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**Variation in silicosis prevalence in South African gold miners –  
an industry-wide study**

**by**

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## DECLARATION

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## Abstract

**Introduction:** This study investigates the prevalence of silicosis in the South African gold mining industry. Gold mining is an important industry in South Africa, yet has been blighted by silicosis and tuberculosis in miners since its inception in 1887. There have been two previous studies conducted in black in-service miners using modern epidemiologic methods that found high prevalences of silicosis. The objectives of our study were three-fold. Firstly, to determine silicosis prevalence stratified by certain variables. Secondly, to compare silicosis prevalences to these two previous studies conducted in order to determine whether any secular trends are present. Thirdly, to report on any variation in silicosis between mining shaft, mining company or mining region, and to generate hypotheses for any variation found.

**Methods:** A cross-sectional study was conducted as part of the Thibela-TB project in a sample of gold miners in three South African gold mining companies in three South African mining regions across 10 mining shafts or clusters. 9,599 participants were randomly selected from 10 clusters, (or mine shafts with associated hostels). The clusters were chosen from mine shafts with a predicted lifespan of more than 5 years and with a workforce of at least 1,000 people. A validated questionnaire was administered to capture covariates associated with silicosis and tuberculosis. Chest radiographs (CXR) were read by an experienced reader according to the International Labour Organisation (ILO) Classification of Radiographs of Pneumoconiosis (2000). Pulmonary tuberculosis (PTB) was read according to an internal Thibela-TB trial classification system. Crude prevalence of silicosis was reported. Prevalences stratified by certain covariates were also reported. Prevalence odds ratios were reported at the cluster and regional levels. Pearson's Chi-Squared Test was applied to 2 x k tables. Two sample t-tests were applied for hypothesis testing of numerical variables. **Results:** The *crude* prevalence of silicosis is 3.86% for ILO category 1/1 and above, and 5.22% for ILO category 1/0 and above. The mean length of service for all cases read was 17.3 years, (n = 9,531; SD = 10.3), and 27.0 years for cases with radiographic silicosis, (ILO category  $\geq$  1/1) (n = 367; SD 7.1). The radiographic prevalence of silicosis, (ILO category  $\geq$  1/1), ranged from 0.19% in the 0-4 year service group to 11.55% in the 30+ year service group. There are 15 cases of miners, who may have silicosis, (ILO category 1/0 and above), with less than 10 years in the industry. The radiographic prevalence of

silicosis, (ILO category  $\geq 1/1$ ), ranged from 0.19% in the younger than 26 years age group to 12.6% in the older than 56 years age group. A total of 20.4% (n = 1,958) of the participants had either radiological signs of PTB or a history of current or previous TB treatment. The prevalence of PTB evidence on CXR ranged from 14.68% in participants with no radiographic silicosis to 36.21% in participants with ILO category 2 & 3 silicosis. This study generally found a lower prevalence of silicosis for both definitions used, compared to the Cowie study conducted in 1984 for the age stratified groups above the age of 30 years.<sup>21</sup> This study has found a lower prevalence of silicosis of 11.6% in the 40+ year age group compared to the Churchyard (2004) study's silicosis prevalence of between 18.3-19.9% in a similar age group in the same mine shaft conducted around 2000.<sup>2</sup> This study found a significant three-fold difference in silicosis prevalence, (ILO category  $\geq 1/1$ ), between the highest prevalence (GN MK) and lowest prevalence (Kloof 7) clusters, (prevalence odds ratio 3.0, 95% C.I. 1.8 to 5.2,  $\chi^2 = 19.6$ ,  $p < 0.0001$ ). At a regional level this study found a significant 2.8-fold difference in silicosis prevalence, (ILO category  $\geq 1/1$ ), between the highest prevalence (Orkney) and the lowest prevalence (Welkom) regions, (prevalence odds ratio 2.8, 95% CI = 1.97 – 4.19,  $\chi^2 = 35.5$ ,  $p < 0.0001$ ). **Discussion:** There is still an unacceptably high prevalence of silicosis in black in-service gold miners in South Africa, with the *crude* prevalence reported probably being an underestimate due to a healthy worker effect. This study found a downward trend in silicosis prevalence compared to the two previous studies conducted in black working mining populations. This does appear to show that recent progress has been made in combating the scourge of silicosis that has afflicted the South African mining industry. However, a healthy worker survivor effect could also possibly explain this trend owing to the maturing HIV epidemic selecting out silicosis cases. Furthermore, this study has found that there is significant variation in silicosis prevalence between gold mining clusters (shafts) and between mining regions that requires further research. This variation is probably real, and not due to confounding or chance. The reason(s) for this variation is probably differences in respirable crystalline silica exposures, and possibly differences in respirable dust toxicity between the clusters and regions. These are two key areas that require further research. In addition, the 15 cases of silicosis in participants with fewer than 10 years of exposure to dust would suggest that there are still jobs and tasks in the industry where very high silica dust

exposures are occurring. The South African government and mining industry have set a target of no new cases of silicosis in miners exposed to dust after 2008. This seems unachievable.

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## **Acronyms**

ACGIH – American Conference of Governmental Industrial Hygienists

CXR – Chest X-Ray or Chest Radiograph

DME – South Africa Department of Minerals and Energy

DOL – South African Department of Labour

eCRF – Electronic Case Record Form

HIV – Human Immunodeficiency Virus

ILO – International Labour Organisation

MBOD – Medical Bureau of Occupational Diseases of South Africa

MHSA – Mine Health and Safety Act of 1996

MMR – Mass Miniaturised Radiographs

NIOSH – National Institute of Occupational Safety and Health of America

NUM – National Union of Mineworkers of South Africa

ODMWA – Occupational Diseases in Mines and Works Act of 1973

OSHA – Occupational Safety and Health Administration of America

PTB – Pulmonary Tuberculosis

TB – Tuberculosis

USA – United States of America

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# 1 Introduction

Prior to 1984 no studies had been reported using modern epidemiologic methods on silicosis prevalence in black in-service mine workers in the South African gold mining industry. The first to do so, by Cowie in 1984, found a crude prevalence of 1.4%.<sup>1</sup> A second more recent study by Churchyard (2004) and others conducted on a sample of 520 miners from one shaft in 2000, found an extremely high prevalence (about 20%) of silicosis in older in-service black miners. The participants in the Churchyard study had on average more than 20 years service duration in the industry.<sup>2</sup>

Currently in South Africa a large study is being conducted on tuberculosis (TB) prophylaxis called the Thibela-TB project. An opportunity was afforded to describe silicosis prevalence as part of a sub-study within the Thibela-TB study. The Thibela-TB study is a prospective cohort study with a final sample size of about 80,000 Southern African gold miners. The Thibela-TB study involved an initial baseline study from which information on silicosis was captured.

This study describes current silicosis prevalence in gold miners in South Africa on a large sample (9,599) across 10 shafts, in three mining companies, and in three different mining regions in South Africa. It is the first to be able to look at intershaft variation in silicosis prevalence, and as such can discuss potential reasons for any variation across shaft, company and region. It also provides important and current information on secular trends in silicosis prevalence in light of stated aims by industry and government to eliminate silicosis.

