronic [23 pp474-480,169,170]. Heat has also been implicated in occupational lung disease [171]; and the ambient temperature in the Orange Free State gold mines is generally high with rock temperatures sometimes in excess of 50 degrees C. Dust levels in the Orange Free State mines have been stable since the start of mining in the area 35 years before the present study, and dust levels on the Witwatersrand mines are said to have changed little since 1936 [10,21]. A recent publication gives average figures for respirable dust in South African gold mines ranging from 0.24 to 1.26 mg per cubic metre [146]. The free silica content of the respirable dust probably varies and is quoted as being 30% by Sluis-Cremer [21] and 75% by Wiles and Faure [22]. There appears, also, to be some uncertainty about the validity and relevance of dust measurements made in the South African gold mines. Against the opinions that dust levels have been well-controlled and constant for many years [10,21], there has been the suggestion that levels had increased between 1950 and 1969 [172] and there is also doubt as to whether the konimeter in use in the South African mines [146] provides the most relevant estimates of the dust with the potential to produce disease [172,173]. However, specific dust levels, quality of dust, aspects of dust control and the pathogenesis of silicosis and other occupational disorders are not aspects which have been addressed by the present study.

8.5.5.1 Intensity of dust exposure

It is generally accepted from the work of Beadle [26,174] that the intensity as well as the duration of mine dust exposure correlate well with the degree of silicosis. In the present study, the highest intensity of dust exposure, that of the machine men who operate the drills at the rock face, was not found to be associated with the greatest prevalence of silicosis. The assessment of the intensity of dust exposure was fairly crude, compared with that made for white South African gold miners, [26,103,175] in that no detailed work records exist for the black, migrant mine worker. It is thought possible that men may have tended to exaggerate their employment as machine men, as that is a prestigious occupation on account of its high physical demands and more unpleasant and more dangerous working environment. On the other hand, men do tend to remain in similar occupations and the question asked about their predominant occupation seemed to be confirmed by the limited amount of validated data obtained from the recently started mine computer records. One possible reason for the failure to distinguish between the men on the basis of the level of dust exposure in their workplace, could be the wide differences in energy expenditure, minute ventilation, dust inhalation and dust retention of the individuals within each workplace [79,176,177]. Thus, a locomotive driver sitting in his locomotive will have a lower minute ventilation than that of the 'lasher' shovelling rock into the hoppers attached to his locomotive. As a result, the amount of dust which the locomotive driver inhales will be less than that inhaled by the 'lasher'. Similar contrasts exist in the workplaces reflecting all of the different levels of dust exposure. A report concerning granite workers [178] also emphasises the great difficulty in characterising individual dust exposures. On the other hand, the white gold miners who were the subjects of most of the published studies from South Africa [21,22,26,82,87,96,98,174,175, 179] are involved almost exclusively in supervisory positions and have similar levels of minute ventilation, and thus have a dust load which should more closely reflect their workplace. Nevertheless, Wiid [180] reporting on white gold miners had difficulty in relating the man, his physique, his workplace, the number of shifts worked and the presence and extent of silicosis. Chatgidakis [181], also reporting on white gold miners, found a poor correlation between the duration of their service and the extent of silicosis found at autopsy. Dobreva et al [176] found differences in the quantity and quality of dust in the lungs of men with similar exposure.

A closer examination of the lung function data in relation to the intensity of dust exposure shows that the only measurements which reached significance, although only at the 5% level, were the FVC and DlCO and that in each case, the higher mean was found in the men who worked in the highest of the three grades of dust intensity. This finding suggests, as was previously noted (p135), that the healthiest and strongest men select themselves for the dustiest and most physically demanding work [24]. It would seem to be intuitively correct to assume that these men exposed to the highest levels of dust [10,26] and expending the greatest physical effort with high working minute ventilations, would be more likely to have silicosis and the higher categories of silicosis. In fact, multiple regression analysis with the intensity of exposure controlled for the duration of exposure, confirmed that those with exposure to both the intermediate and to the highest levels of dust had a significantly greater category of silicosis than those exposed to the lowest level. However, the intermediate intensity exposure exceeded the highest intensity exposure in terms of the potential to predict silicosis. There is probably no reason to believe the "New Rand Miners" concept that fitter men are less prone to develop silicosis [6,7]. In fact, the contrary view has been supported by a report showing that men with the highest FEV1 have the greatest penetration of small dust particles into their alveoli [182], and an experimental study with hamsters has shown a 6-fold increase in dust retention in the alveoli when the animals are exposed to dust during exercise compared with exposure at rest [183].

