

SAFETY IN MINES RESEARCH ADVISORY COMMITTEE

SIMRAC

DRAFT FINAL REPORT

Title: RESPIRATORY HEALTH EFFECTS OF EXPOSURE TO
CRYSTALLINE SILICA

EPIDEMIOLOGY

PRINCIPAL INVESTIGATOR: Eva Hnzido

COLLABORATORS: Jill Murray, Alison Davison

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Executive Summary

The golden ore in the South African gold mines is embedded in a rock that contains 80-90% of quartz, and consequently the dust that results during the mining processes contains high percentage of crystalline silica (silica dust). The primary health concern in subjects exposed to silica dust is with the fibrogenic capacity of the inhaled silica particles that can lead to the development of silicosis. Inhalation of silica dust can also lead to the development of chronic obstructive lung disease (COLD), to lung cancer, and increased susceptibility to develop pulmonary tuberculosis.

Silicosis was a disabling disease that often lead to death in South African gold miners exposed to dust prior to the 1940s. Substantial dust exposure reduction during the 1930s resulted in decreased occurrence and severity of silicosis in gold miners employed after 1940. Although dust levels have declined to some extent since the 1940s, there was no substantial decrease. Epidemiologic studies done on South African gold miners who were employed from 1940 to 1970 and who had almost lifetime follow-up contribute significantly to our current knowledge on the lifetime morbidity and mortality from respiratory disease associated with silica dust exposure. Especially important are studies that were able to link health effects with relatively good estimates of cumulative dust exposure, and estimate exposure-response relationships. These studies used the exposure levels for occupational categories estimated by a study done by Beadle in the late 1960s, and linked these with the occupational history of individual miners to calculate cumulative dust exposure. Cumulative dust exposure estimated in this way correlated well with respiratory diseases.

Several epidemiological studies of white miners employed from 1940 showed that a large percentage of these miners developed mainly simple silicosis after lifelong career of underground mining, and that the risk of silicosis displayed strong exposure-response relationship with silica dust exposure (see Section 5). Generally, the degree of silicosis was not associated with a significant loss of lung function. However, cumulative dust exposure on its own was associated with a significant loss of lung function, with increased mortality from chronic obstructive lung disease, and with increased risk of developing emphysema found at an autopsy. Mortality studies done on white miners have also shown that these miners have an increased risk of dying from pulmonary tuberculosis.

The present report describes two additional studies of exposure-response relationship between respiratory disease and silica dust in gold mines. Section 3 describes a study of pulmonary tuberculosis in relation to silica dust, and Section 4 describes a study of chronic obstructive lung disease in relation to silica dust. Completion of these two studies was partially funded by SIMRAC grant GAP440. For completion, Section 2 provides an overview of respiratory effects associated with silica dust exposure and Section 5 provides a shorten version of a study of silicosis dose-response trend done on white gold miners exposed to dust from 1940 to 1970. This section is intended to give a reader background information on the risk of silicosis in the miners to whom the other studies refer to.

Section 3. Risk of pulmonary tuberculosis (PTB) relative to silicosis and silica dust. In this study a cohort of 2260 white South African gold miners was followed for the incidence of PTB from 1970 to 1995. The exposure-response relationship between the lifetime risk of pulmonary tuberculosis and cumulative silica dust exposure was estimated in subjects with and without silicosis. The study showed the following:

- (1) The risk of PTB is increased in miners with silicosis;
- (2) In the absence of silicosis, the risk of PTB shows an exposure-response trend with cumulative silica dust exposure;
- (3) The diagnosis of PTB was on average 7.6 years after the cessation of exposure, at around 60 years of age;
- (4) The onset of radiological silicosis preceded the diagnosis of PTB in 90.2% of the PTB cases who had silicosis. .

The results of this study have implications for medical surveillance of silica dust exposed workers while employed and after cessation of dust exposure and also for compensation practices.

Section 4 - Chronic Obstructive Lung Disease (COLD). In South Africa chronic obstructive lung disease is a compensable disease. Compensation is based on in life and on autopsy findings at death for COLD. Autopsy findings include emphysema, bronchitis assessed by mucus gland hyperplasia in the main bronchus and bronchiolitis assessed by goblet cell metaplasia. The present study investigated whether the autopsy findings correlated with clinical findings for chronic obstructive lung disease. The results show that emphysema found at an autopsy was the main predictor of in life lung function impairment. After emphysema was adjusted for the findings for bronchitis and bronchiolitis did not contribute to lung function impairment. Tobacco smoking was the main cause of emphysema and was associated with all conditions relating to COLD. The presence of silicosis in the lungs found at autopsy was associated with a restrictive lung function pattern.

Section 5 - Risk of silicosis in white miners exposed from 1940 to 1970. A cohort of white miners exposed to dust from 1940 to 1970 was followed up for the risk of silicosis up to 1990. The study found a strong exposure-response trend with cumulative silica dust exposure. Almost 50% of the miners who developed silicosis diagnosed radiologically did so after dust exposure ceased. The results of this study and the PTB study have implications for medical surveillance of silicosis and PTB in ex-miners and also for the prevention of silicosis and PTB associated with silicosis via the development of dust controls measures.

Applicability of these results to other groups of miners. Although the studies have been done on white miners, they are applicable to black miners also. Even though on average black miners were exposed to higher dust levels than white miners were through those years, in majority of the black miners the extent and severity of silicosis were to some extent controlled by the employment pattern which consisted of intermittent two year contracts. Though there were differences in the exposure pattern between the black and white miners, the autopsy data

from 1974 to 1995 indicate that the extent and severity of silicosis were similar up to 1990. However, the change of an employment pattern onto a more permanent basis in the black miners during the early 1980s is now resulting in an older workforce and increased incidence and severity of silicosis in these miners. The increase in silicosis incidence in the black miners shows that the levels of dust in occupations in which black miners were employed are too high for a lifelong exposure.

In conclusion. The results demonstrate that prevention of silicosis should be a first step in reducing respiratory diseases associated with silica dust exposure. Current exposure threshold limit value (TLV) of respirable silica of 0.1 mg/m^3 in gold mines should be strictly enforced as a first step. However, it needs to be determined whether this is a safe limit in terms of development of silicosis, and in terms of development of other respiratory diseases such as loss of lung function, increased risk of pulmonary tuberculosis and lung cancer. However, because respiratory diseases related to silica dust are progressive in nature and can progress and develop after cessation of dust exposure, safety in terms of lifelong risk need to be determined. According to SIMRAC report GAP 046 the average weighted respirable dust ranged from about 0.20 to 0.70, with average quartz content ranging from 10 to 20%. Thus it is possible that the TLV of 0.1 mg/m^3 is not safe.

Acknowledgements

The authors would like to take this opportunity to express their gratitude to the previous generation of South African researchers who have made it possible to produce this research. Dr Wiles who established the initial miners' cohort. The late Dr Sluis-Cremer who read the X-rays for most of the studies and whose research into occupational lung diseases inspired us to continue. Finally, the pathologists from the National Centre for Occupational Health (NCOH) who performed the autopsies over the years and were interested in research.

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Section 1 - Introduction

The golden ore in the SA gold mines is embedded in a rock which contains 80-90% of quartz, and consequently the dust that results during the mining process contains high percentage of crystalline silica. It is established that inhalation of crystalline silica can lead to respiratory diseases such as silicosis, pulmonary tuberculosis, chronic obstructive lung disease and lung cancer. These diseases are chronic in nature and can develop and progress into a severe disease years after silica dust exposure ceases. It is also recognized that all the above diseases are preventable. To accomplish prevention of these diseases we need to know their epidemiology and the safe exposure levels.

Currently it is still not well established what is the safe exposure level to crystalline silica that prevents development of these diseases during a lifetime. Epidemiologic studies done on South African gold miners have made unique contribution to our current understanding of the epidemiology of silica dust related respiratory diseases; in particular the lifetime risk of the development of these diseases.

This report is related to the epidemiology of respiratory diseases associated with exposure to silica dust and contains the following sections. Section (2): A general overview of respiratory health effects of exposure to crystalline silica; Section (3): Epidemiologic findings from a study of an association between

pulmonary tuberculosis and silica dust exposure; Section (4): Epidemiologic findings from a study correlating inlife lung function impairment with autopsy findings. The discussion of each study is designed to provide an overview of our current knowledge on the epidemiology of these diseases in relation to silica dust exposure. Section (5): For completion of this report we also include a study of risk of silicosis in a cohort of white miners exposed to dust from 1940 to 1970 and followed-up for the onset of silicosis up to 1990. Studies described in Section 3 and 4 were partially funded by SIMRAC grant GAP 440.

We recommend that reader who is interested in an overview only reads the abstracts provided with each section.

Section 2 - Respiratory Health Effects of Exposure to Crystalline Silica - an Overview

The Human Respiratory System

Airborne dust may enter the body by inhalation, but only a fraction of the inhaled particles are deposited in the respiratory system - the remaining dust is exhaled. Some particles are removed from these deposit sites by clearance mechanisms, but others may be transported to reactive sites in the lung to produce lung injury. Soluble particles enter the bloodstream and may be carried to a remote susceptible organ. Particle size and specific gravity largely determine where, and what fraction of particles are deposited.

Understanding the deposition process requires knowledge of the structure of the human respiratory system. This section provides background into the subject that can help to understand some of the epidemiological findings.

Air enters through the nose or mouth and passes through the upper airways where it enters the trachea which divides into the right and left bronchi and these in turn divide into smaller branches called bronchioles (Figure 2-1).

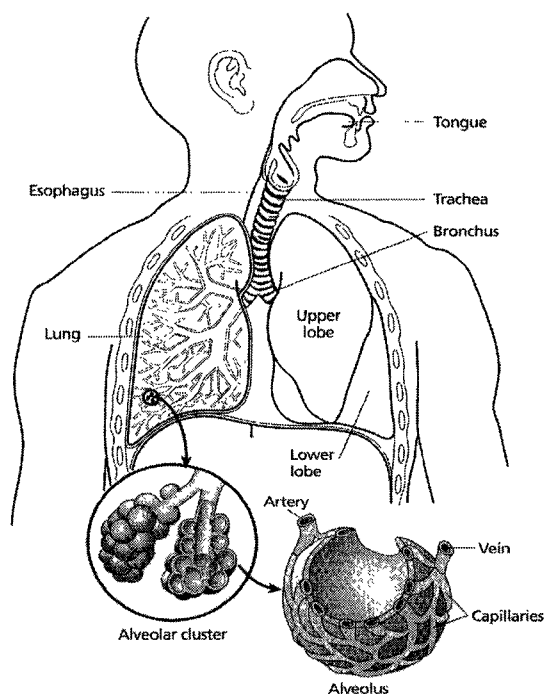


Figure 2-1 The Human Respiratory system

Beyond the terminal bronchioles are alveolar (air) clusters whose walls contain alveoli. The walls of the alveoli contain pulmonary capillaries where oxygen and carbon dioxide interchanges occur. The walls of these alveolar air spaces are very thin and render the lungs extremely vulnerable to airborne substances. Small inhaled particles, which are not deposited in the winding passages and removed by ciliary clearance action along these airways, are deposited in the alveoli and cause adverse reactions.

Most of the coarse airborne particles ($\geq 10 \mu\text{m}$ in diameter) are deposited in the passages are quickly removed by the ciliary clearance action.

The smaller particles, called respirable particles, can penetrate deep into the respirable part of the lungs. The three mechanisms promoting deposition in the lungs, are shown in figure 2-2. 1. Impactation occurs when inhaled particles impact on the airway wall usually at the branching point.

2. Sedimentation occurs under the influence of gravity under minimal air movement. When respirable particles reach this velocity, they are deposited on airway walls or alveolar surfaces.

3. The smallest particles are captured by the diffusion (Brownian motion) process. Under this process airborne particles $< 0.5 \mu\text{m}$ in diameter which reach close proximity of the alveolar wall can be deposited there.

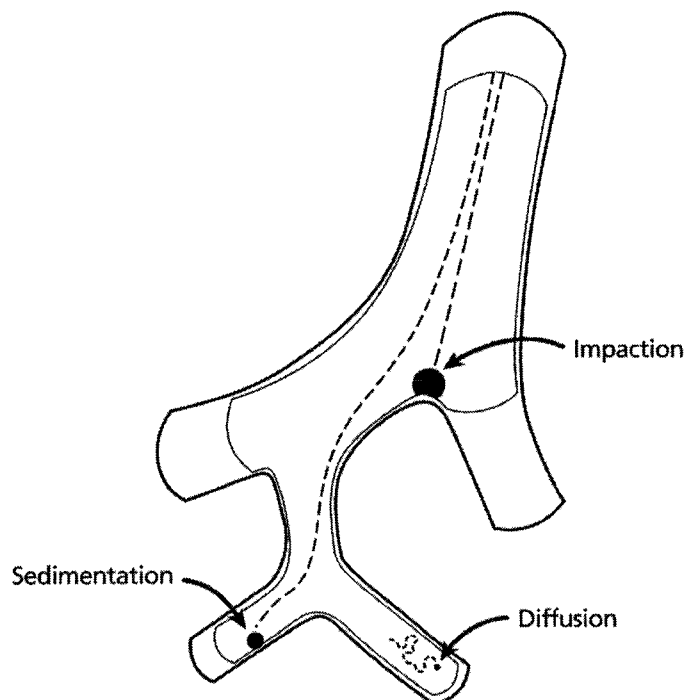


Figure 2-2 Principal Mechanisms of Aerosol Deposition in the Lung

Dust can penetrate to and can be retained in the alveoli for long periods of time, but it can also be cleared from the alveoli by protective mechanisms. Macrophages (phagocytic cells in the alveoli) are released in large numbers by the stimulus of dust particles. The macrophages engulf the particles deposited in the lung and these are then removed from the lung either by mucociliary action after moving to the finer bronchioles, or by entering the lymphatic system and being discharged via the lymph into the blood stream. Hence, a great deal of particulate matter is deposited by the macrophages at the lymph nodes, and it is here that fibrosis of healthy tissues often starts. Other dust-laden cells may be deposited on the alveolar walls where fibrosis can be initiated also.

The physiological reaction to inhaled particles depends on size, form, concentration, and chemical composition of the particles. In the case of silica particles, the primary concern is with fibrogenic capacity of the dust that can lead to the development of silicosis. Other insults to the lungs can lead to the thickening of small airways that can lead to restrictive or obstructive respiratory impairment. Increased destruction of alveolar wall may potentially lead to emphysema, but this mainly happens due to a synergistic effect with tobacco smoking. Other damage to the lung tissue by silica can lead to lung carcinoma. Because of the overwhelming effect of smoking on small airway disease, emphysema, and lung cancer one needs good data on smoking and cumulative dust exposure to establish in epidemiological

studies the size of the effect and dose-response relationships.

An important pathological feature of silica is that it predisposes a subject to infection to pulmonary tuberculosis.

Chronic silicosis is the is the most common disease resulting from excessive inhalation of silica dust. The fibrotic changes in the lungs usually occur after many years, usually 10-30, of inhalation of excessive levels of respirable silica dust. Chronic silicosis is further subdivided into simple silicosis and complicated silicosis.

Simple silicosis is the earliest form of chronic silicosis. The fibrosis occurs predominantly in the upper lung zones and appears on the chest x-rays as small discrete nodules. Simple silicosis is usually not associated with lung function impairment or respiratory symptoms. Complicated silicosis results when the small nodules increase in size and coalesce into larger nodules greater than 1 cm. Clinical changes resulting from complicated silicosis range from minor symptoms to extensive respiratory impairment that can be progressive and ultimately disabling, even fatal.

It is thus important that safe exposure levels for life long caree be determined and maintained. Thus epidemiologic research aimed at solving these issues should have priority.