## 1.1 Historical perspective on silicosis

Mining and quarrying date back 6,000 to 10,000 years. Furthermore, accounts of dust-related occupational lung disease afflicting miners and stonecutters date back to ancient Grecian times. Hippocrates in 466 BC recognised lung disease in quarry workers in Ancient Greece, and Pliny advocated the use of a simple pigskin respirator to protect workers from lung disease associated with dust exposure.<sup>3</sup> In more recent times Agricola, in 1566, described lung disease in stonecutters and miners in his treatise on mining.<sup>3</sup> Likewise Ramazzini, the father of occupational medicine, associated mining with the development of asthma, phthisis,

cachexia and edema.<sup>4</sup> In 1713 Ramazzini made the following prescient observations on the association between dust and lung disease in stone-cutters and other tradesmen exposed to stone dust<sup>5</sup>:

*“Stone-cutters, sculptors, brick-cutters, and all the workers in this line, swallow down, when breathing, the hard, sharp, pointed splinters which come from the rocks. Hence they are almost always affected by cough and some become asthmatic and consumptive. When Diemerbrock performed autopsies on stone-cutters who died from asthma, he noticed that their lungs were full of very minute stones (‘small sand heaps’) so that, under the anatomical knife, the pulmonary ducts looked like sand.”*

More recently Thomas Legge, the first factory inspector of the Home Office in England, reported a high mortality in the miners of ganister, a type of silica rich fire-clay, and noted “*iron grey nodules*” in the lungs of these miners in 1901. He shared the conviction with JS Haldane, who conducted the seminal 1904 study on lung disease in Cornish tin miners, that it was ultimately not the dust, but the consumption by tuberculosis that led to their untimely deaths. AL Cochrane, who pioneered randomised controlled trials, conducted 30 years of meticulous research (with extremely high participant response rates) into pneumoconiosis and tuberculosis in the Welsh valleys of Rhondda Fach in the 1950s. He was particularly interested in the associations between dust, radiological category and disability, and went on to become an international figure pioneering the use of randomised controlled trails.

In assessing recent epidemiology of silicosis, there is evidence that silicosis and silica dust related diseases remain a global public health issue. Countries like Sweden have just about eliminated silicosis through stringent dust control measures.<sup>6</sup> However, many millions of workers in various other countries such as the United States of America (USA), Brazil, India, China and South Africa are exposed to excessively high levels of silica dust.<sup>7</sup> For example, significant silica dust exposure occurs in diverse industries such as mining and quarrying, sandblasting, blast furnaces, construction and stone-cutting. There are an estimated 10 million workers in China exposed to silica dust, with 9,871 new cases of silicosis reported in 1995 alone.<sup>8</sup> The USA alone has an estimated 1.7 million workers exposed to respirable crystalline silica.<sup>9</sup>

In South Africa, silica dust related occupational diseases such as silicosis, progressive massive fibrosis, chronic obstructive pulmonary disease (COPD), and tuberculosis, have relentlessly and severely afflicted gold miners in the South African mining industry since the first discovery of gold on the Witwatersrand in 1887.

Elaine Katz, in her excellent book “*The White Death*”, describes the immense toll that silicosis had on the health of gold miners in the Witwatersrand Gold Mines between 1886 and 1910.<sup>10</sup> Around this period it was estimated that 50% of white miners came from Cornwall in England as a result of the downscaling of the English mining industry. In contrast to the short term contracts held by black miners, the white miners worked continuously underground under relatively long term contracts. This continuous exposure to high concentrations of respirable crystalline silica dust resulted in exceptionally high morbidity and mortality rates from occupational lung disease. The high levels of dust were brought about by poor dust control, compounded by the widespread introduction of pneumatic dry-drilling in the late 1890s.<sup>10</sup> Pneumatic dry-drilling continued until about 1910 when the water-fed axial drill was introduced to try and stem the incredible high death rates in white miners.

The Van Niekerk Commission in 1912, for example, found that the average life expectancy of a white rock driller was just 33 years, and that they had an average working life of only 7 years.<sup>10</sup> Unfortunately, mortality rates were difficult to assess as many of the affected miners moved back to Cornwall once their health had deteriorated to the extent that they could not continue working. However, in 1907 it was estimated that the total *annual* death rate amongst rock drillers was probably in the order of 109 per thousand drillers.<sup>10</sup>

Cornwall exported healthy young men to South Africa, and the Witwatersrand gold mines returned those same Cornish rock drillers just 7 years later in the final phases of their lives, about to die from cardiorespiratory failure from severe silicosis or silicotuberculosis, (or as it was then called – miners’ phthisis).

Although occupational lung disease rates dropped with the introduction of wet-drilling in 1910, improved ventilation and new legislation (Miners’ Phthisis Act

of 1912),<sup>11</sup> the rates of silicosis in miners still remained unacceptably high. This was especially so in white miners with stable contracts and prolonged periods of exposure.

Since the first discovery of exceptionally rich gold deposits at Komatipoort in 1885, the mining industry in South Africa has played a major role in the economic and socio-political development of the country over the last century. By 1898 South Africa was the world's biggest gold producer and by 1970 was producing 79% of the Western World's gold.<sup>12</sup>

However, the gold was difficult to mine owing to the gold-bearing reefs dipping down deep below the surface. This necessitated underground mining. Low margins resulted in gold companies needing to be extremely efficient. Consequently cheap servile labour was used to reduce labour costs. This resulted in the displacement of large numbers of black workers from traditional rural areas to the gold mines during the 20<sup>th</sup> Century. Migrant men working in the mines were accommodated in overcrowded single-status hostels. This led to the breakdown of the family unit and traditional rural political structures, and thus reduced the self-sufficiency of rural communities.

The South African mining industry became the largest in the world, but although a rich capitalist class grew out of this, there was also the formation of a large oppressed labour class that worked for low pay and in unsafe working conditions. This inevitably resulted in increasing friction between labour unions and industry (for example, the mine workers' strike of 1946 involved 73,000 people).

These conditions were aggravated during the time of the apartheid government. The power of the unions was curtailed during the apartheid era, but towards the end of the 1980s after the formation of the National Union of Mineworkers' (NUM) in 1983, the NUM became an increasingly vocal proponent of change in the mining industry.

From the mid-1970s the stabilisation of the black labour force increased considerably, and as a result the average length of service increased.<sup>13, 14</sup> With an increase in service duration came a concomitant increase in cumulative respirable crystalline silica dust loads resident in the lungs of black miners.

The 1994 Leon Commission of Enquiry into the state of health and safety in the mining industry concluded that there was no evidence of improvement in dust levels in the mines over the previous 50 years. It also exposed the terrible burden of occupational disease and injury in the South African mining industry. Leon found, for example, that an estimated 69,000 mine workers had died due to occupational disease and injury from the turn of the century up to 1993.<sup>15</sup>

The findings of the Leon Commission catalysed the development and passing of the Mine Health and Safety Act (MHSA) in 1996. This, together with increasing commitments by the mining industry to combat occupational lung disease, led to the following agreed milestone at the Mines Occupational Health and Safety Summit in 2003: that by the year 2013, “*no new cases of silicosis will occur among previously unexposed individuals*”, (unexposed individuals being defined as “*unexposed prior to 2008*”). In support of this a best practice guideline for the prevention of silicosis was developed.<sup>16</sup>

## 1.2 Rationale for the current study

The current study is a descriptive cross-sectional study using individual level data with a sample size of 14,522 individuals with 9,599 reported chest x-rays (CXR). The objective of this report is to determine silicosis prevalence variation across 10 shafts from three different gold-mining companies in three different regions. The three previous prevalence studies conducted on ex-miners have certain limitations. The Girdler-Brown study used data from more than a decade ago and was limited to one mine with a sample size of 624.<sup>17</sup> The Trapido study<sup>18</sup> and the Steen study<sup>19</sup> were both conducted more than a decade ago with sample sizes of 304 and 238 respectively.