The failure of the present study to show the most advanced silicosis and disturbance of lung function in men exposed to the highest intensity of dust might simply indicate differences in the quality of the dust with regard to the effective particle size and density, and the area of impaction in the respiratory tract [106]. The process of dust collection and measurement may well alter the characteristics of the dust [173] and, in particular, overestimate the quantity of the small particles which are known to cause silicosis [184]. Larger particles will lodge in airways and may lead to bronchitic symptoms from main bronchial impaction and to small airway disease from impaction in the bronchi of less than 2 mm diameter [185]. It has been suggested that the dust particles at the work face are, on account of the water used through the drills, larger particles consisting of small particles adherent to each other [184]. If this is so, these larger particles would be expected to cause bronchitic disease or small airway disease rather than lung parenchymal disease. The analysis of respiratory symptoms in the men exposed to the highest intensity of dust supports these concepts: the men had a greater frequency of sputum production and wheezing, than the men exposed to the intermediate dust intensity. Analysis by logistic regression, while controlling for the other potential determinants, confirmed the association between exposure to the highest dust intensity and sputum production, and also showed a relationship with dyspnoea and a history of variable dyspnoea. Men with intermediate dust intensity exposure could be distinguished from those with the low dust intensity exposure by their greater frequency of dyspnoea. These respiratory symptom data appear to validate the dust intensity information. The failure to demonstrate an effect of high intensity exposure on lung function may be due to the cross-sectional design, which may underestimate the effect of high intensity exposure because of the healthy worker effect, but the lack of association between bronchitic symptoms and chronic airflow limitation is well known [163]. Alternatively, men may move to the lower dust intensity environments as their lung function deteriorates; but evidence for this was lacking and the duration of underground exposure did not differ for men in the three levels of dust intensity exposure. A longitudinal study (which is to be made) might be able to demonstrate, as others have done [107,112], that the men with exposure to the highest dust intensity do, in fact, have a more rapid loss of lung function.

8.5.5.2 Duration of dust exposure

The duration of dust exposure was associated with quite different patterns of outcome from those associated with intensity of exposure. No formula such as that used by Sluis Cremer et al [175] could be designed by combining the duration with the intensity data to permit a more predictive regression equation for the several dependent determinants. This might suggest that the quality of dust associated with the changes in lung function relating to duration of exposure, was present in similar amounts in most of the work places.

In the crude analysis, there were no differences in the frequency of any of the respiratory symptoms in those with less than 25 years of exposure compared with those who had first worked in a gold mine 25 or more years before the study. The men with the greater duration of exposure were older, had smoked more, had more silicosis and had lower mean values for FVC, FEV1, FEV1/FVC% and MMEF but not for DlCO. When analysed by multiple regression controlling for smoking, silicosis and airway reactivity, duration of dust exposure was found to be related to MMEF, FEV1/FVC% and, to a lesser extent, FEV1. These results are similar to those described in men with histological evidence of small airways disease caused by mineral dust in which the MMEF showed greater changes than the FEV1 [86]. In the present study the actual FEV1/FVC% was estimated to decrease by 1.3% per 10 years of mine dust exposure which was comparable with the 1.4% decrease associated with smoking 10 pack years. The percentage predicted, MMEF was estimated to decrease by 6% per 10 years of mine dust exposure and by 5% per 10 pack years of smoking and the FEV1 by 2.1% and 1.6% respectively. In the present study, unlike that described for men exposed to coal mine dust [105], without pneumoconiosis, there was no associated change in the FVC after controlling for other factors. In a study of hard rock miners in Canada, mining exposure was found to exceed the effect of smoking on lung function [81].

The variation in reported findings of symptoms and lung function changes in men exposed to mine dust is similar to that described for men who smoke. Morgan [186] has pointed out that smoking can produce different syndromes and that current smoking habits correlate well with symptoms of chronic bronchitis while the summary exposure data of pack years correlates best with evidence of chronic airflow limitation. It seems probable that the occupational environment to which gold miners are exposed is also capable of producing a range of syndromes including chronic bronchitis [80,82,106], chronic airflow limitation [22,104,109], silicosis [61,131,181,187], and combinations of these syndromes [187].

8.5.6 <u>Silicosis</u>

Silicosis as a determinant of lung dysfunction and respiratory symptoms will be discussed in section 8.6.5

8.6 THE RESPIRATORY DISORDERS ASSOCIATED WITH GOLD MINING

8.6.1 <u>Occupational Bronchitis</u>

In the present study, it was not possible to conduct the standard questionnaire concerning the symptom complex of chronic bronchitis because these subjects give times and dates a low priority and they found the question confusing. Nevertheless, 62% of the subjects stated that they produced sputum and 42% of the subjects stated that they regularly produced sputum on most days and thus appear to qualify for a diagnosis of chronic bronchitis. The non-smokers were not spared; 45% of them produced sputum and 26% produced sputum on most days. These findings are in contrast with those of Sluis-Cremer who found no non-smokers and only 3.5% of the heaviest smokers with a cough and sputum [94]. Paul reporting on black copper miners in Zambia found only 0.1% with chronic bronchitis [188]. The reason that these two studies showed such a low prevalence of chronic bronchitis is not clear but the findings of the present study are consonant with many other reports [22,81,84,87,104]. In a post-mortem study (post-mortems are largely a routine in men who have worked in gold mines), it was found that 66% (616/935) of examinations revealed histological evidence of chronic bronchitis, on the basis of the Reid Index, in black gold miners [80]. Although the authors of that study doubted the significance of their findings, they are compatible with the response to the respiratory questionnaire in the present study. It might be suspected that miners will exaggerate their symptoms in the interest of gaining compensation. In the present study, the matter of compensation was never raised by the investigators nor by the subjects. In general, the small award offered to black miners does not remotely compensate them for loss of earnings and it is far more likely that symptoms would have been under-reported. Wiles and Faure [22] did, in fact, find significant under-reporting of symptoms of bronchitis in white miners when they compared their answers with sputum produced during the period of the examination.