SECTION 3 - PULMONARY TUBERCULOSIS

Risk of Pulmonary Tuberculosis relative to silicosis and exposure to silica dust in South African gold miners

Reference: Occupational and Environmental Medicine;55:496-502.

Authors: Eva Hnizdo and Jill Murray

3.1 ABSTRACT

Objectives - The study was designed to investigate the following questions: (1) Is silica dust on its own, without the presence of silicosis, associated with an increased risk of pulmonary tuberculosis (PTB) in silica dust exposed workers? (2) In the absence of silicosis is the excess risk dose related? (3) What is the predominant chronological sequence between the development of PTB and the development of silicosis after cessation of dust exposure?

Methods - A cohort of 2255 white South African gold miners has been followed from 1968-71, when they were 45-55 years of age, through December 31, 1995 for the incidence of PTB. During the follow-up 1592 (71%) men died. Of these, 1296 (81%) had an autopsy done at the National Centre for Occupational Health (NCOH) to determine the presence of silicosis and PTB. The incidence rate of PTB in the cohort was studied in relation to cumulative dust exposure and the onset of silicosis. For the miners with autopsy, the incidence rate for PTB was studied in relation to the severity of

silicosis found at autopsy.

Results - There were 115 subjects who developed PTB. The total person years of follow-up was 39 319. For the whole cohort, the factors associated with increased risk of PTB were cumulative dust exposure (mg/m^3 -yrs) (the adjusted rate ratio, $\text{RR}=1.07$; 95% confidence interval (CI) 1.04-1.10), silicosis diagnosed radiologically ($\text{RR}=3.96$; 95% CI 2.59-6.06), and tobacco pack-yrs ($\text{RR}=1.02$; 95% CI 1.01-1.03). The RR for PTB increased with quartiles of cumulative dust exposure 1.0, 1.51 (95% CI 0.78-2.91), 2.35 (95% CI 1.28-4.32), and 3.22 (95% CI 1.75-5.90). In miners who did not have radiological silicosis ($n=1934$, $\text{PTB}=74$), the adjusted RR for PTB and cumulative dust exposure was 1.10 (95% CI 1.06-1.13), and the adjusted RR increased with quartiles of cumulative dust exposure as 1.00, 1.46 (95% CI 0.70-3.03), 2.67 (95% CI 1.37-5.23) and 4.01 (95% CI 2.04-7.88). For the subjects who had an autopsy ($n=1296$, $\text{PTB}=70$), the adjusted RR for PTB increased with the severity of silicosis found at autopsy; 1.0 for no silicosis, 1.88 (95% CI 0.97-3.64) for insignificant, 2.69 (95% CI 1.35-5.37) for slight,

and 2.30 (95% CI 1.16-4.58) for moderate/marked degree of silicosis. For subjects who had an autopsy and no silicosis (n=577, PTB=18), the adjusted RR increased slightly with quartiles of cumulative dust 1.0, 1.11 (95% CI 0.31-4.00), 1.42 (95% CI 0.43-4.72), 1.38 (95% CI 0.33-5.62).

Conclusion - Silica dust exposure is a risk factor for the development of PTB even in the absence of silicosis, and even after silica dust exposure ceases. The risk of PTB increases with the presence of silicosis and, in miners without radiological silicosis, with quartiles of dust exposure. The severity of silicosis diagnosed at autopsy was associated with increasing risk of PTB. Even insignificant degree (<5 nodules) that is undetectable radiologically was associated with an increased risk. The diagnosis of PTB was on average 7.6 years after the cessation of exposure, at around 60 yrs of age. The onset of radiological silicosis preceded the diagnosis of PTB in 90.2% of the PTB cases who had silicosis. The results have implications for medical surveillance of silica dust exposed workers after cessation of exposure.

3.2 INTRODUCTION

The association between silicosis and pulmonary tuberculosis (PTB) has been well established.¹ Epidemiologic and case studies have shown that silica dust exposed workers have increased morbidity and mortality from PTB.²⁻¹³ Experimental studies have demonstrated an association

between silica particle induced changes and increased susceptibility to mycobacterial infection.¹⁴⁻¹⁶

Although the association between silicosis and PTB has been shown in many epidemiologic studies, there are still gaps in the epidemiologic evidence. The epidemiologic evidence on the dose-response trend between PTB and cumulative silica dust in the absence of silicosis is limited^{1,17} and no published study has examined the incidence of PTB in relation to the onset of silicosis or cessation of dust exposure.

South African gold miners are exposed to dust containing high levels of silica, and PTB always had a great impact on gold miners' health.^{2,3} A mortality study of 3971 white miners has found increased Standardised Mortality Ratio (SMR) for pulmonary tuberculosis of 153.8 (41.9-394.1) after 9 years of follow-up,⁴ and SMR of 306.4 (192.0-463.9) after 20 years of follow-up.⁵ In black South African gold miners the risk of PTB is even higher than in white miners, because the effect of silica is superimposed on a high population rate of PTB,³ and in more recent years on the high rate of HIV infection.^{11,18} The risk of PTB in black miners was shown to be related to severity of silicosis, and the relative risk due to the effect of silicosis was reported as 2.8 (95% CI 1.9-4.1).³ During a 7 yrs of follow-up, the incidence of PTB increased with age depending upon the category of silicosis; from 1% per year for miners with Category 0 to 6.3% per year in miners with Category 3 silicosis.³ A more recent study of South African gold miners has reported that the adjusted rate ratio for PTB increased with

age, with occupational categories known to have higher dust exposure (for drillers, mining team workers, and stope team workers the incidence rate ratios ranged from 2.25 to 2.56) and with the presence of silicosis the incidence rate ratio was 1.54 (95% CI 1.00 to 2.37).¹¹

In the present study, we followed up a cohort of 2255 white SA gold miners from 1968-71, when they were 45-55 years of age, to 31 December 1995 for the incidence of PTB. The factors studied relative to the incidence rate of PTB were cumulative dust exposure, the onset of radiological silicosis, and autopsy findings for silicosis. HIV was not a confounding factor in this cohort of miners. Objectives of the study were to investigate the following questions. (1) Is silica dust on its own, without the presence of silicosis, associated with an increased risk of PTB in silica dust exposed workers? (2) In the absence of silicosis is the excess risk dose-related? (3) What is the predominant chronological sequence between the development of PTB and the development of silicosis after the end of exposure to dust?

3.3 MATERIALS AND METHODS

3.3.1 Study Subjects

The study subjects comprised a cohort of 2260 white gold miners who were studied in 1968-71 for chronic obstructive lung disease.¹⁹ The study subjects were selected from all white miners who attended the Medical Bureau for Occupational Disease (MBOD) during the four years 1968-71 for a medical examination and who fulfilled the following criteria: (1) MBOD number within

the range B9000-C8999; (2) age 45-54; (3) at least 10 years of underground service; (4) at least 20 years residence in South Africa; (5) less than two years service in mines other than gold mines. An annual medical examination is compulsory for all miners working in dusty occupations in the gold mines. Of the 2260 miners, 2018 were current miners and 240 were inactive miners of whom 107 came to renew their fitness certificate to work underground and 133 came for a benefit examination (a specialized examination to determine disability and eligibility for compensation; this does not mean that they had disability). A mortality follow-up through December 31, 1995 has been done using the Department of Interior records of vital status. Five miners were excluded for the follow-up study of PTB as they were diagnosed with PTB before the start of follow-up in 1968-71. Of the remaining 2255 miners, 1592 (71%) have died and of these, 1296 (81.4%) had an autopsy at the National Centre for Occupational Health (NCOH) to assess the presence of compensable lung disease. There were 49 miners whose vital status was not established. These miners were assumed to be alive.

3.3.2 Incidence of Pulmonary Tuberculosis

PTB is a compensable lung disease in South African gold miners. The miners in this cohort who developed PTB while employed, or after retirement, would have come to the Medical Bureau for Occupational Diseases (MBOD) for medical examination and to apply for compensation. Also by law PTB is a notifiable disease and any doctor treating

a miner for PTB is obliged to notify the MBOD. The records relating to the diagnosis of PTB done at MBOD or by non-MBOD doctors (sputum examination, x-rays, etc) are kept in the miners' medical files at the MBOD. These files were searched for the diagnosis of PTB. There were 180 subjects who were diagnosed with PTB. The x-rays of these miners were re-read blindly for signs of PTB by the same reader who previously read the onset of silicosis in this cohort.²⁰

Autopsy examinations of the cardiorespiratory organs are performed at the NCOH according to a standard procedure. The presence of compensable disease is established by macro- and microscopic examination of the lung. Histological examination is done on six tissue blocks taken from the upper, middle and lower zones of each lung. At autopsy the presence of pulmonary tuberculosis is diagnosed in the presence of epithelioid granulomas associated with caseous necrosis, other causes having been excluded.

Of the 180 miners diagnosed with PTB, 39 had positive histological evidence at autopsy, 76 had a positive sputum finding in life, 5 were diagnosed on radiological findings only, and the remaining 60 miners had only a record of being compensated and date of compensation.

For the purpose of this study we have used only the cases where we could find either positive radiological signs, or a positive sputum test, or a positive autopsy finding in the lung parenchyma and who were diagnosed after 1968-71. There were 115 such cases.

3.3.3 Assessment of Silicosis

Radiological silicosis. While employed, the miners had annual radiological examinations. After retirement most of the miners came for radiological examinations, but less frequently. In the year 1990, the onset of silicosis was determined in the cohort by three experienced x-ray readers for the purpose of establishing the dose-response trend between silicosis and cumulative silica dust.²⁰ They examined yearly x-rays, starting from the most recent x-ray in the medical file, and identified the year of silicosis onset. The silicosis onset was diagnosed when the ILO category was at least (1/1). No detailed ILO grading was performed. The readings of the reader with the highest correlation with autopsy findings for silicosis²¹ were used in this study.

Autopsy silicosis. At autopsy, the presence and degree of silicosis is determined from macroscopic and histological examination of the lung. At the macroscopic examination the degree of silicosis is classified according to the number of palpable silicotic nodules, as follows: no silicosis, insignificant (<5 nodules), slight (up to 14 nodules), moderate (15 to 30 nodules), and marked (more than 30 nodules). The presence of silicosis is confirmed by histological examination.

Estimation of cumulative dust exposure. The occupational histories were coded for each miner from the Chamber of Mines personal records which show the number of shifts worked in the particular mine and the occupation during a given period. Using

estimates of average dust exposure for occupational categories in the SA gold mines derived by a study done by Beadle in 1970 (published by Page-Shipp et al., 1972),²² occupations were grouped into occupational categories and assigned an average dust level and an average time spent underground.²²

Cumulative dust exposure (CDE) in terms of $\text{mg}/\text{m}^3\text{-yrs}$ was calculated as $\text{CDE} = \sum (\text{number of dusty shifts} \times \text{the mean mass respirable dust concentration for an occupational category} \times \text{the average hours spent underground for an occupational category}) / (270 \times 8)$. The summation is over all jobs in which a miner worked, 270 is the average number of shifts per year standardized to an 8 hour shift. CDE was cumulated as a time-dependent variable (see Statistical Analysis).

Smoking habits. Details of smoking habits were obtained by a questionnaire during the 1968-71 examination and answers were checked against smoking histories recorded in the medical file. Tobacco consumption was calculated in terms of cigarettes pack-years up to 1968-71.¹⁹

3.3.4 Statistical Analysis

The proportional hazards model was used to estimate the association between the risk of PTB and the potential risk factors. The SAS programme PROG PHREG was used.²³ The measure of association estimated was the incidence rate ratio (RR). The follow-up time started from the year a subject was enrolled into the cohort study in 1968-71. At each time, $t(l)$, when PTB case was diagnosed, all

subjects who were still at risk of developing PTB and the PTB case formed a risk set, $R(l)$. For each risk set $R(l)$, the explanatory variables (cumulative dust exposure, the presence of radiologically diagnosed silicosis and age) were calculated up to the time $t(l)$.

Because the degree of silicosis was only assessed at autopsy, and the autopsy findings are more reliable than the radiological findings, we analysed the subjects who had an autopsy in a separate analysis. Since the autopsy silicosis was diagnosed at the end of a follow-up (at death), the inclusion of autopsy silicosis in the analysis as a time-dependent explanatory variable would have biased the estimated RR. Only subjects with PTB would be found to have autopsy silicosis, most of those without PTB who were found to have silicosis at death (i.e., the end of follow-up) would be censored before death and their silicosis would not contribute to the calculation of the maximum likelihood statistics. Therefore the autopsy silicosis was treated as if it was present or absent during the whole follow-up and the estimated RRs were adjusted for the years of follow-up and for cumulative dust exposure. The use of this model can be justified by the fact that silicosis is a progressive disease and it is difficult to determine its onset radiologically.

3.4 RESULTS

The miners were born on average in 1919 (S.D. 2.5; range 1913-1924), started mining in the 1940s and retired from dusty occupations in 1971.7 (S.D. 5.3), at around

52.4 (S.D. 5.4) years of age. During the follow-up (from 1968-71 through 1995) 115 miners developed PTB according to the criteria used for the study. Only the first incidence in one person was considered. The total person-years of follow-up was 39 319. Table 1 shows characteristics of the cases with PTB and the rest of the cohort. The cases had more silicosis diagnosed radiologically, 41 (35.6 %) versus 280 (13.1%) in miners without PTB, and were on average younger at silicosis onset, 53.5 (S.D. 6.0) versus 56.2 (S.D. 6.9) years for miners without PTB.

A higher percentage of the cases with PTB than the rest of the cohort died by the year 1995, 85.2% versus 69.8%, but a lower percentage of PTB cases had an autopsy at death, 71.4% versus 82.1%. Silicosis diagnosed at autopsy was found in 52 (74.3%) cases and in 667 (54.4%) miners without PTB. The cases had significantly higher cumulative dust exposure and cigarette pack-yr than the rest of the cohort.

3.4.1 Association between PTB, dust and silicosis

Radiologically diagnosed silicosis. Table 3-2 shows the smoking adjusted rate ratio for PTB estimated from the proportional hazards model for the whole cohort and for those without silicosis. The presence of silicosis (diagnosed radiologically) increased the risk of PTB by about 4 times (RR=3.96) when cumulative dust was adjusted for (Model 3). The RR for PTB increased with increasing levels of cumulative dust exposure in the whole cohort (Model 3 and 4) and also in

miners who did not have silicosis (Models 5 to 8). The effect of cigarette pack-years was statistically significant, and for all models the estimated RR was constant, RR=1.02 (95% CI 1.01-1.03). RR for increasing age at death categories (<60, 61-70, 70+) did not show a statistically significant trend and age at death was not included in the model.

Autopsy diagnosed silicosis. Table 3-3 shows the results for miners who had an autopsy. The RR for PTB increased with the increasing severity of silicosis diagnosed at autopsy (Model 1). However, when cumulative dust was adjusted for, the RR in the highest exposure category decreased from 2.71 to 2.06 (Model 2) and to 2.30 (Model 3). The RR for PTB was increased even for the insignificant degree of silicosis (RR=1.86, 95% CI 0.96-3.58). There were only 577 subjects who did not have any nodules found at autopsy. Though the RR showed some trend with increasing dust levels (Models 4 and 5), this was not statistically significant. However, the number of miners in this group was small.

The distribution of autopsy findings for silicosis according to the PTB diagnosis is as follows. Of the 70 PTB cases who had an autopsy, 18 (25.7%) did not have silicotic nodules and 18 (25.7%) had insignificant, 16 (22.9%) had slight, 14 (20.0%) had moderate and 4 (5.7%) had marked degree of silicosis found at autopsy. Of the 1226 subjects who did not have PTB, 559 (45.6) did not have silicotic nodules, 292 (23.8%) had insignificant, 180 (14.7%) had slight, 140 (11.4%) had moderate, and 55 (4.5%) had marked degree of silicosis at autopsy. This difference in the distribution of autopsy

silicosis in the PTB cases and in the rest of the subjects was statistically significant (Mantel-Haenszel Chi-square=10.7, df=1, p=0.001).