Regarding the two prevalence studies conducted on in-service miners, the following is evident: the study by Cowie<sup>20</sup> in 1987 was not stratified by age (it was in the dissertation<sup>21</sup>), the data were collected over 20 years ago, the duration of service was not reported on, silicosis was not classified according to the ILO system and is thus difficult to compare to other reports, and the denominator was difficult to define; and the study by Churchyard<sup>2</sup> was conducted on data from only one mine shaft with a sample size of 524 miners. Furthermore, in the Churchyard study there is the possibility of bias as employees on sick leave and those on active treatment

for TB were excluded, thus enhancing the healthy worker effect already likely to be present.<sup>22</sup>

This sub-study is therefore novel with respect to its size and generalisability. The large sample size of 9,599 individuals across 10 mine shafts, three regions and three mining companies with stratification by age, duration of service, occupation, and pulmonary tuberculosis (PTB) will greatly increase generalisability to the industry. It is only the third modern study of in-service miners in South Africa, (excluding studies from the first half of the 20<sup>th</sup> Century), and the first to explore variation across mine shafts. The size, generalisability and exploration of variation of silicosis across shafts, therefore makes this study potentially very useful. It will help to provide up-to-date information on how well the industry is doing to reduce the burden of disease from silica dust. Although a cross-shaft risk factor analysis is not possible with a sample size of only 10 shafts, the discussion will explore potential reasons for any variation in prevalence and identify future areas of research.

### 1.3 Objectives

This analysis thus has three objectives:

**Objective 1:** Descriptive objective - to determine silicosis prevalence stratified by age, length of service, and other variables in this study.

**Objective 2:** To compare prevalences stratified by age and length of service to previous studies of in-service gold miners in order to determine whether any secular trend is evident.

**Objective 3:** Any variation in prevalence, (reported as prevalence odds ratios), across cluster, region or company will be discussed, and hypotheses will be generated to explain any variation found.

## 2 Literature Review: Silicosis

This literature review will show that currently there is considerable variation in silica risk estimates. In addition, it will show that there is also considerable variation in silicosis rates in Southern African mine workers as estimated from modern epidemiological studies, and in particular in black in-service miners. The two modern studies on black in-service miners will be reviewed to enable comparisons with this study.

### 2.1 Silicosis and crystalline silica deposition in the lungs

Silicosis is a progressive incurable disease caused by the inhalation of respirable crystalline silica dust into the lungs. “Respirable” refers to dust particles that are of a size small enough to gain access through deposition and diffusion into the small airways of the respiratory tract - specifically the bronchiolar and alveolar regions of the lung. The fractional deposition of dust particles in the lungs is dependant on the aerodynamic diameter, with about 50% of 4  $\mu\text{m}$  particles gaining access into the respirable region of the lungs, but only 5% of 8  $\mu\text{m}$  particles.<sup>23</sup>

The 1994 International Commission on Radiological Protection (ICRP) model indicates that diffusion of particles into the alveolar-interstitial zone (gas-exchange zone) peaks for particles between 0.01 and 0.1  $\mu\text{m}$  in diameter,<sup>24</sup> which interestingly is into the nano-sized range for particles. It is this zone that has the slowest particle clearance rates.

Silicosis comprises one of the *pneumoconioses*, or fibrotic lung diseases caused by mineral dust. The International Labour Organisation (ILO) at the Fourth International Conference on Pneumoconiosis held in Bucharest in 1971 agreed upon the following definition of pneumoconiosis:

*“Pneumoconiosis is the accumulation of dust in the lungs and the tissue reactions to its presence. For the purpose of this definition, ‘dust’ is meant to be an aerosol composed of solid inanimate particles.”*

A distinction must be made between total inhalable dust, respirable dust and respirable crystalline silica dust when assessing exposure: inhalable dust includes all types of dust inhaled into the airways; respirable dust is all types of dust that

enter the respirable region of the lungs; whereas respirable crystalline silica refers only to the crystalline silica portion of the total dust that enters the respirable region.

Crystalline silica dust that enters the respirable region becomes trapped deep in lung tissue. There is no effective detoxification system,<sup>25</sup> apart from a small amount that may be cleared through mucociliary action from the larger airways, and as a result crystalline silica is highly biopersistent. In addition, crystalline silica is fibrogenic, and therefore initiates an inflammatory response that results in fibrosis and nodule formation. The mechanisms are not yet clearly understood, but through animal and human cell line studies it is thought that the surface of the crystalline silica particle promotes the production of Reactive Oxygen Species (ROS).<sup>26-30</sup> ROS-induced oxidative stress turns on certain transcription factors.<sup>31</sup> This in turn promotes the gene expression of pro-inflammatory chemicals and cellular apoptosis. Silica-laden alveolar macrophages are also thought to be less efficient in phagocytosing other foreign bodies and apoptotic cells, thus promoting a persistent inflammatory state.<sup>31</sup> ROS have also been implicated as a cause of DNA damage, and hence mutagenesis and carcinogenesis.<sup>26, 32-34</sup> However, the genotoxicity of crystalline silica in-vitro at concentrations that correlate to exposures found in highly exposed workers is not clear.<sup>32, 34, 35</sup>

As nodules become more profuse, they become evident as small opacities on the CXR. Silicosis can vary radiologically from Category 1 which is conceived of as “early” silicosis and has lower nodule profusion to Category 3 which has the greatest profusion of nodules and is conceived of as “advanced”. This classification has been developed by the International Labour Organisation as an epidemiological tool.

It is important to note that there is no treatment to remove silica dust from the lungs once it is trapped in the lungs.

Nodule formation and fibrosis slowly progress over time, with the length of time since first exposure and the cumulative exposure dose both associated with severity of disease in a dose-response relationship.<sup>2, 36-40</sup> Host factors, the size distribution of respirable particles, and particle surface characteristics and co-contaminants may also play a somewhat uncertain role in the development of

silicosis as discussed below in Section 2.9. Lower degrees of profusion may be relatively well tolerated, (apart from increasing the risk of PTB and possibly lung cancer). However, as the profusion increases and/or the nodules coalesce, so lung function declines.<sup>41-46</sup> Eventually adjacent nodules may coalesce to form a mass which, when greater than 10mm in size, is termed *progressive massive fibrosis*.

## 2.2 Chemical forms of silica and exposure limits

Silica, known chemically as silica dioxide (SiO<sub>2</sub>), is an extremely common substance found in the earth's crust. Silica forms either a crystalline structure or an amorphous structure, with the crystalline form posing the highest risk to health. There are various forms of crystalline silica, with the American Conference of Governmental Industrial Hygienists (ACGIH) in 2005/6 placing quartz, cristobalite and tripoli forms all into one group named "*Silica-Crystalline*". Tridymite was withdrawn owing to insufficient data. Therefore there are now two groups of silica with a recommended ACGIH threshold limit value (TLV): 1) Silica-Amorphous; and 2) Silica-Crystalline. The South African Department of Labour (DoL), Hazardous Chemical Substances regulations, as well as the Department of Minerals and Energy (DME) occupational exposure limits include tridymite as part of "*Silica, crystalline*". In addition to these three forms that make up crystalline silica, there are an estimated 27 other stable and metastable polymorphs of crystalline silica that are known to exist.<sup>47</sup>

Mining exposes and liberates silica dust through grinding, blasting, drilling, cutting, tipping, pouring and chipping. The ACGIH TLV applies to the proportion of dust less than 10 microns in diameter known as "*respirable crystalline silica dust*". It is odourless, may be invisible to the eye at concentrations that cause disease, and can remain airborne for hours after being liberated.

## 2.3 Silica exposure and associations with disease other than silicosis

Silica not only accumulates in the lungs but has also been found in other organs and systems in the body, particularly in the lymph nodes surrounding the lungs.<sup>48</sup> In addition, silica is classified as a human carcinogen (IARC Group 1) with silicosis and silica dust exposure both associated with lung cancer. Steenland's pooled analysis done in 2001 estimated that, "*the excess lifetime risk (through age 75 years) of lung cancer for a worker exposed from age 20 to 65 at 0.1 mg/m<sup>3</sup>*

*respirable crystalline silica (the permissible level in many countries) was 1.1 - 1.7%, above background risks of 3-6%”.*<sup>49</sup> A significant risk, according to the Occupational Safety and Health Administration in the USA (OSHA), is somewhere above 0.1% excess risk of death, (for example, death resulting from lung cancer).