In the present study there was no association between the presence of silicosis and the symptoms of chronic bronchitis (chi sq df1 = 0.67, P = .417), a finding supported by Gilson [79] and by Morgan [106]. Sputum production, expectedly, was associated with smoking and also with the intensity of dust exposure and was especially prevalent in those exposed to the highest levels of mine dust.

8.6.2 Chronic obstructive bronchopulmonary disease

In the present study, evidence of airflow limitation was found to be associated with the duration of dust exposure, silicosis and smoking. There has been some dispute as to the role of mine dust and other mine atmosphere pollutants in the development of chronic airflow limitation (CAL). Elmes [24] and Morgan [106] believe that dust may not be an important cause of CAL in relation to the role of smoking but others have reported findings similar to those of the present study, that dust does cause CAL to an extent which is similar to that associated with smoking [22,86,95,110,171].

The presence of emphysema was not addressed in the present study. Chatgidakis [181] in an 800 autopsy series found that emphysema and silicosis were closely linked. In a more recent case control study, Becklake et al [109] found an association between emphysema and dust exposure, independent from silicosis. In their study, emphysema was found to relate to mine dust exposure and to smoking and not to silicosis nor to a history of bronchitis. It seems probable that emphysema is thus part of the airway disease associated with mine dust exposure contrary to the views of Morgan [106] and Elmes [24].

8.6.3 Acute changes in lung function

Lung function changes in relation to the most recent work shift and the time of that shift have been noted in at least one study of miners [189]. Wiles failed to show any acute airway response to the inhalation of a large amount of mine dust [111]. In the present study, all of the lung function measurements were made at the same time of the day. The men had all worked underground approximately 18 hours before the measurements with the exception of those tested on a Monday when the interval since their last shift varied from 42 to 66 hours. No differences could be found between the men tested on a Monday and those tested on the other days of the week. If there was any acute change in relationship to mine dust exposure, it was no longer apparent 18 hours after the shift.

There is no doubt that the subjects in this study have shown adverse effects from exposure to the mining environment. In theory, these changes, notably the airflow limitation, are far more relevant than silicosis as a potential cause of disability. Silicosis affects less than 2% of this working population [131] but bronchial disease may be more widespread as reflected by the changes observed in the present study after controlling for silicosis. Nevertheless, silicosis affecting those who have been most exposed to mine dust, has the potential to produce additional pulmonary dysfunction in men who may already have CAL and chronic bronchitis.

8.6.4 Silicosis

Although silicosis, in the present study, has been examined as a determinant of the main outcomes, pulmonary dysfunction and respiratory symptoms, it seems appropriate to examine it as the third of the dust-induced syndromes. The presence and extent of silicosis was predicted by the duration of dust exposure. The intensity of dust exposure was a significant factor and although the high intensity was slightly less predictive of silicosis than the intermediate intensity they were each more likely to be associated with silicosis than was the low intensity of exposure. No association could be demonstrated between age or smoking after controlling for duration of dust exposure. In the present study as well as in others [177,180], the presence or extent of silicosis was not influenced by the age at which the man had started work as a gold miner. It has been suggested that bronchitic symptoms are protective against the development of silicosis [88,89] but in the present study as in other studies [22,91] no such effect was detected.

The distribution of the categories of silicosis in the study sample are likely to reflect the distribution in the working population of black gold miners on the Orange Free

State goldfields. There are few men with the Category 3 silicosis [120] and few with large opacities. Whether this reflects a selective tendency for men with these more severe grades of silicosis to leave the industry or whether they are really uncommon will have to be determined by the longitudinal study. Advanced disease is uncommon in the white gold miner [34] and may also be an infrequent finding in the black miner. However, the present study has shown an increasing risk of tuberculosis with increasing profusion of silicotic nodules. Until recently, men with silicosis who developed tuberculosis were not permitted to continue with their underground work and many of them left the industry. It is thus probable that there had been a differential loss of men with more advanced silicosis in the years preceding the study.

8.6.5 Pulmonary dysfunction and symptoms in relation to silicosis

In the present study relationships between silicosis and lung dysfunction and respiratory symptoms were apparent.