Diagnosis of tuberculosis in relation to the cessation of dust exposure and onset of silicosis.

In the cases with TB, the average age at the last dust exposure was 52.7 (S.D. 5.2) and the age at PTB diagnosis was 60.3 (S.D. 5.7). There were 15 subjects who were diagnosed with PTB prior to cessation of dust exposure, 6 subjects were diagnosed in the same year as dust exposure ceased, and 99 subjects were diagnosed after cessation of dust exposure. Figure 3-1 shows the distribution of age at last exposure to dust for the cohort, of age at the onset of radiological silicosis for silicotics, and of age at the diagnosis of PTB.

Of the 115 cases with PTB, 41 (35.7%) had radiologically diagnosed silicosis. In 4 cases, the onset of radiological silicosis was during the same year as the diagnosis of PTB, and in 37 cases the diagnosis of PTB was after the onset of silicosis. On average the age at silicosis onset in the PTB cases was 53.5 (S.D. 6.0) years, and the average age at PTB diagnosis was 60.3 (S.D. 5.7). The 52 cases in whom silicosis was first diagnosed at autopsy only were excluded from this analysis as the relation between the onset of silicosis and PTB could not be determined.

3.5 DISCUSSION

Epidemiologic studies have shown that subjects with silicosis have a substantially increased risk of developing PTB,^{3,7,10,11,12} and that the risk of PTB increases with increasing severity of radiological category

for silicosis.³ However, epidemiologic evidence is still limited on whether subjects exposed to silica dust who do not have silicosis also have an excess risk of developing PTB, and whether the excess is dependent on the amount of dust to which they have been exposed.¹⁷

A study of foundry workers from Denmark has shown that the morbidity from PTB increased with the duration of silica dust exposure in nonsilicotic workers.⁷ The shortcoming of this study is that the presence of silicosis was established during the initial examination while the incidence of PTB was established during a follow-up period of almost ten years. Thus the silicotic status might have changed during the follow-up period. Our study shows that silicosis is a progressive disease and might become radiologically visible years after dust exposure ceased and also that a large percentage of silicosis found at autopsy is not diagnosed radiologically.

A case-control study based on U.S. national mortality surveillance database in which mortality data for PTB was related to occupational exposure to silica dust also found that silica dust exposure is associated with increased mortality from PTB after pneumoconiosis was adjusted for.¹² The limitation of this study is that silicosis was established from the death certificates and that occupational exposure was obtained indirectly by interviewing the next of kin. Thus misclassification of disease and exposure was likely to have been present in this study.

The first two objectives of our study were to investigate whether silica dust on its own, without the presence of silicosis, is

associated with an increased risk of PTB and whether the excess risk is dose-related, using radiological and autopsy data for the diagnosis of silicosis.

The results show that the risk of PTB increases with the presence of radiologically diagnosed silicosis, with increasing cumulative silica dust exposure, and with tobacco pack-yrs. The presence of silicosis diagnosed radiologically increased the risk of PTB by about 4 times when cumulative dust and smoking were adjusted for (Table 3-2, Models 3 and 4). The RR for PTB showed a significant trend with quartiles of cumulative dust exposure (Table 3-2, Model 4). The results indicate that the miners in the highest dust exposure category who were diagnosed with radiological silicosis had 13.4 times (3.22x4.18) increased risk of developing PTB during the follow-up period than the miners who did not have radiological silicosis and had the lowest dust exposure level.

Although the results in Table 2 show that dust remains a significant risk factor after silicosis is considered in the model (Model 4), it can, however, be argued that in this model cumulative silica dust can be acting as a surrogate variable for increasing severity of silicosis. In the next step in the analysis we therefore estimated the association between PTB and cumulative dust in miners who did not have radiological silicosis (Models 5 and 6) and in miners who had neither radiological nor autopsy diagnosed silicosis (Models 7 and 8). For both sets of models the association between PTB and cumulative dust exposure was statistically significant and close to that observed for the whole cohort. Of the 1388

subjects used in Models 7 and 8, 572 (41.2%) had an autopsy, thus potentially there might have been few subjects who developed silicosis after their radiological follow-up ceased.

We therefore analysed separately only subjects who had an autopsy, to investigate whether silica dust remains a significant risk factor after the degree of silicosis found at autopsy is taken into account. The results show that after the degree of silicosis found at autopsy is taken into account, dust still remains a significant risk factor and that the trend in RR with increasing dust levels persists (Table 3-3, Models 2 and 3). A miner with moderate or marked silicosis found at autopsy who had high dust exposure has $2.30 \times 2.54 = 5.8$ times increased risk of developing PTB after cessation of dust exposure. Although the miners without autopsy silicosis do not show a significant trend with increasing dust levels (Table 3-3, Models 4 and 5), the number of these miners in this group is small and we can not exclude the possibility of exposure misclassification.

Thus the results obtained for the whole cohort using radiologically diagnosed silicosis, and for the autopsy subjects using silicosis diagnosed at autopsy demonstrate that silica dust without the presence of silicosis is an important risk factor for the development of PTB and that the effect is dose dependent.

The above findings confirm, in humans, the *in vitro* and animal experimental evidence that silica dust may increase the risk of PTB via its direct effect on the pulmonary macrophage. The current knowledge on the mechanism by which silica particle

potentiates the increased susceptibility to mycobacterial infection suggests that depending upon the silica dust dose, silica particles can cause destruction of the pulmonary macrophage, or in lower doses alteration of its metabolism and function, thereby reducing its capacity for an effective antibacterial defence.¹⁴⁻¹⁵ The presence of silica particles in the lung has also been shown to lead to an alteration of cell-mediated immunity.¹⁶

The role that silicosis, or the susceptibility to develop silicosis, plays in pulmonary tuberculosis is uncertain. It has been suggested that the bacilli may be encapsulated in the silicotic nodules and cause increased risk of future reactivation of the disease,²⁴ or that the altered immunological profile in the lungs of the silicotic person might predispose a person to the PTB infection.¹⁶ It is noteworthy that even an insignificant degree of silicosis (<5 nodules) is associated with an increased risk when compared to those without silicosis. This result seems to suggest that the effect of silica dust, rather than that of those few silicotic nodules, is causing the increased risk. Because epidemiologic studies cannot estimate the effect of silicosis in the absence of silica dust, and the effects of silicosis and dust are correlated, it is not possible to determine by epidemiologic studies whether silicosis itself is the causal factor or whether silicosis is acting as a surrogate variable for the effect of dust.

Our previous study of this cohort of miners has shown that many subjects not diagnosed radiologically had silicotic nodules found at autopsy.²¹ Using additional autopsy results since that study, we have

found now that only 34% of 719 subjects found to have silicosis at autopsy had been diagnosed radiologically (although this cohort had annual radiological examinations while exposed to dust and most miners had radiological follow-up after cessation of dust exposure, although less regularly²¹). The percentages not diagnosed radiologically according to the severity of silicosis found at autopsy were 97.8% for insignificant, 75.4% for slight, 51.6% for moderate and 30.0% for marked silicosis (there were 61 with marked silicosis). Thus, to demonstrate the relationship between silica dust in the absence of silicosis and the risk of PTB, it is necessary to have autopsy data.

The third objective of the study was to investigate what is the predominant chronological sequence between the development of PTB and the development of silicosis after cessation of dust exposure in silica dust exposed workers. It needs to be pointed out that this cohort of miners had been selected for fitness at the initial medical examination and for having had at least 10 years of mining, thus miners who developed PTB before completing 10 years of underground mining would not be included in this study as previously those miners were not allowed to return to underground work. The average age at the cessation of dusty occupation was 53.1 (S.D. 4.2) for the cases versus 52.6 (S.D. 5.2) for the rest of the cohort. The age of silicosis onset (radiological silicosis only) was 53.5 versus 56.2, respectively. The average age at the diagnosis of PTB was 60.3 (S.D. 5.7). Thus PTB was diagnosed on average 7.6 years after cessation of dust exposure and 6.8 years after the onset of silicosis. There

were only 4 cases who developed PTB at the same year when the onset of silicosis was diagnosed on the x-rays, the rest (37) developed PTB after the onset of silicosis. Figure 3-1 shows the distribution of the ages at last exposure for the whole cohort, of the age at radiological silicosis onset in silicotics and of the age of diagnosis of PTB.

Limitations of the study are that miners who developed pulmonary tuberculosis before they worked 10 years underground would not be included in this study as at the time these workers were employed underground, miners who developed PTB were not allowed to continue underground service. Although most of the retired miners came for radiological examination after retirement from dusty occupations this would not be on a regular basis, thus the onset of silicosis might be affected by this, but most miners came for medical examinations²¹. Also miners who were awarded second degree compensation for pneumoconiosis would not benefit from a visit to MBOD. There is also the possibility that not all the miners who developed PTB were notified to the MBOD, although this number would be small since notification of PTB is compulsory by law.

3.6 CONCLUSION

The results indicate that the silica dust which miners accumulate in their lungs during exposure is a lifelong risk for the development of PTB, even if silicosis is not present in the lungs. Further more, even after exposure to dust ceases, ex-miners continue to be at risk for developing silicosis

and the development of silicosis places them at even greater risk for developing PTB. More over, the data show that miners with very few silicotic nodules (insignificant and slight degree of silicosis) have significantly increased risk of getting PTB and that this degree of silicosis is seldom diagnosed radiologically.

The results of this study show that even after silica dust exposure has ceased, life long surveillance for silicosis and especially for pulmonary tuberculosis is important in silica dust exposed workers. In the Southern African setting where the population of ex-miners is extensive, it is important that health care providers are informed about the increased risk of pulmonary tuberculosis in ex-miners, so that patients with respiratory symptoms who have a previous mining history are rigorously investigated for PTB. Furthermore, if resources are available, miners and ex-miners should receive prophylactic antituberculous treatment as suggested by the American Thoracic Society.²⁵

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Table 3-1 Characteristics of the cases with PTB and the rest of the cohort

Characteristics	Pulmonary TB (n=115) mean (S.D.)	Rest of the cohort (n=2140) mean (S.D.)
Year of birth	1918.8 (2.4)	1919.1 (2.5)
Years gold mining	27.6 (6.0)	26.5 (6.4)
Year last in dust	1971.9 (4.1)	1971.7 (5.3)
Radiological silicosis, N (%)	41 (35.6%)	280 (13.1%) *
Age at radiological silicosis onset	53.5 (6.0)	56.2 (6.9) +
Deaths by 1995 , N (%)	98 (85.2%)	1494 (69.8%)*
Age at death	65.2 (6.4)	64.9 (7.4)
Autopsy done at death, N (%)&	70 (71.4%)	1226 (82.1%)*
Age at autopsy	65.0 (6.2)	64.5 (7.3)
Silicosis found at autopsy, N (%)	52 (74.3%)	667 (54.4%)*
Cumulative dust mg/m3-yrs	17.5 (6.4)	14.3 (6.1) #
Quartiles of total CDE mg/m3-yrs		
<=9	16 (13.9%)	542 (25.3%)
10-13	20 (17.4%)	547 (25.6%)
14-17	31 (27.0%)	528 (24.7%)
18+	48 (41.7%)	523 (24.4%)
		X ² (1)=20.3, p=0.001
Cigarettes pack-yrs	23.3 (16.0)	20.3 (16.3) +

+ p<0.05. * p<0.001. # p<0.0001. & Percentage is out of those that died. CDE= cumulative dust exposure.

Table 3-2 Adjusted relative risk and 95% confidence intervals for pulmonary tuberculosis and associated risk factors, for the whole cohort and for those without silicosis

Model	Silicosis	Cumulative dust exposure (continuous variable)	Quartiles of cumulative dust exposure			
			1	2	3	4
All subjects n=2 255, cases with PTB=115						
1	6.01 (4.08-8.85)					
2		1.103 (1.07-1.13)				
3	3.96 (2.59-6.06)	1.071 (1.04-1.10)				
4	4.18 (2.75-6.36)		1.0	1.51 (0.78-2.91)	2.35 (1.28-4.32)	3.22 (1.75-5.90)
All subjects without radiological silicosis, n=1934, cases with PTB=74						
5		1.10 (1.06-1.13)				
6			1.0	1.46 (0.70-3.03)	2.67 (1.37-5.23)	4.01 (2.04-7.88)
Subjects without radiological or autopsy silicosis, n= 1388, cases with PTB=40						
7		1.093 (1.04-1.15)				
8			1.0	1.59 (0.62-4.08)	2.39 (0.97-5.89)	3.78 (1.57-9.42)

Table 3-3 Adjusted relative risk and 95% confidence intervals for pulmonary tuberculosis and associated risk factors, for subjects who had an autopsy

Model	Silicosis Degree				Cumulative dust mg/m³-yrs	Quartiles of cumulative dust exposure			
	None n=577	Insignificant n=310	Slight n=196	Moderate/Mar ked n=213		1	2	3	4
All subjects who had an autopsy at NCOH, n=1296, cases with PTB=70									
1	1.0	1.86 (0.97-3.58)	2.62 (1.36-5.03)	2.71 (1.41-5.20)					
2	1.0	1.86 (0.96-3.58)	2.51 (1.25-5.01)	2.06 (1.04-4.11)	1.07 (1.03-1.11)				
3	1.0	1.88 (0.97-3.64)	2.69 (1.35-5.37)	2.30 (1.16-4.58)		1.0	1.24 (0.54-2.84)	1.96 (0.92-4.17)	2.54 (1.20-5.42)
All subjects who had an autopsy at NCOH and did not have silicosis diagnosed at autopsy, n=577, cases with PTB=18									
4									
5						1.0	1.11 (0.31-4.00)	1.42 (0.43-4.72)	1.38 (0.33-5.62)