There is some debate, however, around how strong the association between silica exposure and lung cancer is, as there may be other carcinogenic chemicals in hardrock mining that are acting as confounders that have not been properly controlled.<sup>50-52</sup> The ACGIH (2006) consider that an acceptable exposure limit for preventing silicosis will also be acceptable for preventing excess risk of lung cancer, and thus exposure limits have generally been set with silicosis as the sensitive endpoint.

Silica exposure has also been associated with kidney disease and arthritis,<sup>53-55</sup> and with systemic sclerosis and scleroderma.<sup>20, 56</sup>

Silica exposure and silicosis have in numerous studies, been strongly associated with the development of tuberculosis. Studies in Southern African gold miners for example have found between a 1.6 and 6.3 times increased risk of tuberculosis in miners with silicosis.<sup>57-60</sup> Furthermore, these studies have found an increased prevalence of tuberculosis in miners *without* radiographic silicosis but *with* silica dust exposure,<sup>59-61</sup> and even in the absence of negligible silicosis at autopsy but with silica dust exposure.<sup>60</sup> The landmark study by Hnizdo and Murray<sup>60</sup> reported on a cohort of 2,255 white miners followed up over a period of approximately 25 years, with 1,296 autopsies having been performed in 81% of the deceased miners. The study reported a 4-fold increased risk for PTB in the presence of radiographic silicosis, and a 2.7-fold and 2.3-fold increased risk in the presence of slight and moderate to marked silicosis at autopsy respectively. For those with no radiographic or pathological evidence of silicosis there was a cumulative silica dust dose-dependant increase in risk of PTB.

There is some evidence to show that TB may bring out the silicosis on CXR.<sup>62</sup> Presumably this occurs when TB infection stimulates alveolar macrophages into secreting various interleukins, chemokines, tumour necrosis factor and growth factors, thus simultaneously amplifying the fibrotic response to incarcerated silica particles. Conversely, alveolar macrophages and lung epithelial cells with

phagocytised silica particles do not seem to function effectively in phagocytising apoptotic cells and mycobacteria,<sup>31</sup> hence increasing the risk of active TB.

It must be noted that white miners generally have fewer risk factors for TB than black miners. This is mainly owing to much lower rates of HIV infection, (although HIV is a more recent epidemic and would not have been a factor when the Hnizdo and Murray study was conducted). However this reduced risk is also due to better socio-economic status related determinants for TB, such as better housing and nutrition, and greater access to quality health care.

It would therefore be expected that the risk for PTB in the presence of silica exposure in black miners could be even higher. For example, trends in autopsy data report that in 2007 about 40% of black miners have active PTB at death.<sup>63</sup> Interestingly the Hnizdo and Murray study also found that about 90% of white miners developed radiographic silicosis before the onset of PTB, with an average of 7.6 years from the end of exposure to dust to the diagnosis of PTB.

It has also been shown that HIV infection and significant silica dust exposure interact in a multiplicative way to increase the risk of tuberculosis.<sup>57</sup> Furthermore it has been shown that the presence of silicosis is a significant risk factor for death in miners with PTB (controlled for HIV), and therefore that control of silicosis would not only reduce PTB incidence but also TB related mortality.<sup>64</sup> This is important to note for mining operations in high prevalence TB countries where silica control should play an important role in workforce PTB control<sup>a</sup>, but unfortunately often does not.

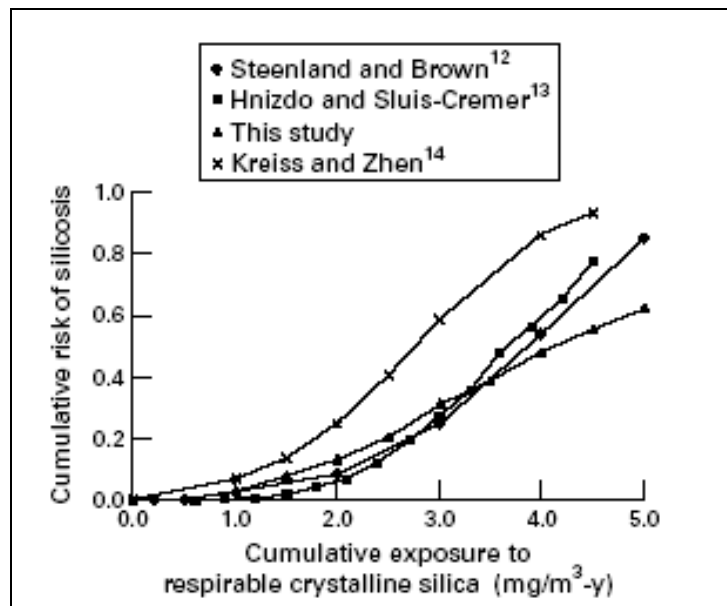
#### 2.4 Silica risk estimates

Dose-response curves calculated from 5 different studies,<sup>2, 8, 37, 39, 65</sup> excluding a cohort study done on Ontario hardrock miners,<sup>66-68</sup> estimated risks that were roughly similar, and led to the same conclusion: that an exposure limit standard of 0.1 mg/m<sup>3</sup> for respirable crystalline silica was not sufficiently protective to worker health over a 45-year working life. Exposure at an OEL of 0.1mg/m<sup>3</sup> respirable silica dust over a 45-year working life would result in a *cumulative* respirable dust exposure of 4.5 mg/m<sup>3</sup>-yrs. Curves generated from

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<sup>a</sup> See the International Council on Mining and Metals (ICMM): *Guideline on HIV, Tuberculosis and Malaria*, 2008

selected cohorts of silica-exposed workers in North America, China and South Africa are shown below in Figure 1 from Chen in 2001.<sup>8</sup> These curves show the cumulative risk of silicosis at various cumulative exposures to respirable crystalline silica dust. A cumulative exposure of 4.5 mg/m<sup>3</sup>-yrs translates into a risk of silicosis of between 55% in Chinese tin miners in the 2001 Chen study,<sup>8</sup> 70% in the Steenland and Brown study from North America,<sup>37</sup> 77% in the Hnizdo and Sluis-Cremer study in white South African gold miners,<sup>39</sup> and 92% risk of silicosis for the Kreiss and Zhen study on Chinese miners.<sup>65</sup>



**Figure 1:** Dose response curves for silicosis from 4 major studies: Cumulative risk of silicosis versus cumulative exposure to respirable crystalline silica dust. Courtesy of Chen (2001).<sup>8</sup>

The cumulative risk in a cohort of Chinese tin miners was, however, considerably less in a later study by Chen in 2005,<sup>40</sup> with a cumulative risk of about 33% at 4.5 mgm<sup>3</sup>-yrs of respirable silica dust. The difference may be explained by the fact that the 2005 dataset was different. More specifically, there were more mines added to the 2005 dataset than were in the 2001 dataset, (personal communication, E Hnizdo, National Institute of Safety and Health USA). The Chinese datasets required the conversion of exposure measurements from a Chinese methodology to a USA methodology to allow comparable analysis of respirable crystalline silica as explained in the 2005 Chen paper.<sup>40</sup> This may have introduced additional imprecision.

Finally, the prevalence survey of in-service mines by Churchyard and others in 2004 indicated a very high (32%) prevalence of silicosis at a midpoint cumulative quartz exposure of 2.28 mg/m<sup>3</sup>-yrs in older black South African gold miners.<sup>2</sup>

Although these studies indicate risks of silicosis that are roughly similar, there is still variation between these studies. Furthermore, there are other international studies in considerable disagreement with regards to the risk posed by silica dust exposure for silicosis. Ontario hard-rock miners were found to have a much lower risk of silicosis, with only a 2% risk of silicosis at about 5 mg/m<sup>3</sup>-yrs cumulative exposure to respirable crystalline silica.<sup>66-68</sup> The Ontario cohort, however, only included in-service miners and may have underestimated risk as a result.