Crude comparison of the frequency of symptoms showed that silicosis was associated only with an increased frequency of dyspnoea. This was also true of the subjects with simple silicosis reported by Koskinen [187]. Analysis by logistic regression confirmed the association between silicosis and dyspnoea, after controlling for other variables.

The subjects with silicosis differed significantly from the those without silicosis in respect of their mean levels of all the indices of lung function measured. Analysis by multiple regression showed that silicosis was associated with decreases in FVC, FEV1, FEV1/FVC%, MMEF and DlCO, after controlling for duration and intensity of dust exposure, smoking, airway hyper-reactivity and age. Similar findings were reported by Louw et al [144] in shale workers with pneumoconiosis and by Koskinen [187] in men with simple silicosis. Irwig and Rocks [104] examining white South African gold miners were not able to attribute a decrease in lung function to silicosis. The discrepancy in the findings between black and white South African gold miners raises questions about the comparability of the disease in the two groups. It would seem that black gold miners are exposed to greater intensities of mine dust than are white miners [5]. It has been said that their greater exposure is not important because they are migrant labourers, not career miners, and thus, have short total durations of exposure [5]. The present study is the first which has examined, albeit crudely, the duration of the working life of the black gold miner and it would appear that there are those who remain in service for long periods (study mean 25 years). It is possible that the disease which has been examined in the black South African miner differs from that in the white miner by being of more rapid onset. Although a mean duration of exposure of 25 years places the disease, by definition, into the category of chronic silicosis [19], there may be differences within that category on the basis of duration of exposure. To determine whether a spectrum of silicosis existed in the present study sample, 49 men with silicosis who had apparently worked for 15 years or less were examined to determine whether they differed from the other men with silicosis. No differences could be found in the indices of lung function nor in the frequency of pulmonary tuberculosis in the men with the shorter dust exposure. The reason for the discrepancy between the studies of white South African gold miners and the present study of black gold miners is thus not clear but the results of the present study conform with those of two other modern studies of silicosis [144,187].

8.7 PULMONARY DISABILITY

Because this was a working population, it was not expected that more than a few subjects would have significant pulmonary impairment [116]. More than mild impairment was apparent in 50 subjects of whom 7 had severe impairment. This impairment correlated well with the major determinants of lung function in this study, namely, silicosis, duration of dust exposure and smoking but not with age. It is difficult to comment about the extent to which this occupational exposure causes disability until completion of a longitudinal study which examines men who leave the industry as well as those that remain employed. However, the general impression gained is that older men are very reluctant to leave the industry. Few alternative employment opportunities exist for the older labourer and none offer salaries which are comparable with those paid to miners. The policy in the 5 years prior to the present study, was to inform men with silicosis that they were eligible for compensation should they decide to retire from mining. In fact, only 9 men were compensated for silicosis alone (as opposed to silicosis with tuberculosis) during the 2 years before the study. This suggests that few men with silicosis voluntarily leave the industry for any reason and that the prevalence of disability demonstrated by the present study may be similar to that in the study population.

8.7 PULMONARY TUBERCULOSIS

The cross-sectional study showed that pulmonary tuberculosis was more common amongst men with silicosis than in the non-silicotic comparison group. There was also an increasing prevalence of pulmonary tuberculosis in the past with increasing categories of silicosis. It remained uncertain as to whether silicosis increasingly predisposed to tuberculosis or whether tuberculosis had contributed to the presence and severity of silicosis [14,19]. Several reports suggest that tuberculosis is a cause or at least an aggravating factor in the development of silicosis. Göthe [74] has reported that Bacillus Calme-Guerrin does, at least experimentally, interfere with dust transport from the lung parenchyma to the hilar nodes and also causes an increase in total dust retention by the lungs. Watkins-Pitchford [7] believed that by interfering with the ability of the lung to incarcerate silica in fibrous tissue, tuberculosis actually caused the development of silicosis. However, it is generally agreed that silicosis predisposes to the development of tuberculosis. In the present study, this view was supported by the follow-up of the cohort defined by entry into the cross-sectional study. Incident cases of pulmonary tuberculosis in the cohort confirmed that silicosis which had been determined and categorised prior to the onset of tuberculosis predisposed to the development of tuberculosis and that the degree of predisposition increased with increasing categories of silicosis. This finding conforms with that of other studies [12,60,61,62,181]. The actual mechanism of this predisposition is controversial. The conventional view that silica interferes with the ability of the lung macrophage to counter *Mycobacterium tuberculosis* [65,66] is based on experimental work which might match the situation in acute silicosis but not necessarily that of simple or chronic silicosis [19] which is the subject of the present study. Davis has also challenged the conventional view with studies showing that lung macrophages from silica-dust exposed men have normal viability and function [185].