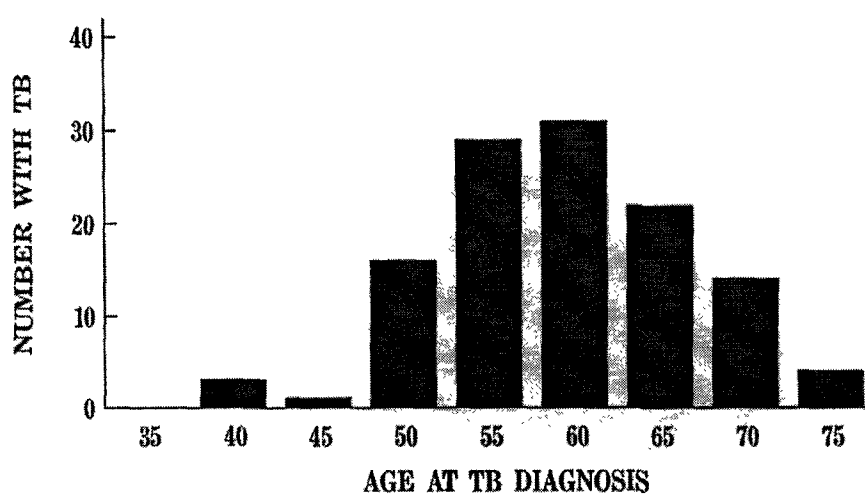
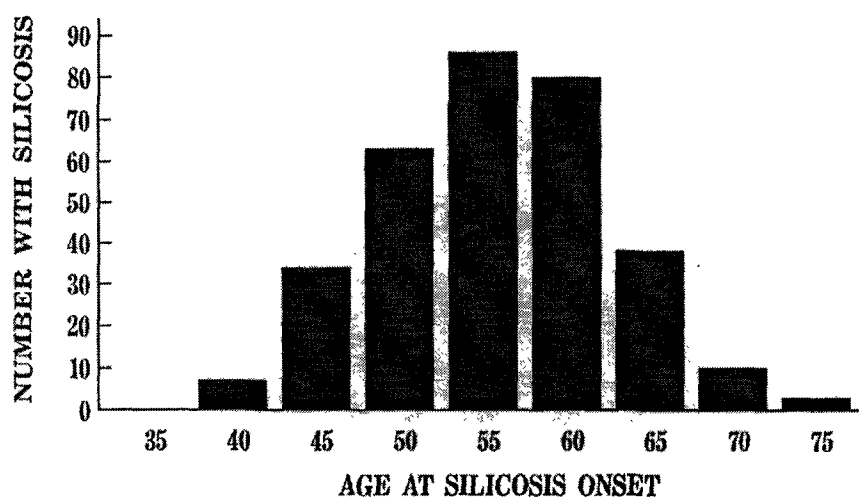
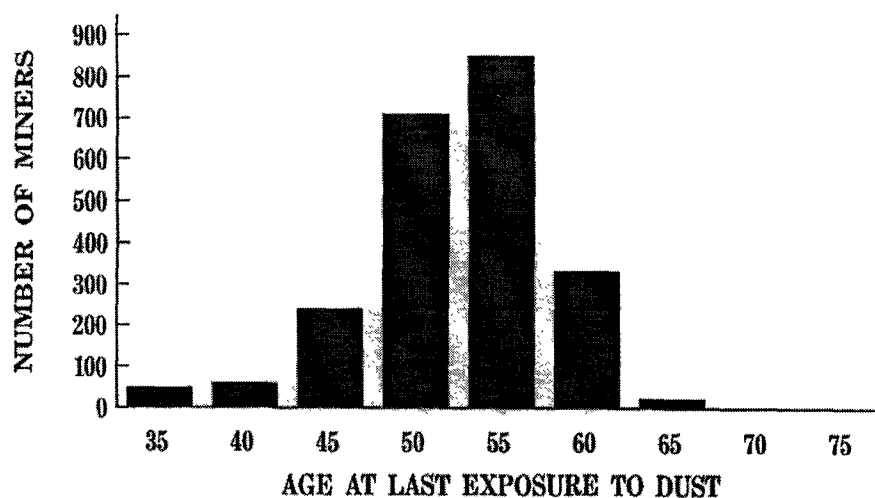


Fig 1. Age distribution for all the subjects at last exposure to dust, at silicosis onset and at TB diagnosis

SECTION 4 - CHRONIC OBSTRUCTIVE AIRWAYS DISEASE

Correlation between autopsy findings for chronic obstructive airways disease and in life disability in South African goldminers

Authors: Eva Hnizdo and Jill Murray

4.1 ABSTRACT

Objectives. In South Africa chronic obstructive airway disease (COAD) which could be due to work in a dusty atmosphere in scheduled mines or works is a compensable disease. Miners are compensated for in life disability and for findings for COAD at autopsy which include emphysema, bronchitis assessed by mucus gland hyperplasia in the main bronchus, and bronchiolitis assessed by goblet cell metaplasia. The question arises as to whether the autopsy findings correlate with in life impairment. The objectives of the study were: (1) to determine whether autopsy COAD outcomes relate to lung function and to respiratory symptoms and signs; (2) to quantify the individual contributions of emphysema, bronchiolitis and bronchitis to lung function; and (3) to assess the contribution of smoking, silicosis, and dust exposure to autopsy findings.

Methods. Pathological findings for COAD - emphysema, bronchitis and bronchiolitis, were related to lung function measurements and respiratory symptoms and signs observed within five years prior to death on 724 gold miners.

Results. Emphysema diagnosed at autopsy was associated with airflow impairment. The mean forced expiratory volume in one second expressed as percentage predicted (FEV₁%) decreased with emphysema score categories 0-5, 5-35, 35-65 and >65 as

follows: 78.8%, 66.2 %, 52.0% and 46.0%, respectively. Of the respiratory symptoms, mainly the prevalence of dyspnoea increased with the emphysema categories as 14%, 24%, 38%, and 53%, respectively. Bronchitis was also associated with airflow impairment. However, in subjects without emphysema, the presence of moderate or marked bronchitis was associated with a mild impairment only. Of the respiratory symptoms, mainly rhonchi, sputum and cough showed association with the degree of bronchitis. Only a slight association was found between bronchiolitis and lung function impairment and this disappeared when emphysema and bronchitis were adjusted for. Of the respiratory symptoms only sputum was associated with bronchiolitis. Tobacco smoking was associated with all the COAD outcomes.

4.2 INTRODUCTION

Epidemiological studies of South African gold miners have shown that silica dust exposure and silicosis are risk factors for lung function impairment and for mortality from chronic obstructive airway disease (COAD).^{1,2,3} Since 1973, COAD which could be due to work in a dusty atmosphere in scheduled mines or works has been a compensable disease. COAD is a progressive disease and respiratory disability due to dust often develops after cessation of dust exposure. Because many miners do not have medical follow-up after cessation of employment, current legislation allows for autopsy compensation. Deceased miners with adequate service who have a moderate or marked degree of emphysema, bronchiolitis, or bronchitis diagnosed at autopsy are eligible for compensation. The question has been raised whether the autopsy COAD outcomes correlate with lung function abnormalities in life.

The main objective of the study was (1) to determine how the pathological diagnosis of COAD correlates with clinical observations (chiefly lung function tests and recorded respiratory symptoms and signs), (2) to quantify the individual contributions of emphysema, bronchiolitis and bronchitis to lung function impairment in life, and (3) to assess the contributions of smoking, silicosis and dust exposure to these diseases. The results are discussed in relation to current compensation policies.

4.2.1 Chronic obstructive airways disease - definitions.

COAD is characterized by abnormal tests of expiratory airflow that do not change markedly over several months of observation. Three disorders are incorporated in COAD: emphysema, peripheral airway disease, and chronic

bronchitis.⁴ Emphysema is characterised by abnormal permanent enlargement of the airspaces distal to the terminal bronchiole, with destruction of their walls and is assessed morphologically at autopsy. Peripheral airways disease includes pathological features such as inflammation of the terminal and respiratory bronchioles, fibrosis of airway walls with narrowing, and goblet cell metaplasia of the bronchiolar epithelium. Correlations suggest that small airway disease contributes to airflow obstruction, but that their importance on lung function is secondary to that of emphysema. Chronic bronchitis refers to "the condition of subjects with chronic or recurrent excess mucus secretion into the bronchial tree".

4.2.2 Compensation practice for COAD in South African miners

Compensation for COAD is based on functional disability in life and on autopsy findings, provided that there has been a minimum of 10 years service in conditions of high dust or 13 years in low dust. Smoking history is not taken into consideration.

In life compensation criteria. COAD first degree is assigned for moderate impairment of lung function and second degree for severe impairment. Pulmonary impairment is graded according to percent of predicted value for FEV₁, forced vital capacity (FVC) and the observed FEV₁/FVC ratio, respectively, as follows: normal ($\geq 80\%$, $\geq 80\%$, $\geq 75\%$), mildly impaired (79-65%, 79-65%, 74-65%), moderately impaired (65-52%, 65-52%, $<65\%$), severely impaired ($<51\%$, $<55\%$, $<55\%$).

Autopsy compensation criteria. Autopsy criteria for COAD compensation are based on the degree of emphysema, bronchitis and bronchiolitis. Emphysema is graded by a score ranging from 0 to 100. COAD first degree is assigned for moderate

emphysema, (score 35-64), and second degree for marked emphysema (score $\geq$ 65). Bronchitis is assessed as the amount of mucus gland hyperplasia in a main bronchus graded by the Reid index⁵

COAD first degree is assigned for moderate bronchitis (Reid index = 0.6-0.7), and second degree for marked bronchitis (Reid index >0.7). Bronchiolitis is assessed by the presence of goblet cell metaplasia in bronchioles. COAD first degree is assigned when 50-75% of bronchioles are involved and second degree when over 75% are involved.

4.3 MATERIALS AND METHODS

4.3.1 Selection of study subjects.

By South African law, autopsy examination of the heart and lungs is required for all miners and ex-miners provided the next of kin agrees. For subjects dying within 100 km of Johannesburg a full autopsy examination is offered. For those dying further afield, the organs are removed locally, preserved in formalin and sent to the National Centre for Occupational Health (NCOH) in Johannesburg. Autopsy examinations are performed by pathologists at the NCOH according to a standard procedure and the results are sent to the Medical Bureau for Occupational Disease (MBOD) for determination of compensation. Since 1974 autopsy results have been computerised on a database called PATHAUT.⁶

Study subjects were selected from the PATHAUT database if they fulfilled the following criteria: (1) autopsy performed between 1975 and 1986; (2) 80% of mining service on gold mines; (3) less than one year asbestos mining; (4) lungs inflated at autopsy; (5) tissue adequately preserved to enable histological assessment of bronchiolitis and bronchitis; (6) lung function tests within 5 years of death. Because lung

function tests were mainly available on white miners, black miners could not be included in this study. There were 8462 miners who satisfied criteria 1-4. Of these, 2427 did not have adequately preserved tissue to satisfy criteria 5, leaving 6035 miners who fulfilled criteria 1-5. Of these, 3384 did not have any pathological findings for COAD and a random sample of 500 was selected from these miners. The remaining 2651 were categorized into 7 categories according to possible combinations for the presence or absence of emphysema, bronchitis, or bronchiolitis and all were considered for the study. From the 3151 (500+2651) miners, we excluded miners without lung function tests within 5 years of death and also cases with cardiac failure, leaving 724 miners in the study.

4.3.2 Autopsy examination.

The presence of compensable disease is established by macro- and microscopic examination of the lungs.

Emphysema. Emphysema is assessed on all lungs, however for the present study only men who had a full autopsy were eligible, because whole lung sections, which are required for meticulous assessment of emphysema must be prepared on lungs which are inflated when removed from the thorax. The lungs are inflated with formaldehyde and a paper mounted whole lung section is made of one lung with the Gough-Wentworth technique.⁵ Emphysema is graded by a score between 0 and 100. The degree of emphysema is categorised as absent (<10), insignificant (10-34), moderate (35-64), and marked (≥ 65). To obtain exact emphysema scores for the study subjects, their whole lung sections were reassessed and scored by Dr. B. Goldstein from NCOH.

Bronchitis. Bronchitis is assessed by mucus gland hyperplasia in a main bronchus. It is

categorized according to the ratio of the thickness of the mucous gland layer to the thickness of the wall between the epithelium and the cartilage (i.e. the Reid Index) as absent, insignificant (<0.6), moderate (0.6-0.7), and marked (>0.7).

Bronchiolitis. Bronchiolitis in small airways (< 2 mm diameter), is assessed mainly by goblet cell metaplasia. Bronchiolitis is graded by the ratio between the number of goblet cells and the total number of cells seen, as absent, insignificant (up to 50%), moderate (50-75%), and marked (>75%).

Because the lungs are already at varying stages of decomposition when preserved in formalin, the assessment of airways disease is compromised. This is particularly so for small airways as often only small loose pieces of bronchiolar epithelium can be seen. This study only used cases with adequate tissue preservation. The computerized records indicate whether the tissue preservation was adequate.

Silicosis. Silicosis is graded according to the number of palpable silicotic nodules as absent, insignificant (<5 nodules), slight (6-14 nodules), moderate (15-30 nodules) and marked (>30 nodules). The presence of silicosis is confirmed by histological examination.

All information on pathological findings was extracted from the PATHAUT database, except for the emphysema score which was re-assessed for this study.

4.3.3 Clinical findings and lung function tests

For each eligible study subject we extracted lung function tests done within 5 years prior to death and information on respiratory symptoms and signs from the MBOD medical files.

Lung function measurements. The MBOD

has a well equipped lung function testing laboratory, with experienced technicians. Tests included in this study were FEV₁, FVC, and FEV₁/FVC, expressed as percentage predicted FEV₁%, FVC%, FEV₁/FVC%, and the observed data for total lung capacity (TLC) and FEF_{25-75%}. Each individual's height, age and weight at the time of testing were recorded. Percentages of predicted were obtained directly from the lung function records.

Clinical data. Data on respiratory symptoms (dyspnoea, sputum and cough) and signs (rhonchi) were obtained from the periodical medical examinations which routinely included questions on cough, sputum and dyspnea. The questions were not, however, asked in a standard epidemiologic format to establish the presence of chronic bronchitis.

4.3.4 Silica dust exposure

A complete work history for each miner was extracted from the Chamber of Mines personal records. These accurately record the number of shifts worked in each mine and the miner's occupation. During the 1960s, a study done by Beadle (1971)⁷ estimated the average dust exposure, in terms of respirable surface area (RSA), for occupational categories in South African gold mines. Cumulative dust exposure (CDE) calculated up to the age of 50 in RSA-years was calculated by weighting the number of shift spend in each occupational category by the Beadle's average dust measurements for occupational categories (see details in ¹).

4.3.5 Smoking history

Smoking history was obtained from the MBOD medical files. Smoking habits have been recorded at each periodical examination since 1960. Smoking was calculated as tobacco pack-years and

years of smoking.

4.3.6 Statistical analysis

Analysis of lung function and clinical findings.

To establish the reliability of in life symptoms and signs, we first assessed the associations between these and the known risk factors (smoking, dust, and age). The association was measured by the adjusted odds ratio, estimated in the logistic regression (SAS proc LOGIST).⁸ Next, we determined the association between respiratory symptoms and signs and lung function tests. The mean lung function values for increasing severity of symptoms were calculated and a test for trend performed with the regression analysis. To determine which of the respiratory symptoms and signs best predict lung function, we applied the linear regression model which included all the symptoms and signs, and height, weight, age, pack-years tobacco smoking, and dust exposure.

Relationship between in life and autopsy findings.

The analysis of variance and multiple comparison tests were used to test whether the severity of autopsy findings is associated with increasing lung function impairment. The lowest severity category was used as a comparison group in the multiple comparisons of the means. The association between the severity of autopsy findings and the presence of symptoms and signs in life was assessed by the chi-square test for trend. Risk factors associated with autopsy findings (emphysema, bronchitis, bronchiolitis, and silicosis) were identified by the logistic regression. To determine which of the pathological findings are most strongly associated with lung function, the stepwise linear regression model was applied.

4.4 RESULTS

There were 724 subjects who fulfilled the selection criteria. Lung function tests were invalid in 21 miners, thus only 703 miners were analysed for lung function. Table 4-1 summarises the characteristics of the subjects. On average, the miners were 64.2 years old at death and the mean duration of service was 23.7 years.

4.4.1 Validity of clinical findings

Table 4-2 shows the age adjusted odds ratios for the association between the presence of in life COAD outcomes (dyspnoea, rhonchi, sputum, cough) and smoking and CDE. Smoking was associated with all the in life COAD outcomes, especially in miners who had smoked ≥ 20 pack-years. Dust showed slight association with dyspnoea and rhonchi. Table 4-3 shows the association between lung function tests and increasing severity of symptoms and signs. The mean lung function values decreased significantly with increasing severity of all clinical findings. Table 4-4 shows the in life predictors of lung function which were selected into the regression model at the $p=0.15$ level. Rhonchi was the most significant predictor followed by dyspnoea. Sputum, cough and CDE were not selected into the model (even if rhonchi and dyspnoea were not included in the model). The model explained 37% of variability in FEV₁%, 31% variability in FVC% and 30% in FEV₁/FVC%.

4.4.2 Association between autopsy findings, lung function and clinical findings

Table 4-5 summarises the association between autopsy findings, lung function tests, and clinical findings. The moderate and marked categories for bronchitis, bronchiolitis and silicosis were combined because of the small numbers of miners in these categories.