Western Australia has reported no compensable case of silicosis in miners whose first dust exposure began during or after 1974, despite a very well-established and extensive mining industry with about 45,000 miners working in 1998, and notwithstanding a respirable crystalline silica exposure limit standard as high as 0.2mg/m<sup>3</sup>.<sup>69, 70</sup> However, medical surveillance for silica in Western Australia has fallen away since 1996 due to a change in the legal environment.<sup>69</sup> This, together with the relatively recent increase in the size of the mining workforce since the late 1980s, may have led to an underestimation of silicosis prevalence and/or may result in silicosis rates increasing substantially in the years to come once the cohort from the 1990s has had sufficient time to develop silicosis.

## 2.5 Silicosis incidence and length of service

Prior to 1984, there were no reliable estimates of silicosis prevalence or incidence in black miners. Virtually all reasonable quality data came from studies and compensation statistics generated on white miners. This was partly due to lack of data generated on black miners, and partly due to the withholding of data from public consumption by the Chamber of Mines and private mining companies.<sup>13</sup>

Regarding the estimation of rates, numerator data that was reported on black miners was mostly in the form of *compensation* cases recorded with silicosis. The data grossly underestimated the true frequency of silicosis cases<sup>14</sup> as most black miners: 1) were never followed up after leaving service; and/or 2) did not have

access to compensation services; and/or 3) developed PTB and were dismissed on medical grounds and were never followed up for silicosis; and/or 4) were undiagnosed during service for reasons discussed below.

The denominator data required to calculate incidence or compensation rates was uncertain due to frequent and intense migration into or out of the mine workforce. Many black miners, especially prior to the 1970s, did not work permanently on the mines and spent periods of each year back in their home villages. For example, Watkins-Pitchford made mention of this practice as far back as 1927, and more recently, Cowie in 1987.<sup>21, 71</sup> Many workers were not South African and came from Mozambique, Botswana, Lesotho and other neighbouring countries and returned home regularly. In addition, human resource data were often not robust enough to capture this constantly evolving workforce with sufficient accuracy to allow calculation of the true denominator. The denominator problem and issues surrounding it are well described by Cowie.<sup>1</sup>

Studies on white miners indicated that the average length of service had increased from around nine and a half years in 1919 to just below 25 years in 1969.<sup>72</sup> Further, that silicosis compensation rates, (included “coloureds” after 1962), had remained stable at between 5-15 per 1000 workers per year from 1935 to 1985.<sup>13</sup> Dust levels must have fallen somewhat during this period as compensation rates remained stable despite increasing length of service.

For black miners the data are very limited, although the average length of service in 1985 was around 14 years, and corresponding compensation rates were around 5 per 1000 workers for this period. JP Leger came to the conclusion that black miners must have been exposed to much higher dust levels on average, (similar to those experienced by white miners in the 1930s by extrapolation of the data), as their average length of service in the mid 1980s was about half that of white miners, yet they seemed to have silicosis compensation rates approaching those of whites.<sup>13</sup>

Compensation data with regards to silicosis are, however, unreliable for black miners in South Africa. Black miners found to have compensable occupational lung disease were statutorily unfit to work underground. For white miners to be found unfit for underground work, the Occupational Diseases in Mines

and Works Act of 1973 (ODMWA) required certification with second degree pneumoconiosis (i.e. more than 40% incapacity) or PTB in combination with a compensable disease. However, for black miners it required just the presence of a compensable disease.

As the compensation system was geared to benefit white miners, and made access very difficult for black miners<sup>b</sup>, dismissal or retrenchment on medical grounds for black miners would result in their losing their source of income, and in most cases consigning them to poverty. Thus it was widely held that black workers would try to avoid medical examinations and that doctors sympathetic to their plight would be reluctant to diagnose them with an occupational lung disease.<sup>13, 21</sup>

The legislation has since changed, and currently only miners found to have second-degree compensable occupational lung disease are required under the amended ODMWA legislation to be found unfit to work underground. Recently there are efforts to try and place some of them. For example, the AngloGold Ashanti gold mining company in its 2007 report states that out of a total Southern African workforce of about 31,000 people: 462 new cases of silicosis were detected and submitted to MBOD; 414 cases of *early* occupational illness were detected, of which 42% “*chose to be medically discharged*” and the rest were placed or continued in their current job; and 911 employees were found permanently unfit, of which 16% were accommodated.<sup>73</sup>

Currently some South African mining companies apparently submit silicosis with an ILO category  $\geq 1/1$  and others only submit cases that are  $\geq 2/2$ . Thus there are still currently discrepancies in how companies submit cases of silicosis for compensation.

## 2.6 Silicosis prevalence

With regard to prevalence, the first study done on silicosis prevalence in South Africa, and the first internationally to use chest radiographs, was conducted in 1911 on a sub-sample of 326 miners from an original sample of 3,163 white miners as part of the Miners’ Phthisis (Medical) Commission. The commission found pronounced phthisis in 26% of miners and suspected phthisis in 5.5% of

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<sup>b</sup> Up to 1992, black miners had no access to the Medical Bureau for Occupational Diseases (MBOD)<sup>13</sup>

miners, with the average length of service for the phthisis cases being 8.2 years. It is not clear whether this was radiographic silicosis or radiographic silicosis plus clinical opinion. It seems to have been the latter, as Elaine Katz states that 24 cases of miners phthisis were reported in the radiographic survey which would result in a prevalence of radiographic silicosis of 7.4%.<sup>10</sup> It is probable that the radiographic survey underestimated the prevalence, as interpretation of CXRs for silicosis was not standardised and the quality of CXRs was uncertain, thus casting doubt on both the sensitivity and specificity of early radiographic surveys for silicosis.

A second radiographic prevalence study was reported in 1970 by Beadle and Harris where 10% of a sample of long-exposed older white miners was found to have “*P<sub>I</sub>, M<sub>I</sub>, N*” or higher radiographic evidence of silicosis.<sup>74</sup> The radiographic survey was conducted on the cohort in 1968. All participants had worked more than 3,000 shifts underground and had more than 30 years service, with 36% still working underground in 1968 when the cohort was analysed. Survivor curves were also calculated, in what was the first dose-response analysis of silica dust and silicosis. In addition, 9% had been certified at autopsy and were therefore not captured in the cross-sectional survey. The total with silicosis (radiographic and autopsy) was therefore probably closer to 19%.

There are three studies describing silicosis prevalence in black former migrant ex-miners in labour sending areas of Southern Africa<sup>17-19</sup>, and two modern studies describing silicosis prevalence in in-service black gold miners in South Africa.<sup>1,2</sup> These are described in detail in the next section.

Finally, South Africa has a unique autopsy database, with legislation requiring that any deceased person that worked in a controlled mine, with consent of next of kin, has their cardiorespiratory organs submitted for examination. Trends show a rise from about 15% prevalence of silicosis at autopsy in black gold miners in 1977 to 30% in 2007.<sup>7, 38, 63</sup>

## 2.7 Prevalence in ex-miners

The three studies in ex-miners found a prevalence in the order of 25%.<sup>17-19</sup> The Steen study was conducted on 227 ex-miners in Thamaga village in Botswana in 1994, with an average age of 55.8 years, an average of 14.6 “years in mining” and an average of 15.7 “years since last service”.<sup>19</sup>

**Table 1:** ILO readings pertaining to former mineworkers in Thamaga, Botswana and Libode, South Africa (%): adapted from NW White<sup>14</sup>

<b>ILO readings</b>	<b>Thamaga<sup>19</sup></b> (n=227)* (%)	<b>Libode<sup>18</sup></b> (n=228)† (%)
0/0-0/1	68.2	63.6
1/0-1/2	18.1	21.1
2/1-2/3	10.1	14.5
3/2-3/3	3.5	0.9
Signs of PTB	23.9	33.3
*Seven Thamaga radiographs were unreadable		
†10 Libode radiographs were unreadable		

Thus we can infer that the average ex-miner would have started work on the mines around 1964, a period well before the stabilisation of black miners' service contracts.