It would have been expected, given the high number of incident cases of tuberculosis in the cohort of the present study, that there would have been a greater prevalence of tuberculosis in the past in the cross-sectional study. The discrepancy between these data is likely to have been the result of the regulations which existed at the time of the study [119]. These regulations prevented a man who had both silicosis and tuberculosis from continuing to work in an occupation in which he was exposed to silica-containing dust. Very few 'non-dusty' occupations are available on the mines and as most of these are menial, poorly paid positions, the status-conscious, former underground employee generally prefers to leave the industry than to accept this alternative form of employment. The prevalence data for tuberculosis was also diminished by the acceptance only of confirmed cases of tuberculosis. As a result, men who claimed to have developed tuberculosis while employed on other mines or while at home were not included as there was insufficient evidence to support the diagnosis by the criteria used in this study [118]. Nevertheless, the distribution of prevalent cases was similar to that of the incident cases.

A number of the subjects in the present study had been included in a concurrent study of short-course chemotherapy for pulmonary tuberculosis. Fifty-five of the subjects with silicosis had been treated with short-course chemotherapy and two of them had relapsed. Life table analysis of these subjects showed that their outcome did not differ significantly with the outcome of treatment in a general group from the tuberculosis study [54]. This finding conforms with that of another study from the same working population [78] and with that of Jones [77] which show that pulmonary tuberculosis is as responsive to treatment with modern rifampicin-containing regimens as is pulmonary tuberculosis without silicosis. The finding from these three studies and from another predating the use of rifampicin [76] is in conflict with earlier studies and reports [14,190,191] but is supported, although without specific confirmatory references, by Seaton [192, p645] and by Parkes [23 p158].

Disability is an aspect of tuberculosis and silicosis which has not been addressed since the earlier days when tuberculosis was recognised as being the factor which converted simple, benign silicosis to a disabling and lethal disease [7,12,29]. In the present study, pulmonary tuberculosis, although fully treated, was found to be associated with a significant reduction of all the indices of lung function apart from the FVC. This reduction in lung function was not apparent when comparing those who did not have pulmonary tuberculosis with the subjects who subsequently developed tuberculosis and is therefore unlikely to be entirely due to the tendency for those with more severe silicosis, and thus worse lung function, to get tuberculosis. When the tuberculosis effect on lung function was examined while controlling for the degree of silicosis and duration of exposure to mine dust, a trend towards decreased lung function remained although it only reached statistical significance for DlCO. Nevertheless, it seems probable that even with modern and apparently effective anti-tuberculosis treatment, pulmonary tuberculosis does cause respiratory impairment in men with silicosis.

8.8 OTHER DISEASES ASSOCIATED WITH MINE DUST EXPOSURE

The present study has not addressed the subject of lung carcinoma [15,62,181,193], rheumatoid arthritis [19,179,181] and scleroderma [19,175,194,195]. Lung carcinoma has not been shown to be associated with the occupation of gold mining in South Africa [181,193]. Chatgidakis [181] found no association between silicosis and rheumatoid arthritis but Sluis-Cremer et al [196] have shown that the two diseases are associated, with silicosis being more prevalent and more severe in men with rheumatoid arthritis. Scleroderma has been known to be associated with gold mine dust exposure in South Africa since the report of Erasmus in 1957 [194]. A recent report has confirmed that association for black gold miners from the same population which has been the subject of the present study [195].

CHAPTER 9

CONCLUSION

The original purpose of this study was to determine whether silicosis in black gold miners was associated with pulmonary dysfunction and disability. Evidence from South African and other modern gold mining industries has suggested that chronic silicosis is not a significant disease [34,36,192]. However, the working conditions for black South African miners differ in that they are the labourers in a labour-intensive industry and are thus subjected to higher personal exposures of dust.

The present study has clearly shown that silicosis is associated with changes in all the measured indices of lung function and that men with silicosis have an increased prevalence of dyspnoea.

The well-recognised association between silicosis and pulmonary tuberculosis has a special significance in this working population with its origins in areas where tuberculosis is endemic [197]. An important finding of the present study was the development of further respiratory impairment in men who had been successfully treated for pulmonary tuberculosis. This additional impairment occurs notwithstanding the excellent surveillance and treatment facilities for tuberculosis available to this working population. Measures to *prevent* pulmonary tuberculosis are urgently required and it is hoped that the findings of the present study will provide some impetus for their introduction.

In the present study, the examination of determinants of lung disease other than silicosis was necessary for the more precise definition of the role of silicosis. Although the study was not designed to examine the influence of mine dust on lung function and on the frequency of symptoms, a relationship was detected. The question of the degree to which mine dust can affect lung function cannot be fully answered by the present study. The longitudinal study which is to follow may be able to evaluate the extent to which individual susceptibility, smoking and particular levels of exposure influence the development of lung dysfunction and disability. The constraints of the design of the cross-sectional study have discounted the true extent [138 pp56-8] of the influence of mine dust. Nevertheless, the changes in lung function which can be directly attributed to occupational exposure in a gold mine are similar to or even in excess of the lung dysfunction caused by tobacco smoking. The relevance of this effect of dust exposure is that, while silicosis affects less than 2% of this working population, the chronic airflow limitation and chronic bronchitis associated with exposure to the underground mine environment probably affects all black gold miners.