Emphysema score was significantly associated with airflow impairment (FEV₁%).

and FEV₁/FVC %), and with dyspnoea. Figure 4-1 shows the trend between FEV₁% the emphysema score, and indicated are the compensation categories for FEV₁%. Bronchitis was associated also with some airflow impairment in the moderate/marked category and, of the symptoms, rhonchi, sputum and cough showed the strongest association with bronchitis. A moderate/marked degree of bronchiolitis was associated with slightly reduced airflow and with sputum only. The degree of silicosis was not associated with any of these COAD outcomes (not shown).

The risk factors tested for an association with emphysema, bronchitis and bronchiolitis were smoking pack-yrs, age, silicosis, and CDE. Only smoking was significantly associated with all the autopsy outcomes for COAD (results not shown). Figure 4-2 shows the association between smoking and emphysema score.

Of the subjects with dust exposure 279 had no silicosis, 202 had insignificant, 105 slight, 69 moderate and 24 marked degree. Silicosis was associated with increasing age at death and with CDE. The adjusted odds ratios (95% CI) for increasing quartiles of years of age (<57, 57-62, 62-67, >67 years) were 1.0, 1.7 (1.01-2.9), 1.8 (1.1-3.2), 3.3 (1.9-5.7), respectively. The adjusted odds ratios (95% CI) for increasing quartiles of CDE were 1.0, 4.5 (2.2-9.2), 7.2 (3.6-14.5), 17.6 (8.9-35.0). The strong association between silicosis and CDE indicates that the CDE variable is reasonably reliable.

Table 4-6 shows the autopsy findings for COAD and silicosis as predictors of the observed lung function measurements. Predictors for total lung capacity and FEV₂₅₋₇₅% are also shown. Emphysema score was the main predictor for tests of airflow. The categories shown in Table 4-5, for bronchitis and bronchiolitis, were entered into the regression model. Silicosis categories insignificant and slight, and moderate and marked were combined and compared to no silicosis

category.

To determine whether bronchitis in the absence of emphysema is associated with significant lung function impairment, we selected subjects with low emphysema score 0-5 (n=91), and tested for trend between bronchitis and lung function. The mean FEV₁% (S.D.) decreased with bronchitis score none, insignificant, and moderate/marked as follows: 88.8% (22.4), 82.4% (13.5), p=0.19, and 75.2% (17.4), p=0.01, respectively. (P-values are for multiple comparison of the means using the lowest category as a baseline.) The FEV₁/FVC% (S.D.) also decreased from 97.3% (8.3), to 97.7% (8.5), p=0.89, and 90.0% (11.6), p=0.001. The data indicate that in the absence of emphysema, even a moderate/marked degree of bronchitis is only associated with mild lung function impairment.

4.5 DISCUSSION

In South Africa, according to the Occupational Diseases in Mines and Works Act of 1973 and 1993, COAD is compensable. Compensation is based on lung function impairment in life and on autopsy findings. At autopsy, the pathological changes used for compensation are emphysema, bronchitis assessed by mucus gland hyperplasia, and bronchiolitis assessed by goblet cell metaplasia. The main objective of the study was to evaluate whether the autopsy findings for COAD correlate with lung function impairment and respiratory symptoms and signs observed within 5 years prior to death.

Firstly, we assessed the reliability of the lung function and respiratory symptoms data to which the autopsy findings were correlated. This was done by assessing the associations between the in life COAD outcomes, and known risk factors for COAD (smoking, silica dust, age), and also by

testing the associations between respiratory symptoms and signs and lung function tests. Of the risk factors only smoking was significantly associated with respiratory symptoms, signs and lung function impairment (see Table 4-2). In the univariate analysis all respiratory symptoms and signs were associated significantly with decreasing lung function (see Table 4-3). However, in the multivariate analysis only rhonchi and dyspnoea, but not cough and sputum, were selected as predictors; rhonchi accounting for 15% and 13% of the variation in FEV₁ % and FEV₁/FVC%, respectively, and dyspnoea for 6% and 3.5% of the variation, respectively (see Table 4-4).

In the next step of the analysis we compared autopsy findings with in life COAD outcomes. The degree of emphysema was associated with lung function impairment. The mean values for FEV₁% decreased with emphysema score categories 0-5, 5-35, 35-65, and >65 from 78.8%, to 66.2%, 52.0%, and 46.0%, respectively (see Table 4-5). These values are comparable to the lower limit of the FEV₁ % ranges used for in life compensation viz. normal ($\geq 80\%$), mild (79-65%), moderate (65-52%) and severe ($< 52\%$) impairment. A continuous exponential relationship between FEV₁ % and emphysema was observed (see Figure 4-1). Already small amount of emphysema identifiable at autopsy causes measurable lung function impairment. This suggests that even the small degree of emphysema visible at autopsy is a marker of a slow continuous process of elastic tissue destruction taking place in the lungs over the years.⁹ The categories of impairment used for compensation and the amount of emphysema observed at autopsy are also indicated. Of the respiratory symptoms and signs, dyspnoea showed the strongest association with emphysema (see Table 4-5).

In the univariate analysis, the degree of bronchitis was associated with

impairment in FEV₁% (see Table 4-5). However, in subjects without emphysema (score 0-5), even moderate/marked bronchitis was associated with mild airflow impairment only (FEV₁% of 75%). Of the respiratory symptoms and signs, rhonchi, sputum and cough showed the strongest association with bronchitis. Only moderate/marked degree of bronchiolitis was associated with airflow impairment (FEV₁% of 62.8%). Of the symptoms and signs, only sputum was significantly associated with bronchiolitis (Table 4-5).

In the multivariate analysis (Table 4-6), of the autopsy outcomes, emphysema was the most important predictor of lung function and accounted for 20% of the variation in FEV₁% and 30% of the variation in FEV₁/FVC%. Bronchitis accounted for 1.3% and 1.8% of the variation, respectively. Bronchiolitis was not selected as a predictor of lung function. There were 93 subjects with moderate or marked silicosis at autopsy and these subjects had decreased FEF_{25-75%} and total lung capacity (TLC) at $p < 0.10$ significance level (see Table 4-6). Of the potential risk factors for COAD, only smoking was significantly associated with the autopsy COAD outcomes. Neither silicosis nor CDE were associated with any of the autopsy COAD outcomes. There was, however, a strong association between silicosis and CDE.

The study has the following limitations: (1) selection of the subjects was determined by the availability of autopsy results. Only miners with whole lung sections were selected, and of these, only those with lung tissue which was adequately preserved to enable assessment of bronchitis and bronchiolitis were included. There is no obvious reason, however, how this could have biased the results. (2) At the time when the study subjects underwent lung function tests, lung function tests were mainly done on men who were trying to obtain compensation, or who had medical problems. Thus the study would probably

include both relatively healthy miners trying to get compensation, and miners with respiratory problems. Also miners with the highest degree of compensation obtained in life are likely to be under represented.

It is likely that the above limitations reflect on the lack of association between the COAD outcomes and cumulative dust exposure and silicosis. The above limitations are, however, unlikely to bias the association between autopsy findings and clinical findings. The evidence in the literature shows that the pathological changes in the lungs of subjects exposed to silica dust include emphysema, silicosis, airways disease and also tuberculosis, and that there is an association between these and silica dust exposure.

The precise nature of the pathological changes due to inhalation of silica dust is however complex and not completely understood. According to the ATS standards,⁴ emphysema is the most important pathological determinant of lung function impairment and tobacco smoking is the main risk factor in the etiology of emphysema. The results of our study support this. The association between emphysema and silica dust has been investigated in several autopsy based studies. Becklake et al.¹⁰ reported that South African gold miners with 20 years of working in high dust had a 12.7 (95% CI 3-52) times higher risk of having moderate emphysema in comparison to miners who never worked in high dust. No association between emphysema and silicosis was found. When the data from the Becklake's et al. (1987) study were adjusted for a selection bias, the odds ratio decreased to 3.06 (95% CI 1.14-8.23).¹¹ This revised result is more in line with a second autopsy study on South African gold miners, which found that miners with the highest dust exposure had odds ratio of 1.6 (95% CI 0.8-2.0) for developing moderate/marked emphysema and, in addition, miners with moderate silicosis had a risk of emphysema of 2.0 (95% CI 1.2-3.5).¹² According to this

study, miners with both high dust exposure and silicosis had 3.2 times higher odds of developing moderate emphysema than miners with low dust exposure and no silicosis. The effect of dust, relative to the effect of smoking was, however, small.¹² Smoking 20 or more cigarettes per day increased the odds of developing moderate emphysema 28.3 times. Another study of non-smoking South African gold miners found little emphysema, and the emphysema was not associated with dust or functional impairment;¹³ silicosis showed however slight association with emphysema. These and other studies on living miners,³ suggest that silica dust on its own probably causes only insignificant emphysema, whereas smoking alone, and the synergistic effect of smoking and dust can cause moderate and marked emphysema.

The slight association between emphysema and silicosis, observed in two of the above studies^{12,13} might be due to silicosis acting as a surrogate variable for the effect of silica dust on emphysema. There is supporting evidence for this. In studies which used computer tomography silicosis appeared to be associated with obstructive functional impairment but, after emphysema was adjusted for, the association disappeared and only emphysema remained correlated with impairment.^{14,15,16} In a case control study of silicosis and COAD, silicosis was associated with obstructive impairment, but when cumulative dust exposure was adjusted for, the association between silicosis and lung function disappeared and only dust exposure was a significant predictor of lung function.¹⁷

Previous studies on white South African gold miners did not observe that silicosis per se was associated with impairment of FEV₁ or FVC,^{17,18} but silicotic subjects were found to have impairment in FEF₂₅₋₇₅%.¹⁷ A case control study of silicotic and non-silicotic South African gold miners matched for smoking and dust exposure

found that, of all the comprehensive lung function tests done, only the slope of the alveolar plateau (phase 3) and the closing volume were significantly higher in silicotic subjects.¹⁸ These two studies as well as a study of Chinese silica dust exposed workers,¹⁹ point to an association between silicosis and small airways disease.

Experimental and case studies demonstrated the existence of a small airway lesion specific to mineral dust, namely mineral dust airway disease (MDAD).^{20,21} MDAD is reported to be morphologically distinguishable from small airway disease caused by tobacco smoke, and consists mainly of marked fibrosis and pigmentation of the respiratory bronchioles. Patients with MDAD can have significant abnormalities of FEV₁, FEF₂₅₋₇₅, vital capacity (VC) and nitrogen washout.²⁰ Lesions in the small airways can be reliably detected by tests of closing capacity and the slope of alveolar phase III of the single breath washout curve even when other tests are normal.²²

Epidemiologic studies done on black South African miners, however, report that silicosis is associated with a substantial lung function loss.^{2,26,27,28} Men with category 3/3 silicosis, compared to men without silicosis, had reduction of FEV₁ of 447 ml after controlling for the effect of tobacco smoking and duration of dust exposure.² The differences between the two groups of miners may be due to more severe silicosis in black miners. However, age adjusted autopsy data collected from 1974-1995, on some 70 000 miners, do not show that black miners have substantially higher prevalence or severity of silicosis during this period. Black miners, do, however, have a much higher incidence of pulmonary tuberculosis which increases substantially with the severity of silicosis^{23,24} and with increasing dust exposure.²⁵ A significant association between a past history of tuberculosis and loss of lung function was observed in a study of former gold miners from Botswana.²⁶ In

our current study of the effect of tuberculosis on lung function impairment in black gold miners, we observed large losses of lung function increasing with the number of pulmonary tuberculosis episodes (Section 8). Thus the effect of silicosis on lung function in black miners is likely to be worse due to complications with associated tuberculosis and with massive fibrosis.

In conclusion, the data from our study suggest that pathological assessment of emphysema, as done at NCOH, correlates strongly with lung function tests for airflow obstruction. Although there is some association between lung function and bronchitis and bronchiolitis, the degree of impairment remains statistically insignificant after emphysema is taken into account. The lack of association between emphysema and dust exposure is likely because of the study limitations, since other studies supports the existence of an association between emphysema and silica dust. However, relative to the effect of smoking, this association is small and dependent on the presence of tobacco smoking. Mineral dust airway disease, reported to be associated with small airways type lung function impairment, was not assessed at autopsy at NCOH. If MDAD on its own is however important in the development of significant respiratory disability in silica dust exposed workers, then workers with functional impairment due to this condition would not be identified at autopsy examinations done by NCOH. However, more studies are needed to quantify the effect of small airways disease due to silica dust on functional impairment. It is clear from this data that in prevention of COPD due to emphysema, emphasis should be placed on smoking intervention. The loss of lung function associated with simple silicosis as seen in these miners is mainly of restrictive nature. However, because silicosis, complicated by pulmonary tuberculosis and massive fibrosis, leads to large losses of lung function, and any silicosis

infection,²⁹ especially in South African gold mines, any degree of silicosis should be prevented by keeping dust exposures low.

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Table 4-1 Characteristics of the study population

CHARACTERISTIC	n	MEAN (S.D.)		RANGE
GENERAL				
Year of birth	724	1916	(8.6)	1880 - 1945
Age at death (Yrs)	724	64.2	(8.3)	38 - 102
SMOKING HISTORY				
Pack-years smoked	724	31.8	(21.1)	0 - 119
WORK HISTORY				
CDE by 50 yrs (RSA-yrs/1000)	724	23.30	(14.10)	0 - 67.84
Total CDE (RSA-yrs/1000)	724	28.56	(17.49)	0 - 96.15
Years of gold mining dust exposure	706	23.7	(18.0)	0.1 - 44.7
LUNG FUNCTION				
Age at lung function test (Yrs)	703*	61.5	(8.3)	35 - 99
Years prior to death	703	2.2	(1.5)	0 - 7#
FEV ₁ (% predicted)	703	65.3	(22.4)	13.0 - 130.0
FVC (% predicted)	703	83.4	(16.6)	39.0 - 150.0
FEV ₁ /FVC (%predicted)	703	60.9	(15.6)	18.1 - 109.8
FEF _{25-75%}	703	1.53	(1.14)	0.14-7.30
Total lung capacity (L)	524	7.10	(1.23)	3.72-12.43
IN-LIFE SYMPTOMS AND SIGNS	n	n(+ve)	(%)	
Dyspnoea (marked)	722	180	24.9	
Rhonchi	715	326	45.6	
Sputum	723	438	60.5	
Cough	722	467	64.7	

* 21 subjects were found not to have acceptable lung function after they were selected into the study.