The Trapido study was conducted on 228 ex-miners in the Libode district in South Africa in 1996, with an average age of 52.8 years, average "years in mining" of 12.2 and average "years since last service" of 11.9.<sup>18</sup> From this study we can estimate that the average miner started work on the mines around 1972, just before the period when stabilisation of the black workforce started, (the significance of stable job contracts will become apparent later). The radiographic silicosis prevalence in these 2 groups is summarised in Table 1 adapted from NW White.<sup>14</sup>

The Girdler-Brown study was conducted on 779 ex-miners from Lesotho in 1999, with an average age of 49.4 years, an average "duration of employment" of 25.6 years, and the ex-miners were studied about 18 months since last employment when they were laid off on economic grounds.<sup>17</sup> The radiographic silicosis prevalence ( $\geq$  ILO category 1/1) was 24.6%. The prevalence cannot be directly compared to the Trapido and Steen studies as they reported on an ILO reading that included 1/0.

## 2.8 Prevalence in in-service black miners

The study by Cowie on in-service black miners in 1984 found a prevalence of silicosis of between 0.87% and 1.38% (lower and upper bound estimates from two different methods used to estimate prevalence).<sup>1</sup> 1.38% was thought to be a minimum estimated prevalence and most probably an underestimate of the true prevalence. The study was conducted on gold miners in the province of the Orange

Free State (now called the Free State). The study was not conducted as a cross-sectional survey of a sample of miners, but rather by two methods: 1) on a series of 100,880 consecutive 100mm CXRs (mass miniature radiographs or MMRs) taken over a 6-month period as part of routine medical surveillance; and 2) on 12 months of reported silicosis cases from routine medical surveillance. The paper does not report on length of service or age, but information on age is available from Cowie's dissertation.<sup>21</sup> The dissertation reported a mean age for silicotics of 45.4 years, with a minimum of 26 years. In the general workforce the estimated mean age was 28.7 years. In those aged between 51 and 55 years Cowie found a silicosis prevalence of 15%.

The study has a number of problems which Cowie acknowledged: 1) the denominator was difficult to ascertain and was thought to be an overestimate, and thus the prevalence was underestimated, and 2) MMRs were read instead of large film CXRs as used in the ILO classification. However, a validation study was performed and indicated the MMR had 93% sensitivity in detecting silicosis compared to the large film and a Kappa statistic of 0.89.

The third problem, (that is not identified by Cowie in the study or dissertation), is that the definition of silicosis is not clear, (he defines it as, "...radiological abnormality consisting of regular nodular opacification..."). Cowie's definition does not relate directly to the ILO classification, and hence the prevalence is not easily comparable to other studies. This could be due to the fact that there is no ILO reference standard for MMRs.

The Churchyard study (2004), done on a sample of older in-service black gold miners from one shaft in the Orkney region in 2000/2001, found a high prevalence of radiographic silicosis of between 18.3% and 19.9% depending on the reader.<sup>2</sup> Furthermore, it reported silicosis in 48% of miners with over 30 years mining experience. The average age was 46.7 years, with a mean duration of exposure of 21.8 years. The minimum age reported was 37 years, with 40 years being set as the entry point into the study.

## 2.9 Variation in silicosis rates and risk estimates

As suggested earlier, the literature review highlights considerable variation in risk estimates and in prevalence in in-service miners. With regards to prevalence,

the Cowie study<sup>1</sup> found a prevalence of 1.4% in in-service miners, and the dissertation reported a stratified prevalence of 15% in the 51 to 55 years age group from the same sample<sup>21</sup>. Sixteen years later, the Churchyard study<sup>2</sup> however found a much higher prevalence of around 20% in miners over the age of 37 years (from a different mine shaft). If one takes the Churchyard group with 25 to 30 years of mining experience to approximate the age group 51-55 years in the Cowie study, the Churchyard prevalence was over double at around 35%. It was, however, in a different shaft and the selection of cases was not necessarily equivalent.

With regards to the variation in the risk estimates, the question that arises is: are there risk factors involved in determining silicosis development other than cumulative respirable crystalline silica exposure?

There has been speculation, for example, that: 1) the difference in risk estimates in Chinese pottery workers from those of Chinese miners is due to the co-contamination of silica dust with clay that reduced the biological toxicity of the silica particles in the former<sup>40</sup>; 2) different silica polymorphs have different biological effects<sup>47, 75</sup>; 3) host factors play a role, especially regarding genetic polymorphism determining alveolar macrophage performance<sup>76, 77</sup>; and 4) the surface properties of quartz particles and their resultant biological toxicity are modified by various factors such as the age of the particle, the temperature and pH it has been exposed to, and adjuvant actions of other chemical contaminants.<sup>29, 30, 78-</sup>

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For example, aluminium contamination has been found to reduce the toxicity of quartz in rat lungs,<sup>89</sup> while iron contamination has been shown to enhance quartz toxicity in rat lungs.<sup>90</sup>

Extrapolating animal data to humans is problematic, but recent advances in *ex vivo* testing of human cell lines including human lung epithelial cells exposed to various polymorphs and sizes of silica particles could advance our current understanding of silica toxicity. There could also be epidemiological differences between the studies, with bias and confounding also accounting for the variation, either partially or completely.

Regarding the objectives as set out in Section 1.3, the literature review has shown that silicosis prevalence estimates vary considerably in black in-service gold

miners in South Africa. It has also reported on the high prevalence of silicosis found in retired black miners. The variability in prevalence reported in working black miners is of concern, as silicosis is a significant public health problem in Southern Africa, and in other regions, and there is now a commitment in South Africa to try and eliminate silicosis. This study will report on silicosis prevalence in an industry-wide sample, and as such will allow secular trends to be determined by comparison of prevalence with previous studies. Furthermore, this literature review has shown the considerable variability in risk estimates, and uncertainty in the toxicology of crystalline silica. There is debate at present on whether the variability in risk estimates for silica are purely due to differences in estimating cumulative exposure to respirable crystalline silica, or whether variation in dust toxicity plays an important role. This study's third objective aims to generate hypotheses for future research in the event that variability in silicosis prevalence differences are found at the cluster, company or regional levels. Future research into exposure assessment could allow a review of the exposure-response curves, as this study should generate a reliable estimate of outcome responses (silicosis prevalence).

### **3 Methods**

This study was conducted as a sub-study derived from the parent Thibela-TB study currently being conducted on gold miners in the Gauteng, Free State and North West provinces of South Africa. The Thibela-TB study is an open cluster randomised prospective cohort study. Three mining companies are involved – Company A, Company B and Company C, with each company contributing five clusters to the Thibela-TB study. Each cluster comprises a mine shaft with its associated hostel housing the mine workers. The clusters were chosen from mine shafts with a predicted life span of more than five years, and with a workforce of a minimum of 1,000 people. The aim of the Thibela-TB study is to compare the efficacy of isoniazid preventative therapy as a community-wide intervention with the current standard of care for TB among gold miners in South Africa.