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APPENDIX

DIAGNOSTIC CRITERIA FOR PULMONARY TUBERCULOSIS [118]

Category	Subcategory	Score
A Chest radiograph	1. Lesions in upper or lower lobe apex	
	a) Infiltration or scarring with cavitation	5
	b) Non confluent infiltration or scarring without cavity	3
	2. Lesions elsewhere - not apical	
	a) with cavitation	2
	b) without cavitation	1
	3. Diffuse lung lesion	
	a) miliary	3
	b) non miliary	2
	4. Lesion in upper or lower lobe apical segment which is new or enlarging and shows no resolution on a 2 month follow up	5
B Sputum	1. Smear positive for AFB* (ZN#)	
	a) once	3
	b) twice	7
	c) 3 times	10
	2. Culture positive for *Mycobacterium tuberculosis*	
	a) once	7
	b) twice	10
C Tuberculin test	1. Heaf Test	
	a) grade 3	2
	b) grade 4	4
	2. Mantoux test (5tu)	
	a)10-19mm	2
	b) >19mm	4
D Histology	1. Lung liver or lymph node	
	a) epithelioid/giant cell granuloma	5
	b) granuloma with necrosis	7
	c) granuloma with AFB*	10
	2. Pleura	
	Epithelioid /giant cell granuloma	10
E Therapeutic trial	Radiological improvement at 2 months of treatment as compared with chest radiograph at one month	3

Note: A total score of 10 was required for the diagnosis of active pulmonary tuberculosis. Only one score was used from each category.

*AFB acid and alcohol-fast bacilli #ZN Ziehl Neelsen stain

MINE ______________________

SILICOSIS STUDY

MINE: ______

CO. No. ______ ______ ______

PP No. ______________________

NAME ______________________

EMPLOYEE'S HISTORY (his own recollection)

YEAR OF FIRST EMPLOYMENT ON A GOLD MINE ______________

or

NUMBER OF YEARS EMPLOYED BY GOLD MINES ______________

MINES AT WHICH HE HAS WORKED
(include coal, asbestos etc.) ______________ ______________

______________ ______________ ______________

HIS USUAL JOB (the one he has done most often)
(for example machine, lasher, winch) ______________________

HAS HE EVER WORKED WITH ASBESTOS? YES / NO

IF YES GIVE THE ACTUAL YEARS WORKED (e.g. 1964 to 1966) ______________

OR

THE NUMBER OF YEARS WORKED AND APPROXIMATELY HOW LONG AGO

____

PLEASE SUBMIT THIS SHEET TO THE RECORDS DEPARTMENT FOR CONFIRMATION OF EMPLOYMENT ON ANGLO AMERICAN MINES

SEND THIS SHEET WITH THE CONFIRMATION PRINT-OUT TO Dr. COWIE.

THANK YOU.

SILICOSIS STUDY

MINE: ______________________ CO. NO.: ______________

1. **DID HE EVER SMOKE ?** YES/NO IF NO GO TO 2.

   IF YES: When did he start ______________

   Does he smoke now ? YES/NO

   IF NO: When did he stop ? ______________

   DID HE / DOES HE SMOKE : More than 15 cigs/day *
   5 - 15 cigs/day *
   less than 5 cigs/day*

   - a pipe
   - homemade cigs
   - bought cigs
   - dagga

2. **IS HE EVER SHORT OF BREATH ?** YES / NO IF NO GO TO 3.

   IF YES: Does it vary from day to day ? YES / NO
   Is it worse at work ? YES / NO
   Is it present at night ? YES / NO
   DOES IT OCCUR
   - at rest *
   - on dressing or washing *
   - walking on level ground *
   - walking up stairs or up hills*
   - with heavy work or with running*

3. **DOES HE COUGH ?** YES / NO IF NO GO TO 4.

   IF YES: Does he cough
   - occasionally*
   - most days*

   - mornings only*
   - through the day*

   - at night YES / NO

4. **DOES HE PRODUCE SPUTUM ?** YES / NO IF NO GO TO 5.

   IF YES: Is sputum produced
   - occasionally*
   - Most days*

   - mornings only*
   - through the day*

5. HAS HE EVER WHEEZED ? YES / NO
6. HAS HE EVER COUGHED UP BLOOD ? YES / NO
7. HAS HE EVER HAD PHTHISIS ? YES / NO
8. HAS HE EVER HAD TUBERCULOSIS? YES / NO
9. DID HE HAVE ANY CHEST ILLNESS AS A CHILD ? YES / NO
10. DID HE SMOKE THIS MORNING ? YES / NO

* CROSS ONLY ONE ANSWER IN EACH GROUP

The Prevalence of Silicosis in Orange Free State Gold Miners

R. L. Cowie, MB, ChB, and M. G. van Schalkwyk, MB, ChB

The prevalence of silicosis in the migrant laborer in the South African, Orange Free State gold mines has not previously been estimated. Two methods were used to estimate the prevalence of silicosis in this population. The two techniques are described. The difference between the two estimates illustrates the difficulty of epidemiologic studies in this type of working population. It is noted that the highest estimate of 138 cases per 10,000 workers is certainly less than the true prevalence of the disorder. The use of routine miniature (100-mm) chest radiographs for the detection of silicosis was validated through comparison with normal size (125-kV radiographs and through analysis of the consistency of reading of second miniature films from the same subjects.