Table 4-2 Adjusted odds ratios for factors associated with clinical findings (symptoms, signs and lung function)

RISK FACTOR	TOTAL (n = 724)	DYSPNOEA Marked (n = 180)		RHONCHI Any (n = 326)		SPUTUM Any (n = 438)		COUGH Any (n = 467)	
		n	OR (95% C.I.)	n	OR (95% C.I.)	n	OR (95% C.I.)	n	OR (95% C.I.)
SMOKING (Pack-Yrs)									
None	73	12	1.0	17	1.0	32	1.0	39	1.0
< 20	146	32	1.41 (0.67 - 2.98)	57	2.05 (1.07 - 3.93)	90	1.89 (1.05 - 3.37)	93	1.44 (0.81 - 2.58)
20 - 30	137	43	2.23 (1.08 - 3.79)	69	3.25 (1.70 - 6.20)	85	1.99 (1.11 - 3.56)	92	1.71 (0.95 - 3.07)
30 - 40	143	38	1.82 (0.88 - 3.79)	71	3.21 (1.68 - 6.13)	90	2.01 (1.12 - 3.60)	93	1.57 (0.88 - 2.82)
> 40	225	55	1.68 (0.84 - 3.37)	112	3.38 (1.84 - 6.22)	141	2.17 (1.26 - 3.72)	150	1.78 (1.04 - 3.06)
CDE BY AGE 50 (RSA-rs/1000)*									
< 13.72	178	39	1.0	71	1.0	108	1.0	110	1.0
13.7 - 23.2	175	39	0.94 (0.58 - 1.53)	82	1.41 (0.93 - 2.15)	109	1.04 (0.68 - 1.59)	113	1.03 (0.67 - 1.59)
23.2 - 33.4	177	39	0.93 (0.57 - 1.51)	86	1.49 (0.98 - 2.26)	104	0.91 (0.60 - 1.39)	114	1.05 (0.68 - 1.61)
> 33.4	176	56	1.53 (0.96 - 2.43)	80	1.33 (0.87 - 2.04)	104	0.95 (0.62 - 1.45)	114	1.08 (0.70 - 1.66)

*18 subjects who did not have any dusty shifts were excluded from the analysis

Table 4-3 Trends in mean lung function measurements with increasing severity of respiratory symptoms and signs

LUNG FUNCTION MEASURE	DYSPNOEA			RHONCHI			SPUTUM			COUGH		
	None (n=112)	Some (n=414)	Marked (n=175)	None (n=376)	Some (n=280)	Marked (n=38)	None (n=275)	Some (n=414)	Marked (n=13)	None (n=247)	Some (n=430)	Marked (n=24)
FEV ₁ % Mean (S.D.)	78.20 (18.82)	67.12 (20.85)	53.01**** (22.35)	73.23 (19.86)	57.14 (21.19)	44.16 **** (20.24)	70.85 (22.09)	62.18 (22.00)	51.39 **** (17.84)	70.41 (22.13)	63.04 (22.13)	54.00 **** (19.49)
FVC % Mean (S.D.)	90.14 (15.81)	84.86 (15.61)	75.61**** (16.84)	87.47 (15.97)	79.30 (16.25)	72.37 **** (15.62)	86.77 (16.56)	81.25 (16.38)	79.54 **** (16.68)	86.39 (17.07)	81.80 (16.17)	80.25 *** (17.43)
FEV ₁ / FVC% Mean (S.D.)	86.57 (14.21)	78.65 (19.11)	68.46**** (20.92)	83.43 (17.29)	71.13 (19.49)	59.50 **** (19.48)	80.87 (18.63)	75.50 (20.16)	64.15 **** (17.35)	80.70 (18.62)	76.03 (20.10)	66.71 **** (18.78)

* p < 0.05. ** p < 0.01. *** p < 0.001. **** p < 0.0001

Table 4-4 Significant predictors of lung function obtained within 5 years of death

PREDICTOR	FEV ₁ (n = 692)			FVC (n = 692)			%FEV ₁ /FVC (n = 692)		
	β Coefficient	Std. Error	Partial r ²	β Coefficient	Std. Error	Partial r ²	β Coefficient	Std. Error	Partial r ²
Rhonchi	-0.4423	(0.0437) ***	0.1531	-0.2630	(0.0451) ***	0.0385	-8.5805	(0.8721) ***	0.1336
Dyspnoea	-0.3138	(0.0414) ***	0.0620	-0.2644	(0.0428) ***	0.0802	-4.5080	(0.9259) ***	0.0350
Height (cm)	0.0101	(0.0043) *	0.0049	0.0388	(0.0040) ***	0.1356	-0.4365	(0.0872) ***	0.0233
Weight (Kg)	0.0114	(0.0019) ***	0.0840	-	-	-	0.3801	(0.0379) ***	0.0950
Age (Yrs)	-0.0974	(0.0256) ***	0.0444	-0.1027	(0.0266) ***	0.0386	-0.1172	(0.0623)	0.0036
Age ²	0.0006	(0.0002) **	0.0098	0.0007	(0.0002) **	0.0113	-	-	-
Pack-yrs smoked	-0.0042	(0.0012) ***	0.0118	-0.0031	(0.0013) *	0.0062	-0.0596	(0.0242) *	0.0083
Model r ² (p value)	0.3700	(p=0.0001)***	0.3700	0.3104	(p=0.0001)***	0.3104	0.2989	(p=0.0001)***	0.2989

- a variable was not selected into the model at 0.15 probability level

* p < 0.05. ** p < 0.01. *** p < 0.001. **** p < 0.0001

Table 4-5 Relation of autopsy findings to lung function (mean values) and in-life symptoms and signs (percentage).

AUTOPSY FINDINGS	LUNG FUNCTION TESTS#			CLINICAL FINDINGS&			
	FEV ₁ (% predicted)	FVC (% predicted)	% FEV ₁ /FVC (% predicted)	DYSPNOEA marked (n=180)	RHONCHI any (n=326)	SPUTUM any (n=438)	COUGH any (n=467)
	Mean (S.D)	Mean (S.D)	Mean (S.D)	n (%)	n (%)	n (%)	n (%)
EMPHYSEMA SCORE							
0 - 5 (n=179)	78.8 (18.2)	84.7 (14.2)	92.7 (13.1)	25 (14.0)	61 (34.7)	103 (57.5)	113 (63.1)
5 - 35 (n=329)	66.2 (21.6) ****	84.8 (18.0)	77.2 (17.6) ****	78 (23.7)	162 (50.0)	191 (58.5)	203 (61.9)
35 - 65 (n=170)	52.0 (19.4) ****	80.1 (16.5) *	63.9 (17.4) ****	65 (38.2)	89 (52.4)	116 (68.2)	121 (71.2)
> 65 (n=18)	46.0 (18.7) ****	77.2 (15.1)	59.1 (21.5) ****	9 (52.9) ***	4 (23.5) *	13 (76.5)*	13 (76.5)
BRONCHITIS							
None (n=126)	70.6 (22.7)	84.2 (15.3)	82.6 (18.5)	23 (18.3)	43 (34.4)	62 (49.2)	67 (53.2)
Insignificant (n=350)	66.3 (21.9)	83.7 (16.8)	78.3 (19.7) *	88 (25.1)	150 (43.2)	209 (59.7)	224 (64.2)
Mod/ marked (n=248)	61.4 (22.4) **	82.5 (17.1)	73.4 (19.8) **	69 (28.1) *	133 (54.7) ***	167 (67.6) ***	176 (71.3) ***
BRONCHIOLITIS							
None (n=70)	66.6 (19.1)	84.1 (13.6)	78.9 (17.7)	18 (25.7)	35 (50.7)	35 (50.0)	42 (60.0)
Insignificant (n=363)	67.1 (21.7)	84.1 (16.1)	79.0 (19.3)	90 (24.9)	148 (41.5)	217 (59.9)	231 (63.8)
Mod/ marked (n=291)	62.8 (23.8) *	82.3 (17.9)	75.0 (20.6) *	72 (24.7)	143 (49.5)	186 (63.9)*	194 (66.9)

a multiple comparison test in analysis of variance was done using the lowest autopsy category as a comparison group.

& a chi-squared test for trend was used.

* p < 0.05. ** p < 0.01. *** p < 0.001. **** p < 0.0001

Table 4-6 Autopsy-diagnosed findings as predictors of lung function

PREDICTOR	FEV ₁ β Coefficient (S.E.)	FVC β Coefficient (S.E.)	%FEV ₁ /FVC β Coefficient (S.E.)	FEF _{25-75%} β Coefficient (S.E.)	Total Lung Capacity β Coefficient (S.E.)
Emphysema	-0.017 (0.001) ****	-0.003 (0.001) **	-0.430 (0.026) ****	-0.027 (0.002) ****	0.022 (0.002) ****
Bronchitis	-0.126 (0.041) ***	-0.029 (0.044)	-2.800 (0.759)	-0.224 (0.058) ****	0.138 (0.066) **
Bronchiolitis	-0.056 (0.046)	-0.052 (0.048)	-1.143 (0.839)	-0.040 (0.064)	0.032 (0.074)
Silicosis 1 & 2	0.056 (0.059)	0.036 (0.062)	1.284 (1.082)	0.045 (0.083)	-0.040 (0.094)
Silicosis 3 & 4	-0.050 (0.087)	0.027 (0.091)	-1.617 (1.586)	-0.220 (0.121)*	-0.253 (0.139)*
Model r²	0.28****	0.20 ****	0.33 ****	0.29 ****	0.38****

* p < 0.10. ** p < 0.05. *** p < 0.01. **** p < 0.0001.

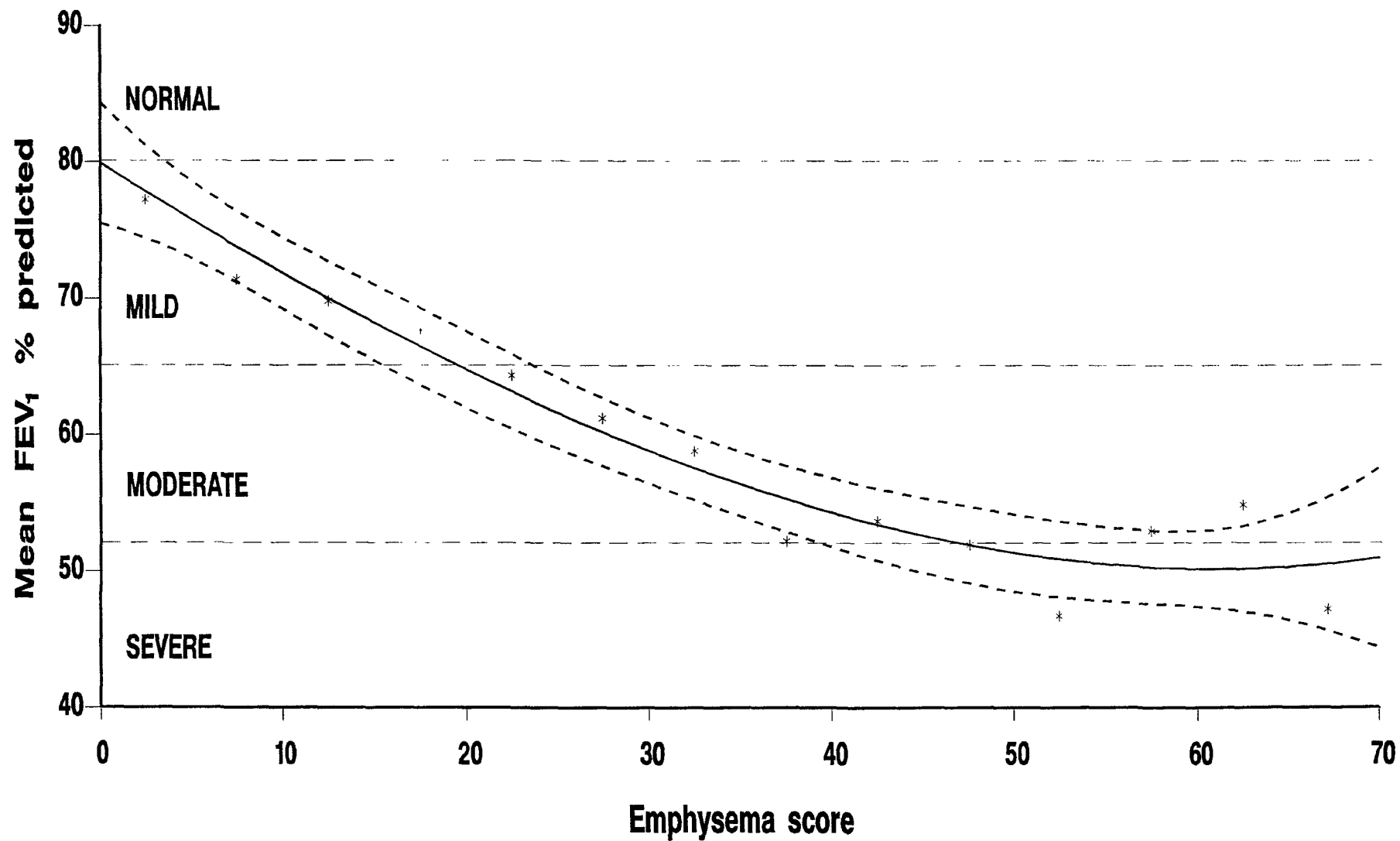


Figure 4-1 Mean FEV₁ (% predicted) by emphysema score, compensation impairment categories (normal, mild, moderate, severe) are indicated

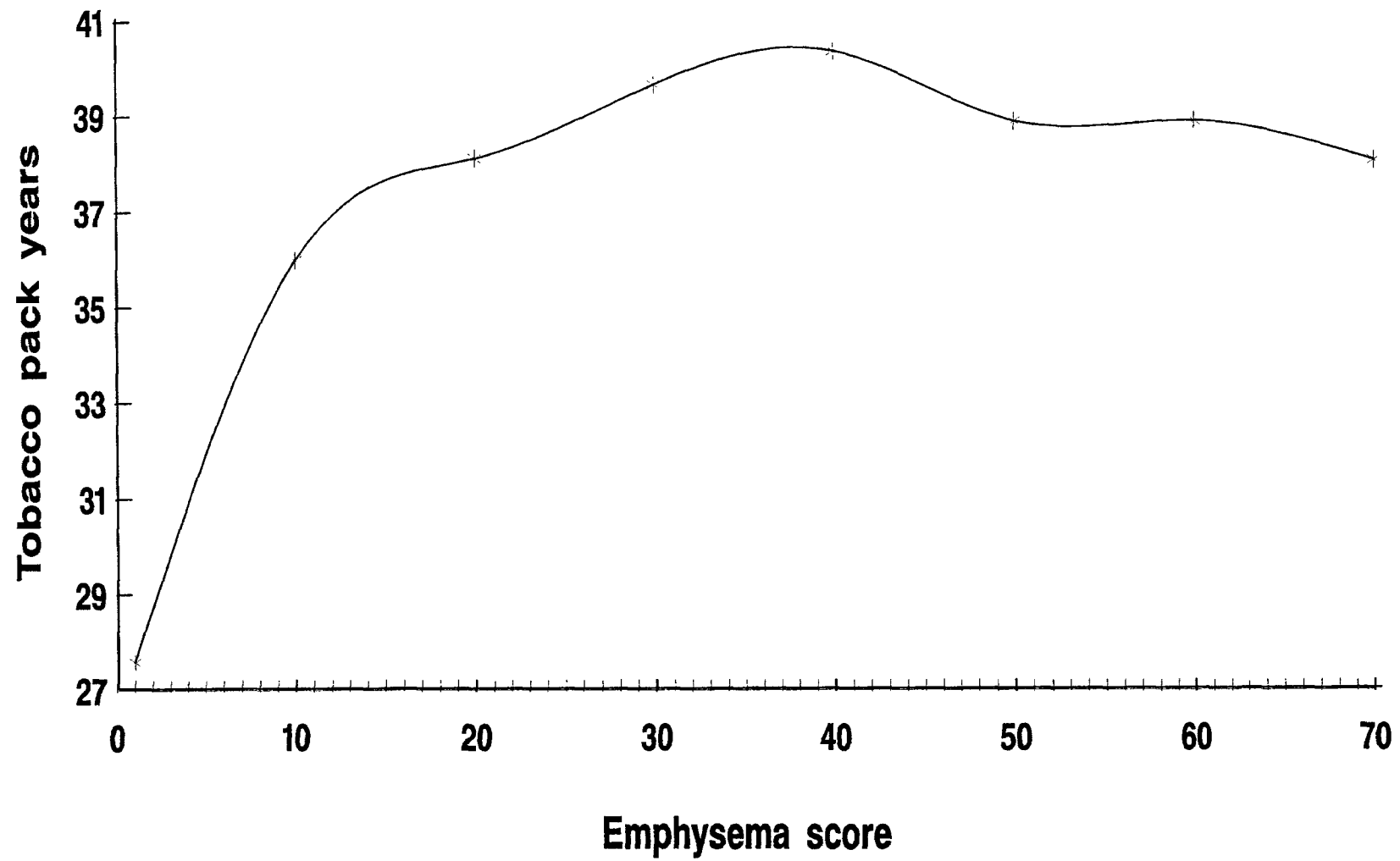


Figure 4-2 Relationship between tobacco pack - yrs smoked and emphysema found at autopsy

SECTION 5 - RISK OF SILICOSIS

Risk of silicosis in a cohort of white South African gold miners

Eva Hnizdo and G.K. Sluis-Cremer

5.1 Abstract

The risk of silicosis was investigated in a cohort of 2,235 white South African gold miners who had, on average, 24 years of net service from 1940 to the early 1970's and who were followed up to 1991 for radiological signs of onset of silicosis (ILO Category 1/1 or more). There were 313 (14%) miners who developed signs of silicosis at an average age of 55.9 years. The latency period was largely independent of the cumulative dust exposure. In 57% of the silicotics, the radiological signs developed on average 7.4 years after mining exposure ceased. The risk of silicosis increased exponentially with the cumulative dust dose, the accelerated increase being after 7 mg/m³-years. At the highest exposure level of 15 mg/m³-years, which represents approximately 37 years of gold mining at average respirable dust concentration of 0.4 mg/m³, the cumulative risk for silicosis reached 77 percent. In conclusion, the risk of silicosis was strongly dose dependent, however, the latency period was largely independent of the dose.