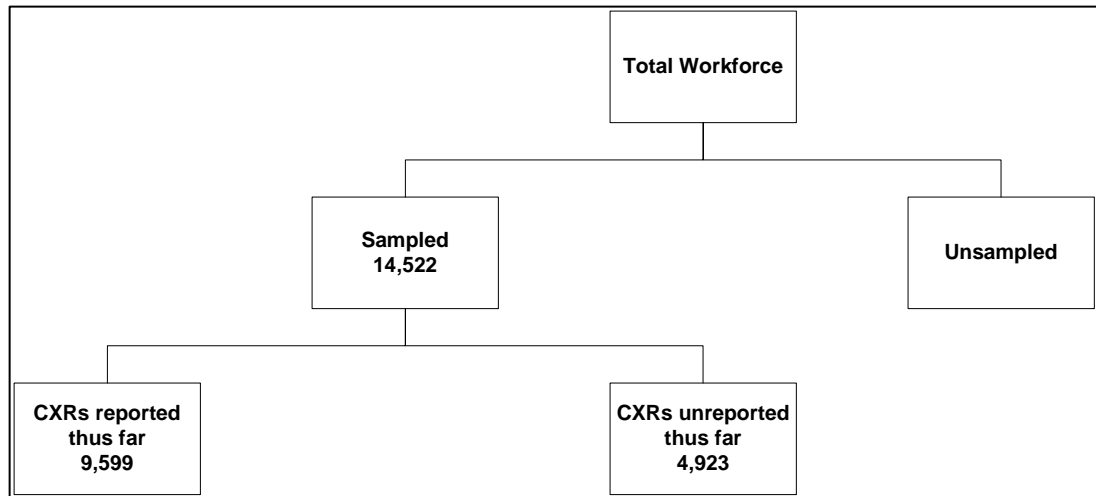
#### **3.1 Baseline survey**

A baseline cross-sectional survey for radiological silicosis and tuberculosis was performed on a sample from all clusters in both the intervention and control groups. The aim of the baseline survey was to determine the prevalence of radiographic silicosis and tuberculosis at baseline, as there are synergistic effects between silica dust exposure, silicosis and tuberculosis. The presence of HIV infection, which is also associated with the development of tuberculosis, was not determined from biological samples owing to labour union opposition. HIV status was originally intended to be included in the baseline survey.

#### **3.2 Sample selection**

The sample size was around 1000 individuals per cluster, and was selected randomly from a list of employees provided by the Human Resources departments of the three companies. Miners of any age and gender were included in the sample, and a detailed history was taken from each miner with a focus on variables relevant to TB risk, but also including variables relevant to silicosis risk. The most recent chest radiograph taken by the mining company was identified and converted into digital format for reading by an experienced reader to determine the presence and grade of silicosis and features compatible with old or new PTB. The sample

selection process did not exclude any participants, with both mine employees and contractors being eligible for selection.



**Figure 2:** Sample selection

### 3.3 Consent and ethics approval

Participants were provided with information about the study in their native language, and informed consent was obtained. Ethics approval was obtained for the Thibela-TB study from the University of Kwa-Zulu Natal and London School of Tropical Medicine and Hygiene. Ethics approval for the dissertation was obtained from the University of Cape Town.

### 3.4 Data management

Electronic case record forms (eCRFs) were used to capture all the data into a database by trained staff. The database was hosted by a client/server architecture using a software application, and personal identifiers were removed prior to analysis. Data monitoring, validation and quality control procedures, both internal and external, are detailed in the Thibela-TB study protocol version 4.0. Data was double captured and analysed using STATA version 10 and Microsoft Office Excel 2003.

Missing data and suspect entries were identified by the data manager during data auditing. The person(s) responsible for primary data capture was/were informed and asked to verify entries and complete missing data points where possible, with the assistance of the investigators.

### 3.5 Measurement of prevalence of radiographic silicosis and PTB

Full-size posteroanterior chest radiographs were used, and were read according to International Labour Organisation (ILO) International Classification of Radiographs of Pneumoconiosis (2000) criteria, that were modified to exclude the subcategories of profusion between 1/1 and 3+. Progressive massive fibrosis was not specifically coded, but could be included on the eCRF as a comment. Other parenchymal and pleural abnormalities were coded according to a system developed by the study team. Features compatible with PTB were graded as definite, probable or possible, and as active or previous PTB. Active definite PTB included cavities, soft cotton-wool type consolidation, and a miliary pattern. Active probable PTB included a pericardial effusion, pleural disease along with other radiographic features consistent with PTB, and hilar adenopathy. Active possible PTB included diffuse infiltrates which are more hilar in distribution, changes in the apical segment of the lower lobe, pleural disease without other radiographic features of PTB, and mediastinal lymphadenopathy. Previous definite PTB included evidence of a primary complex, scarring of one or both upper lobes, apical pleural thickening, and bilateral upper lobe volume loss. Previous probable PTB included old upper lobe cavitation. Previous possible PTB included a miliary pattern with fibrotic changes, changes in the apical segment of the lower lobe, and loss of the pleural angle and pleural scarring.

Chest radiographs were read by one experienced lay reader who had previously demonstrated excellent intra-individual consistency and whom had read on previous epidemiological studies.<sup>91-94</sup> The reader has been screening radiographs using the ILO system and referring cases for compensation since 1974, and has thus graded many thousands of radiographs. The reader was blinded to the participant's history.

A validation study is currently being conducted by a second reader on a subset of chest radiographs.

### 3.6 Analysis

A descriptive analysis was performed. Radiographic silicosis was defined as small rounded or mixed rounded/irregular shaped opacities of ILO category 1/1 and above. The prevalence of radiographic silicosis was classified into four ILO nodule

profusion categories: no silicosis (0/0 and 0/1); ILO category 1/0; ILO category 1 (excludes 1/0); and ILO categories 2 and 3 combined, with no subcategories reported in the ILO classification above 1/0.

ILO category 1/0 was reported separately, as: 1) some studies uses this subcategory as a cut-point for defining silicosis; and 2) correlation between radiographic silicosis and silicosis on autopsy has shown that including ILO category 1/0 in South African gold miners, (a dust exposed working group), increases the sensitivity of radiography for silicosis, without much trade-off in specificity.<sup>95</sup> Interestingly, including 1/0 did not increase sensitivity much but had a marked impact on the positive predictive value and specificity in another study on South African gold miners using MMRs rather than large film radiographs.<sup>91</sup> Silicosis was also analysed as a binary categorical variable – “silicosis” and “no silicosis”.

Histograms were constructed for silicosis prevalence stratified by length of service. Summary statistics, including mean, median, inter-quartile range and minimum and maximum values were calculated for the numerical variables age and length of service stratified by region, company and cluster (shaft). The prevalence of radiographic silicosis was then stratified according to various risk factors such as age, years in industry, and occupational history. In addition, the association between silicosis and PTB was explored, and PTB prevalence in silicotics and non-silicotics was described. Crude prevalence odds ratios were calculated for silicosis as a binary outcome variable, and Pearson’s Chi-Squared Test was applied to 2 x k tables. Two sample t-tests were applied for hypothesis testing of numerical variables. The Royston ptrend command was used to generate a Chi-Squared test of trend in STATA 10 for some of the 2 x r tables.

In terms of precision of the estimate, 95% confidence intervals were reported, and a p-value of <0.05 was generally considered significant, but also taking into account the confidence interval and the sample size.

**Table 2:** Matrix of Covariates

<b>Variable</b>	<b>Type</b>	<b>Form</b>	<b>Comment</b>
Region	Categorical	Nominal	3 regions
Company	Categorical	Nominal	3 companies
Shaft	Categorical	Nominal	10 clusters/shafts
Age	Categorical	Nominal	5-year intervals
Gender	Categorical	Binary	
Ethnic group	Categorical	Nominal	4 ethnic groups
Country of origin	Categorical	Nominal	6 countries
Year of first employment	Numerical	Discrete	Correlates to length of service
Type of work	Categorical	Binary	Underground versus surface
Frequency of work underground	Categorical	Ordinal	Graded from “full time” to “never” in 7 categories
History of PTB	Categorical	Binary	Current or past history
Radiological evidence of PTB	Categorical	Binary	Active or Previous – with each being graded as “definite”, “probable” and “possible”

## 4 Results

### 4.1 Missing data and sample comparisons

In general the quality of the dataset was excellent with very few missing or dirty data. For example: the age variable had only 0.81% missing datapoints (n = 78); the years in industry variable had only 0.71% (n = 68) missing datapoints; cluster, company and region variables had no missing datapoints; history of PTB variable had only 0.15% (n = 14) missing datapoints; and radiographic evidence of PTB variable had no missing datapoints. There was only 1 missing datapoint for ethnic group.