The black gold miner in South Africa is a migrant worker. These migrant workers constitute approximately 90% of the employees in this labor-intensive industry. They work for contract periods of up to 2 years and then return home to renew their contracts. In the past, workers would often remain at home for 6 months and sometimes for even longer periods. At present, the economic climate and a change in conditions of service have produced a more stable work force with workers chosing to spend shorter periods at home between contracts. There is, however, no general rule that can be applied to estimate an average ratio of time spent working to time spent at home. As a result, the total number of individuals contributing to the work force is unmeasured and probably unmeasurable and, thus, the denominator for any prevalence study is uncertain.

The objective of this study was to measure the prevalence of silicosis in migrant black gold miners. Given the nature of the population and a variety of other reasons, the data previously available concerning the prevalence of silicosis in black gold mine workers in South Africa has been incomplete. In this paper we describe the difficulties in making this measurement and present two methods which were used to estimate the prevalence of silicosis.

Methods

For this study we have defined silicosis as a radiologic abnormality consisting of regular nodular opacification of the lung in a subject with a history of exposure to silica-containing dust.[1] The diagnosis was based on a reading of the routine miniature chest radiographs required by law for all gold mine employees. These radiographs were read on a daily basis by one of us (M.G.vS.).

In calculating prevalence, two methods were used. In the first method we determined the proportion of radiographs with features of silicosis in a 6-month sample of radiographs. We used the miniature (100-mm) chest radiographs which are taken at the start of each new work contract (initial films) and at intervals of 6 months throughout the contract (periodical films). The sample consisted of the total initial and periodical chest radiographs for the first 6 months of 1984 and should have included radiographs of all of the current work force. When a radiograph showed changes that were considered to be compatible with silicosis, the identity of the subject was noted and his radiograph packet was labeled to prevent resampling.

The second estimate of the prevalence of silicosis was based on the total number of subjects with silicosis identified during 1984. This 12-month sample included the silicotic subjects in the 6-month sample used in the first method and those detected in a similar way for the second 6 months of 1984. The denominator for this calculation was an estimate of the total number of individuals contributing to the work force for that year.

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0096-1736/87/2901-44$02.00/0

This estimate was made by adding to the number of the men in the work force at the beginning of the year the number of men who entered the work force during the year.

To assess the value of the miniature chest radiograph in detecting silicosis we used data from another study. In that study, cases of silicosis were identified on a daily basis from the routine initial and periodical films. A control subject was selected from those whose radiographs had been read as normal on the same day to match for age each subject with a radiograph showing silicosis. The subjects and their controls were then invited to attend for further investigation, including a full size 125-kV chest radiograph and an occupational questionnaire. A sample of 200 of these cases and controls was studied to compare the routine reading of their miniature chest radiographs by one reader with that of their full size 125-kV chest films by two independent readers.

In addition we evaluated the repeatability of our detection method as follows: 255 subjects whose miniature radiographs had been judged to show no silicosis were found to have had their next periodical film. We compared the reading of the second radiographs with the reading of the first radiographs to determine whether there had been any change in the reader's assessment of silicosis. These subjects were all older men who had been matched for age with those with silicosis. The radiographs of these control subjects were not marked and were thus not identifiable when the subject attended for his next periodical film.

Results

The first estimate of the prevalence was based on 100,880 radiographs taken during the first 6 months of 1984. The number of films read as silicosis was 941 and the proportion of the miniature chest radiographs showing features of silicosis was .00933 (95% confidence limits 0.00873 to 0.00993). Thus, the prevalence of silicosis was estimated by this method to be 87 to 99 per 10,000 black gold miners.

For the second estimate of the prevalence of silicosis, we used the largest possible number of individuals contributing to the work force. This number consisted of 87,470 employed at the beginning of 1984 and the 45,295 new or returning employees who were given contracts during the year, a total of 132,765. During the same period 1,810 subjects with silicosis were detected, yielding a prevalence rate of 136 per 10,000 gold miners (95% confidence limits 134 to 138).

Of the 200 subjects in whom readings of full-size chest radiographs were compared with the reading of their miniature radiographs, 15 had to be excluded, as the two readers could not agree as to whether or not their large films showed changes of silicosis. Analysis of the radiographs of the remaining 185 subjects showed that the sensitivity of the miniature films for detecting silicosis was 93%. The miniature films were 97% specific for the detection of silicosis (see Table).