5.2 Introduction

Silicosis is an occupational disease of South African (SA) gold miners. The rock mined in SA gold mines generally contains 60-90% of SiO_2 in the crystalline form of quartz. The concentrations of airborne dust were dramatically reduced by the 1930's, to the extent that simple silicosis was no longer a direct cause of death in miners who had started mining after the 1930's. The dust levels have not changed considerably between 1936 and 1960 (Page-Shipp et al, 1972), but they decreased by about 30% during the 1970's when the dust conditions in the mines were used to determine the mine's contribution towards a compensation fund. On average, the content of quartz in the respirable dust is approximately 30% (Beadle and Bradley, 1970).

Currently silicosis is still prevalent (Cowie et al, 1987) and it is a potential cause of disability, particularly through its association with pulmonary tuberculosis. It is known that silicosis can progress even after exposure to silica dust has ceased (Hessel et al, 1988). The extent to which this can occur has not been studied, although the information is of great relevance as the majority of black SA gold miners are migrant labourers whose health status is not followed after they leave the mining industry.

The purpose of the present study was to investigate the risk of silicosis and the latency period in relation to silica dust exposure in a cohort of 2,260 white SA gold miners who had extensive mining exposure, well-recorded occupational history and a long medical follow-up. The cohort started mining after 1938 and was followed for onset

of silicosis to the end of 1991. The study estimates: i) the dose-response relationship between silica dust exposure and the risk of silicosis, ii) the dose-response relationship between silica dust exposure and the cumulative risk of silicosis, and iii) the effect of exposure on the latency period (the time from first exposure to the onset of silicosis) and the age of onset of silicosis.

5.3 Material and Methods

5.3.1 Study subjects.

The cohort studied constituted 2260 white gold miners selected during the years 1968-1971 for a study of respiratory disease (Wiles and Faure, 1977). The selection criteria were: attendance at a compulsory medical examination during the period 1968-71, age 45 to 54 years, and underground service of at least 10 years, with less than two years of service in mines other than gold mines. We excluded 21 miners who had more than two years of mining in mines other than gold mines after 1968-71 and four miners for whom X-rays could not be found. Thus 2235 miners remained in the study.

5.3.2 Determination of silicosis onset.

The miners had an annual radiological examination while working in the mines, and subsequently most of the miners came for an occasional radiological examination. Since the years 1968-1971, 984 miners died and had an autopsy at which the presence and degree of silicosis was determined for medico-legal purposes as follows: 326 were

diagnosed as having slight or higher degree of silicosis, and 658 as having none or only an insignificant degree of silicosis.¹ Of the remaining 1,251 miners who did not have an autopsy, there were 657 miners who were compensated in life for any of the compensable lung diseases, i.e. pneumoconiosis, pulmonary tuberculosis or chronic obstructive lung disease, and 594 who were not compensated in life. Silicosis is compensable if profusion of rounded opacities reaches the ILO category 1/0. A large proportion of those compensated in life were compensated for chronic obstructive lung disease.

To identify the year of onset of silicosis, the radiographs of following groups of miners were read: group 1) all those who were found to have silicosis at autopsy (326); group 2: a systematic sample of 231 from the 658 who did not have silicosis at autopsy; group 3: all the 657 who had a compensable lung disease in life; group 4: a systematic sample of 100 from the 594 who did not have a compensable disease in life. All the miners were sorted together by their bureau number and batches of 30 files were selected at random for radiological reading.

The radiographs of each miner were read blindly, in a chronological order starting from the most recent radiograph, by two independent readers. The onset of silicosis was defined as the year when rounded opacities of ILO Category 1/1 or higher were first read. Only the reader whose readings correlated most strongly

with the autopsy findings was used for further analysis (Hnizdo et al, submitted).

As the false positive rate in group 2 was only 1.3% (Hnizdo et al, submitted) and none of the miners in group 4 were found to have rounded opacities of Category 1/1 or more, we assumed that these miners did not develop radiological signs of silicosis up to death or up to the year of most recent radiograph, respectively. Table I summarizes how many miners were in each group, how many radiographs were read and how many of those that were read were found to have radiological signs of silicosis (Category $\geq 1/1$). In total there were 313 miners identified as having a radiological category $\geq 1/1$.

Among the cohort of 2,235 miners, there were 313 miners who were followed up to the time when radiological signs developed, 658 miners who were followed up to death (year 1981, S.D. 5.4), and 1,264 miners who were followed up to the year of most recent radiograph (year 1982, S.D. 6.6, range 1968-1991).

¹An insignificant degree of silicosis is assigned when at the macroscopic examination of the lungs only an occasional nodule is found, whereas slight silicosis is assigned when few nodules are found. Insignificant degree of silicosis is not radiologically visible, whereas slight silicosis is (Hnizdo et al, submitted).

5.3.3 Evaluation of dust exposure.

Although routine sampling of airborne dust in SA gold mines is done by the government industrial hygienist, this sampling is primarily concerned with dust control and is not usable, as yet, for epidemiological studies. During the early 1960's, a special study was

done by Beadle (1971) to establish the shift-long dust exposure in a random sample of 20 gold mines (Page-Shipp and Harris, 1972). The standard thermal precipitator was used and the amount of incombustible and acid insoluble dust particles, which include mainly quartz and silicates, were measured in terms of the surface area of the respirable dust (RSA) and the number of respirable (sizes 0.5 to 5 μm) particles per m^3 . For the purpose of this study, the two measurements were used to calculate the mass of respirable dust, mg/m^3 (duToit, 1991). The mean mass concentrations of the incombustible and insoluble respirable particles, calculated for the nine occupational categories used, are shown in Table II under the headings of the main occupation in each category.

Three measures of dust exposure were calculated up to the onset of silicosis or up to the end of exposure: i) cumulative dust exposure in $\text{mg}/\text{m}^3\text{-years}$, CDE, ($\text{CDE} = \sum \text{number of dusty shifts} \times \text{the mean mass respirable dust concentration (Table II)} \times \text{the average number of hours spent underground} / (270 \times 8)$), where the summation $\sum$ is over all the occupational categories in which a miner worked, and 270 is the average number of shifts per year multiplied by 8 to obtain eight hour standardized years); ii) the average dust concentration in mg/m^3 , calculated by dividing the numerator in the CDE formula by the total number of hours spent underground; and iii) the net number of years of working in dusty occupations in gold mines, calculated as the total number of dusty shifts divided by 270.

5.3.4 Statistical analysis.

The method of estimation of risk and cumulative risk for pneumoconioses in relation to cumulative dust dose was described by Berry et al (1979) and Finkelstein (1985), and more recently applied to silicosis by Muir et al (1989). The risk of silicosis was calculated for increasing levels of CDE by means of the life table method (SAS Proc LIFETEST), as the fraction of subjects who developed silicosis, relative to the average number of subjects who were at risk of developing silicosis, during a given increase in CDE. Those at risk were those who did not develop silicosis up to a given level of CDE.

The relation between cumulative risk and CDE was estimated by the accelerated failure time model, using the Loglogistic distribution (SAS Proc LIFEREG), as

$$\text{CR}(t) = 1 - \{1 / [1 + \exp(-\mu/\sigma) \cdot t^{(1/\sigma)}]\}, t > 0, \sigma > 0, \quad (1)$$

where $\text{CR}(t)$ = cumulative risk at time t , μ and σ are the intercept and scale parameters, respectively, estimated by the LIFEREG procedure. Here t represents either the CDE or the number of years in dusty occupations. The Loglogistic distribution gave slightly better fit than the Weibull distribution used in the Muir et al (1989) study. The cumulative risk is adjusted for loss of subjects who did not develop silicosis, but whose exposure reached only a certain value (see Table IV). The cumulative risk calculated by the Kaplan-Meier method (SAS Proc LIFETEST) is also given for comparison.

5.4 Results

Table III gives the characteristics of the cohort, their year of birth and mining experience. For the 313 miners who developed rounded opacities, Table III gives the age and exposure characteristics up to the onset of silicosis.

Table IV gives, for the increasing levels of CDE, the number of miners who developed silicosis, the number of miners who were at risk, and the risk per one unit of CDE. For those with silicosis, Table IV gives the age, years of exposure, average dust concentration and latency period at the onset of silicosis.

The age at silicosis onset was constant at around 56 years of age up to 11 mg/m³-years and then increased in the two highest levels to ages 59 and 62 (Table IV). The same pattern was observed for the latency period, which was constant at around 35 years and then increased to 37.4 and 39.8, respectively. The increase in CDE corresponds to a simultaneous increase in the number of years spent in dusty occupations (from 20.5 to 37.0 years) and in the average concentration of respirable dust (from 0.17 to 0.42 mg/m³).

Figure 5-1 shows the increase in the estimated and observed cumulative risk in relation to CDE. The estimated coefficients for the Loglogistic distribution (see Eq. (1)) were: $\mu = 2.439$ (S.E. 0.019) and $\sigma = 0.2199$ (S.E. 0.009). The results from the Kaplan-Maier are also shown. Figure 5-2 shows the cumulative risk in relation to years of dust exposure, according to the mean concentration of

respirable dust.

5.5 Discussion

The study examined the risk of silicosis in a cohort of 2,235 white SA gold miners born 1913-24, who started exposure in the early 1940s, had on average 24 years of net service up to the early 1970s and were followed up to 1991 for the onset of radiological signs of silicosis.

There were 313 miners who developed radiological signs of silicosis (ILO Category $\geq 1/1$) during the follow-up period. The onset of silicosis occurred, on average, at 56 years of age, after 27 years of net service (Table III). In 135 miners (43%) the onset occurred while the miners were still working in the mines, at 51 years of age (range 39-61). In the other 178 (57%) miners, the onset occurred on average 7.4 (S.D. 5.5, range 0.1-25) years after the miners left the mines, at 59 years of age (range 44-74).

Up to the dose of 11 mg/m³-years, the miners developed silicosis at a similar average age (56 years) and latency period (35 years), regardless of the dose (Table IV). The miners in the two highest exposure levels were older at the time of silicosis onset, suggesting that these miners were less susceptible and could thus accumulate higher doses before they developed silicosis. The age at silicosis onset was only slightly correlated with CDE up to the onset (correlation coefficient, $r=0.164$).

The cumulative risk may provide an indication of the expected prevalence of

silicosis at various exposure levels. However, the latency period and the healthy worker effect are strong confounding factors in the association. According to Figure 2, the cumulative risk of silicosis is 25% at the dose of 9 mg/m³-years of respirable dust, a dose reached after an average 28 years of mining at an average dust concentration of 0.33 mg/m³ (Table IV). The cumulative risk then increases steeply, reaching 77% at 15 mg/m³-years, given a latency period of about 35 years.

Our results can be compared with those obtained from a recent study of 2,109 Canadian miners who joined the hardrock mining industry between 1940 and 1959 and in whom silicosis was also diagnosed as Category 1/1 or more (Muir et al, 1989). On average, the miners had shorter service than the miners in our study, about 15 years, ranging from 5 to 40 years, 20 years of follow-up, and their cumulative respirable silica dust ranged from 0 to 6 mg/m³-years (Muir, 1991). If we assume that in South African gold mines, the respirable dust, after heat and acid treatment, contains about 30% silica, then by multiplying the dust concentration in mg/m³ given in Table IV by 0.3 and by years in dust, we get the approximate range of cumulative silica dust for our miners as 1.02-4.66. Thus, it appears that the miners in our study had longer service, but were exposed to lower average concentration of respirable silica dust.

Only about 32 (1.5%) of the Canadian miners developed radiological signs of silicosis. The cumulative risk of silicosis was ~ 2.5 at 5 mg/m³-years and reached ~15% at 12 mg/m³-years. In our study, 14% of the miners developed radiological signs of

silicosis and the cumulative risk reached 77% at 15 mg/m³-years of cumulative respirable dust which is equivalent to ~4.5 mg/m³-years of cumulative respirable silica dust (assuming 30% quartz content). Although the follow-up period was longer in our study, this is unlikely to account for the marked differences in the risk of silicosis. It is possible that the average dust concentrations used in our study underestimated the actual exposures. There are no published measurements of today's exposures in SA gold mines, but an yearly average for the year 1991, from one of the dustier mine's stoping area, was reported as 0.48 mg/m³ of respirable dust with 25% of quartz. This concentration is higher than the one used in our study. Another explanation could be that SA quartz is more toxic than the Canadian quartz. In that case, the internationally determined threshold limit value for quartz of 0.1 mg/m³ may not necessarily be safe for SA gold miners.

The predicted risk values shown in Figure 3 indicate that after 32 years of working in exposures of 0.15 mg/m³ of respirable dust, the expected cumulative risk of silicosis is 5%, in 0.16-0.20 mg/m³ it is 8%, in 0.21-0.30 mg/m³ it is 17%, and in >0.30 mg/m³ it is 38%. These results are very similar to those obtained by Beadle (1971) for similar dust concentrations in a study of 1187 white SA gold miners who started mining in 1934-1938. The comparison with our study may not be valid, however, as the ILO classification was not used then (but the same reader read the X-rays in both studies).

From our previous study (Hnizdo et al, submitted) it was calculated that the reader in our study had the sensitivity and specificity

values of 0.39 and 0.99, respectively, when Category 1/1 was used as a cut-off point. The sensitivity for moderate and marked degree of silicosis diagnosed at autopsy increased to 0.46 and 0.74, respectively. Using these figures we estimated that approximately 280 (12.5%) miners will have moderate and 110 (4.9%) marked silicosis at death.

In addition, we also examined the onset of silicosis and exposure profile of the miners with varying degrees of silicosis found at autopsy. Table V shows characteristics of miners who were found to have rounded opacities Category 1/1 or more and who had also an autopsy. Those with marked silicosis had an onset at an earlier average age and at a lower level of dust exposure than the others; most of whom continued mining after onset, and had died slightly younger. This may reflect a situation where the most susceptible miners get silicosis at a younger age and thus continue exposure after onset which leads to increased severity of their disease. Continuing dust exposure after silicosis onset was found to be a significant predictor of silicosis progression (Hessel et al, 1988). A recent study of prognostic factors influencing survival of compensated silicotic patients from the Province of Quebec in Canada, found that the increasing radiological category was associated with decreasing probability of survival (Infante-Rivard et al, 1991).