Table
Sensitivity of Miniature Film for Detecting Silicosis*

		Large film		
		Silicosis	No silicosis	
Miniature film	Silicosis	106	2	108
	No silicosis	8	69	77
		114	71	185

* The sensitivity of the miniature film for detecting silicosis is 93% (106/114 × 100). The overall agreement of the miniature and the large radiographs is 95%: ([106 + 69]/185) × 100.

At the 6-monthly review of the 255 nonsilicotic subjects, the new radiographs of eight of the subjects (3.1%) were found to show changes of silicosis. Thus, in this unrecognized review by the same reader, 97% of the radiographs were read on both occasions as showing no silicosis.

Discussion

The system of migrant labor has made it very difficult to conduct conventional prevalence studies in the black gold miner, as an unknown number of individuals contribute to the work force. On any given day, some men leave for home and others arrive with new work contracts. In addition, legislation intended to protect the miner has further inhibited our knowledge of the true extent of silicosis. This is because (until a recent change in the legislation) the black miner with chronic or simple silicosis was, upon notification, prevented from continuing with his occupation. In effect, the major disability of poverty replaced the often trivial disability of simple silicosis.[1-4] His earning capacity was reduced to less than half and the compensation he received was equivalent to no more than 1 year's loss of earnings. Thus, the legislation invariably inhibited concerned medical staff from reporting silicosis, except in those instances where it was clearly associated with disability or on the retirement of the mine worker. In the present study, it seemed logical to measure the proportion of subjects with silicosis in a random sample of mine workers. The proportion of the disease in the population could then be calculated without needing to know the size of the population. The subjects having routine miniature chest radiographs were judged to represent a random sample of the population as their presentation for radiographic examination was determined by time and not influenced by age, length of service, type of work, or any other disease-associated factors. A sample period of 6 months was chosen as this is the routine interval between periodical chest radiographs. It was expected that the majority of the current work force would thus be included in the sample and that no more than a few individuals would be sampled more than once. The system of identifying cases effectively removed subjects with silicosis from the sample since subjects labeled as silicotic were not included on subsequent sampling.

Thus, we had expected that the number of unlabeled silicotics would drop sharply at the end of the 6-month sampling period. We realized that this system had not worked in practice when we found no falloff in the proportion of silicotics when we continued to look for subjects after the end of the first 6-month period.

The second method involved an estimate of the total number of individuals contributing to the work force. This was known to be an overestimate as, in the calculation, it was assumed that all new contracts were issued to individuals who had not contributed to the work force at the start of the year, whereas it is known that many of these new contracts were issued to men who were returning after short periods at home. The denominator for this prevalence calculation, the population estimate, was further inflated at the expense of the numerator, the silicotics, because a silicotic once labeled would not be counted again, whereas nonsilicotics remained unlabeled and could be sampled more than once. Nevertheless, the estimate of the prevalence of silicosis by the second method provided a mean rate of 136 cases per 10,000 workers, well above the upper 95% confidence limit of 98 per 10,000 determined by the sample proportion calculation. It is clear from this study that the routine chest radiographs gathered over a 6-month period do not represent a random sample of the work force. In fact, the concern of the worker that he might be disqualified from continuing to earn his living by being declared a silicotic appears to have resulted, understandably, in his being partly successful in avoiding the routine chest radiographs. The nature of the system is such that this avoidance cannot be entirely successful but is clearly most expertly applied by the older, more experienced worker who is also more likely to suffer from silicosis.

In the course of this study we have also demonstrated that the miniature (100-mm) chest radiograph has an adequate sensitivity and an excellent specificity in the detection of the nodular opacification of silicosis. This evaluation was made using nonsilicotic subjects who did not reflect the general working population but a group which represents, like the silicotic group, the oldest of our employees. They are certainly not a random sample of the population and the finding that 3.1% of them were judged on the repeat miniature radiograph to have silicosis is not thought to reflect the proportion of missed silicosis in the population. The silicotics and their matched controls were, in fact, an almost complete sample of the older mine workers. It is likely, therefore, that all the silicotics missed in the initial sample were included in the control group, as this group represented the balance of the age-group in which silicosis is detected. A similar study using the general working population as controls would probably have produced higher sensitivity for the detection of silicosis and higher reproducibility rates for the reading of negative radiographs.

In conclusion, we have shown that prevalence studies are extremely difficult to conduct in the migrant labor situation. We have provided evidence that the prevalence of silicosis in the black miner working in the gold mines of the Orange Free State in South Africa is not less than 134 per 10,000.

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The Future of the English Language

Bemoaning the state of the English language has become a popular pastime ...English is the closest thing the world has to an international language. It is currently spoken by some 403 million persons, second only to Mandarin Chinese. Will its power diminish ... ? ...Change in the language is a significant concern, and there are increasingly powerful forces like computers and mass communications that will shape its development [and stabilize it and spread it around the globe].

—Kevin Finneran in *The Futurist* 1986:20(4):9.