Although the present study involved white gold miners exposed from the early 1940s to the early 1970s, the results are relevant to black miners currently employed

in the SA gold mines. During the year 1990, the compensation rate for silicosis was approximately 500 per 100,000 working miners, and those compensated for silicosis developed silicosis after working on average 16 years in the gold mines (Report, 1990). Cowie et al (1987) reported the prevalence of silicosis of 138/10,000 working black gold miners from Orange Free State gold mines. It is difficult to relate this figure, however, without knowing the age and exposure profile of the population studied. Especially problematic is that most of black miners are employed as migrant labour and stop working in the mines at about 40 years of age, often after they receive their compensation money for an occupational disease. For comparison, the new cases of silicosis diagnosed from 1938 to 1941 in the so called "New Rand Miners", white miners who were specially selected for fitness, had 17 years of service on average. The incidence of silicosis in 1940 in white miners was ≈ 9 cases per 1 000 working miners per year (Report, 1946). Thus, the black miners may be exposed to dust levels to which the white miners were exposed in the early 1940s. However, the severity of silicosis may be reduced in the black miners, as many of them work on a contract basis and have periods away from the mines. On the other hand, since the majority of black miners leave the mines at about 40 years of age and very rarely come for another examination, the full extent of silicosis development and associated complications with pulmonary tuberculosis are not known in these miners. The risk of tuberculous complications in silicosis is particularly great in black gold miners because the

tuberculosis morbidity in the general SA population is high (Cowie et al, 1989).

There are several known biases in the study. Firstly, the estimated cumulative dust exposure has a large error. This is because the industry average dust concentrations measured in 1960's were used and because of the conversion from RSA to mass. Although these indicate the relative intensity of silica dust exposure, the actual values may be somewhat different. Secondly, some miners may have developed silicosis after the radiological follow-up ceased, since not all the miners had follow-up to 1991. On the other hand, more than half of these miners have died since 1970, and 85% of those had an autopsy examination for silicosis. Thirdly, after the miners stopped working in the mines they did not have yearly radiological examinations. This could have increased the age of silicosis onset, but unlikely to the extent to alter the main conclusions.

In conclusion, the results from the present study indicate that:

- 1) the risk of silicosis increased exponentially with increasing cumulative dose of silica dust;
- 2) in dust levels above 7 mg/m³-years, the increase in the risk was accelerated;
- 3) in a large proportion of the miners, radiological signs of silicosis developed only after the miners were over 50 years of age and were no longer working in the mines;
- 4) the age at silicosis onset was not related strongly to the dose.

There are several implications from this and the previous progression study (Hessel, 1988).

- 1) To allow SA gold miners to have a life long

career, the dust levels in SA gold mines should be kept at levels at which the risk of silicosis is considerably reduced. Our data indicate that after 28 years of mining at 0.3 mg/m³ of respirable dust (equivalent to ≈ 0.1 mg/m³ of respirable quartz), which is equivalent to 9 mg/m³-years of respirable dust, about 25% of miners developed radiological signs of silicosis (Figure 2). This risk is unacceptable.

- 2) Because the risk of developing radiological signs of silicosis is age related and because of the strong association between silicosis and pulmonary tuberculosis, it is important that the health of gold miners' be monitored after their mining exposure ceases.

- 3) Miners who have silicosis of first degree should be moved to occupations with lower dust exposure, as continued dust exposure after silicosis onset is significantly related to silicosis progression. This may not happen while the miner is working, but may lead to development of marked silicosis at some later stage when he is no longer working in the mines and when his pulmonary health is no longer monitored.

- 4) The fibrogenic effect of quartz from SA gold mines should be compared to that from hardrock Canadian mines, to determine whether the quartz TLV of 0.1 mg/m³ is safe for SA's miners.

- 5) Epidemiological studies of risk of silicosis be carried out on black gold miners who form the bulk of the labour force.

5.6 REFERENCES

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Table5-1 Distribution of white South African gold miners according to four defined groups*. The number of radiographs read and number of those with ILO category $\geq 1/1$.

	With autopsy		Without autopsy		Total
	$\geq$ slight silicosis	none/ insignificant	compensated in life	not compensated in life	
N	326 ^a	658	657 ^c	594	2235
X-rays read	326 ^a	231 ^b	657 ^c	100 ^d	1314
X rays not read	0	427	0	494	921
Categ. $\geq 1/1$	128	3	182	0	313

* Number of radiographs read and the number of those with silicosis ILO category $>1/1$. See the text.

^a Group 1.

^b Group 2.

^c Group 3.

^d Group 4.

TABLE 5-2 Mean respirable dust concentrations in mg/m³ per shift, by Occupational Dust Categories, in South African Gold Miners

Measure	Shift sinkers developers	Assist. miners/ trammers	Shift bosses	Other Offici- als	Banks/ skips	Workers near shaft	Boiler- makers	Other artisans	
Average hrs in dust	8.0	7.8	7.7	5.2	4.0	7.5	6.5	6.3	5.7
Respirable dust concentration* (mg/m³)	0.48	0.37	0.27	0.30	0.30	0.13	0.10	0.19	0.19

* After heat and acid treatment.

TABLE 5-3 Characteristics of the cohort of 2,235 white South African miners followed from 1968/71 to 1991 and of the silicotic cases

Characteristic	Whole cohort mean $\pm$ SD (Range)	Cases Mean $\pm$ SD (Range)
Cohort	N=2,235	N=313
Year of Birth	1919 $\pm$ 2.5 (1913-1924)	1919 $\pm$ 2.5 (1913-1924)
Net years in dust	23.5 $\pm$ 4.9 (8.7-37.9)	26.9 $\pm$ 4.9 (14 -39)
Cumulative dust,mg/m ³ -yr	6.6 $\pm$ 2.7 (1.2-18.7)	8.4 $\pm$ 2.5 (2.4 -16.5)
Mean dust level, mg/m ³	0.29 $\pm$ 0.08 (0.11-0.47)	0.31 $\pm$ 0.07 (0.12 -0.46)
Year level when last in dust	1971 $\pm$ 5.2 (1948 - 1987)	1972 $\pm$ 4.5 (1957 - 1986)
Age at last exposure	52.6 $\pm$ 5.6 (30-70)	53.6 $\pm$ 4.9 (36 - 67)
Age at silicosis onset		55.9 $\pm$ 6.9 (39 - 74)
Year of silicosis onset		1975 $\pm$ 7.0 (1958 - 1990)

Table 5-4 Life table results for the risk of silicosis and the characteristics of silicotic white South African gold miners followed from 1968/71 to 1991

Midpoint CDE (mg/m ³ -yr)	No. cases	No. at risk	Risk per unit of CDE (mean ± SE)	Silicosis only [mean (range)]			
				Age at onset	Yrs in dust	Dust conc. (mg/m ³)	Latency period
1	0	2218					
3	9	2014	0.002 ± 0.001	56.4 (47 - 68)	20.5 (14-26)	0.17 (0.12-0.22)	36.2 (24-48)
5	48	1540	0.016 ± 0.002	56.1 (41 - 74)	23.5 (15-37)	0.24 (0.18-0.33)	35.1 (18-50)
7	85	984	0.045 ± 0.005	53.4 (39 - 70)	27.2 (16-37)	0.30 (0.22-0.41)	32.3 (18-50)
9	93	515	0.099 ± 0.010	56.6 (44 - 74)	28.0 (19-38)	0.33 (0.23-0.41)	35.1 (22-50)
11	53	197	0.156 ± 0.021	56.4 (45 - 72)	29.4 (23-36)	0.38 (0.30-0.45)	35.1 (23-48)
13	20	55	0.222 ± 0.048	58.9 (49 - 67)	31.5 (28-39)	0.41 (0.31-0.46)	37.4 (29-48)
15	5	11	0.227 ± 0.060	62.0 (57 - 71)	37.0 (36-39)	0.42 (0.41-0.43)	39.8 (35-48)

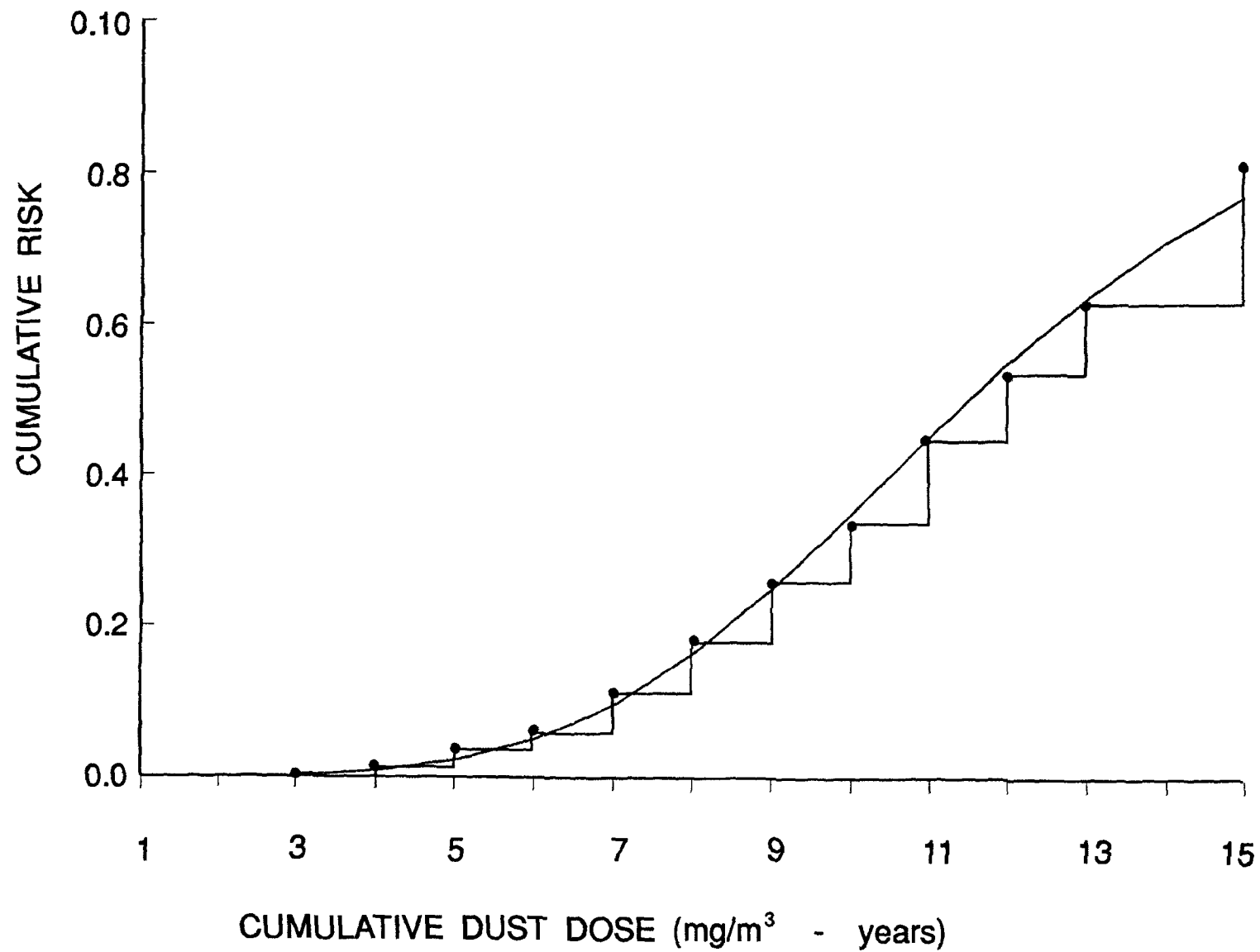


Figure 5-1 Cumulative risk of silicosis in relation to cumulative dust dose in mg/m^3 - years, calculated by the Kaplan-Meier method and estimated by the accelerated failure time model, EG. (1). White South African gold miners followed from 1968/71 to 1991

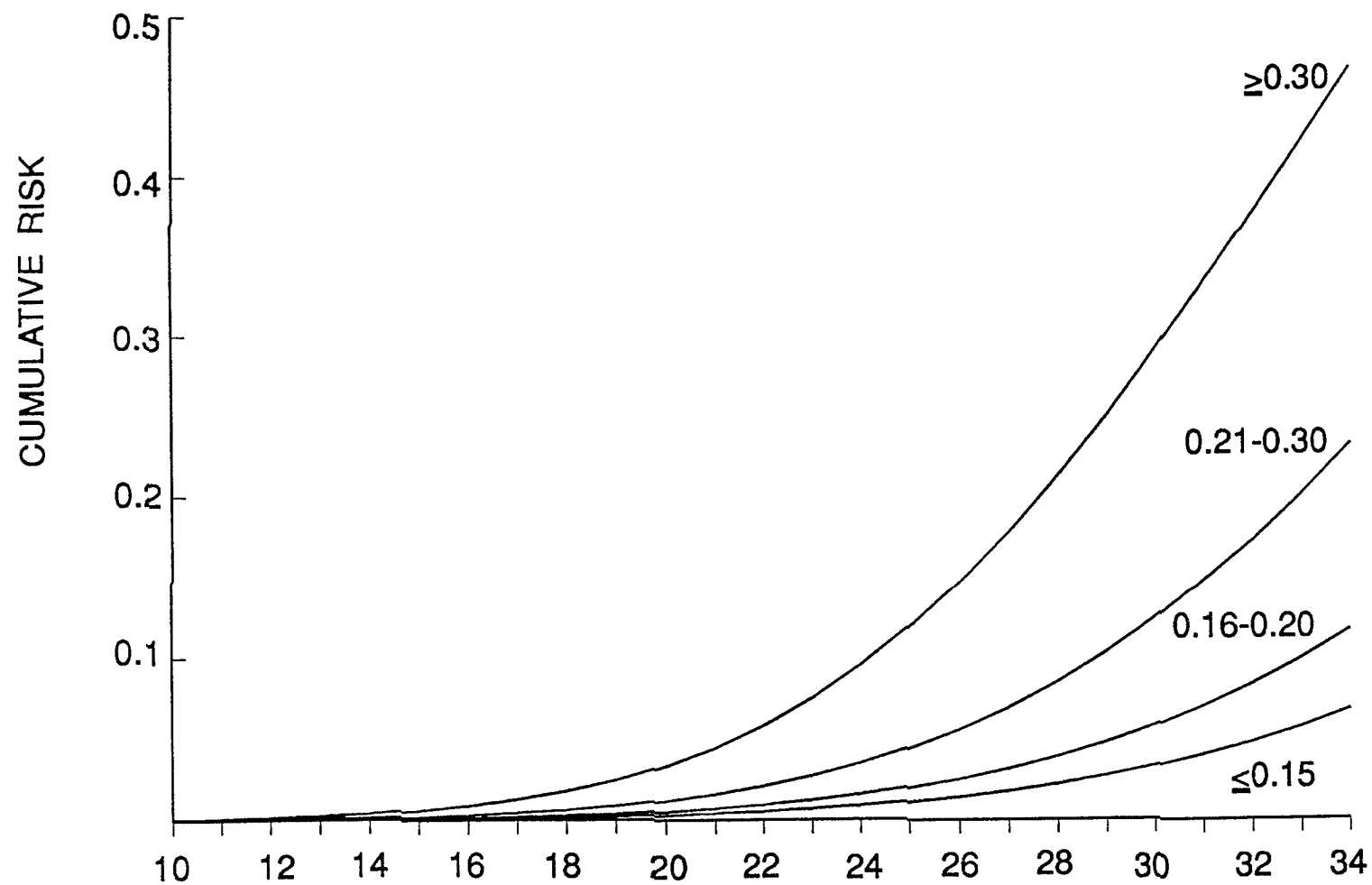


Figure 5-2 Cumulative risk of silicosis in relation to years of gold mining, according to levels of respirable dust. White South African gold miners followed from 1968/71 to 1991