There were no significant differences in age, length of service, and TB rates on history between those participants who had a radiograph reported (n = 9,599) and those who did not (n = 4,923).

### 4.2 Crude prevalence of silicosis

A total of 502 cases were read as ILO category 1/0 and above. The overall (crude) prevalence of silicosis in the participants sampled is shown in Table 3 below. The *crude* prevalence is 3.86% for ILO category 1/1 and above, and 5.22% for ILO category 1/0 and above. 84% (n=313) of cases read as 1/1 or above fell into category 1, 15% (n=56) into category 2 and only 5% (n=2) in category 3. There were no readings of subcategories above 1/1.

**Table 3:** ILO category (n = 9,599)

ILO Category (Freq. / %)				
0/0	0/1	1/0	1*	2 & 3
9,064	33	131	313	58
94.43	0.34	1.36	3.26	0.60

\*ILO Category 1 excludes 1/0

### 4.3 Prevalence of silicosis by years in the industry

The mean length of service for all cases read was 17.3 years (n = 9,531; SD = 10.3) and 27.0 years for cases with radiographic silicosis (ILO category  $\geq$  1/1) (n = 367; SD 7.1). Table 4 reports the radiographic prevalence of silicosis (ILO category) by years in the industry as an ordinal categorical variable. The radiographic prevalence

of silicosis (ILO category  $\geq 1/1$ ) ranged from 0.19% in the 0-4 year service group to 11.55% in the 30+ year service group. There was an ordered increase in the prevalence by increasing years in the industry. There was also an ordered increase in the profusion of nodules for cases read with silicosis with increasing years in the industry. For example, no cases read with radiographic silicosis (ILO category  $\geq 1/1$ ) in the 10-14 year service group had category 2 or 3 profusion nodules, which rose to about 10% of cases in the 15-19 year service group, and to 25% of cases in the 25-29 year group, and dropped back to 18% of cases in the 30+ year group. The Chi-Squared Test showed a highly significant difference in the distribution between ILO categories when tabulated by years in the industry as an ordinal categorical variable ( $\chi^2 = 494$ ,  $p < 0.001$ ). There are 15 cases in this sample of miners, who have developed silicosis (ILO category 1/0 and above) with less than 10 years in the industry. The Chi-Squared test for trend was highly significant for ILO category  $\geq 1/1$  ( $p < 0.0001$ ).

**Table 4:** ILO category by years in industry (ordinal) (n = 9,529)

Years in Industry (years)	ILO category (Freq. / %)			
	1/0	1*	2&3	$\geq 1/1$
0-4	2 0.13	3 0.19	0 0	3 0.19
5-9	4 0.48	6 0.72	0 0	6 0.72
10-14	3 0.21	12 0.84	0 0	12 0.84
15-19	20 1.28	28 1.79	3 0.19	31 1.98
20-24	23 1.51	54 3.54	12 0.79	66 4.33
25-29	31 2.44	76 5.99	19 1.5	95 7.49
30+	45 3.38	130 9.75	24 1.8	154 11.55
<b>Total</b>	<b>128</b> <b>1.34</b>	<b>309</b> <b>3.24</b>	<b>58</b> <b>0.61</b>	<b>367</b> <b>3.85</b>

\* ILO category 1 excludes 1/0

#### 4.4 Prevalence of silicosis by age

Table 5 reports the ILO category by age group as a categorical ordinal variable. There is generally an ordered increase in ILO category with increasing age as one would expect, although there is a flattening in the categories 2 and 3 for the 56+ year age group. The Chi-Squared test for trend was highly significant for ILO category  $\geq 1/1$  ( $p < 0.0001$ ).

**Table 5:** ILO category by age (n = 9,521)

Age group (years)	ILO category (Freq. / %)			
	1/0	1*	2 & 3	$\geq 1/1$
<26	1 0.19	1 0.19	0 0.00	1 0.19
26-30	1 0.11	4 0.45	0 0.00	4 0.45
31-35	1 0.08	6 0.50	0 0.00	6 0.50
36-40	16 0.94	15 0.88	0 0.00	15 0.88
41-45	31 1.47	54 2.55	13 0.61	67 3.16
46-50	43 2.49	121 6.99	19 1.10	140 8.09
51-55	27 2.83	69 7.23	18 1.88	87 9.11
56+	8 2.10	41 10.76	7 1.84	48 12.60
<b>Total</b>	<b>128</b> <b>1.34</b>	<b>311</b> <b>3.27</b>	<b>57</b> <b>0.60</b>	<b>368</b> <b>3.87</b>

\*ILO category 1 excludes 1/0

#### 4.5 Ethnic group and underground work

Ethnic group was self reported by participants. 96.87% (n = 9,289) were Black/African, 2.47% (n = 237) were White/European, 0.63% (n = 60) were Mixed Race, 0.03% (n = 3) were Indian/Asian.

Regarding underground work, 97.6% (n = 9,364) of participants reported working underground and 93.4% (n = 8,944) reported full-time underground work.

#### 4.6 Prevalence of silicosis by country of origin

Table 6 reports the ILO score by country of origin. Interestingly, the prevalence of silicosis (1/1 or greater) in workers from Botswana (7.6%) is over double that of workers from South Africa (3.5%), with Lesotho sitting at 5.6% and Mozambique at 2.2%. Table 7 reports the proportion of workers by country of origin. South Africa, as expected, supplies the majority of workers at 54.5%, with Lesotho and Mozambique being important suppliers of labour at 21.9% and 16.6% respectively.

**Table 6:** ILO category by country of origin (n = 9,585)

Country	ILO category (Freq. / %)				mean age (years)	mean YiI† (years)
	1/0	1*	2 & 3	≥ 1/1		
Botswana	2 1.16	10 5.81	3 1.74	13 7.55	47.3	25.7
Lesotho	39 1.86	99 4.71	19 0.9	118 5.61	42.6	19.9
Swaziland	5 1.02	19 3.87	3 0.61	22 4.48	43	19.9
South Africa	66 1.26	154 2.95	29 0.56	183 3.51	39.3	15.7
Mozambique	19 1.19	31 1.95	4 0.25	35 2.20	42.2	17.2
Zimbabwe	0 0	0 0	0 0	0 0.00	36.8	10.5
<b>Total</b>	<b>131</b> <b>1.37</b>	<b>313</b> <b>3.27</b>	<b>58</b> <b>0.61</b>	<b>371</b> <b>3.88</b>	<b>40.8</b>	<b>17.3</b>

\*ILO category 1 excludes 1/0

†YiI = Years in industry

**Table 7:** Country of origin of workers (n = 9,585)

Country	Freq.	%
SA	5,225	54.51
Lesotho	2,101	21.92
Mozambique	1,590	16.59
Swaziland	491	5.12
Botswana	172	1.79
Zimbabwe	6	0.06
<b>Total</b>	<b>9,585</b>	<b>100</b>

#### 4.7 Pulmonary Tuberculosis

Table 8 reports the prevalence of radiological changes on the CXR that indicate possible, probable or definite PTB. Radiological abnormalities coded as “other” were commented on and allocated to one of the three categories based on the expert opinion of the reader. In total, 16.8% (n = 1,611) of participants were reported to have radiological signs of active (n = 433) or previous PTB (n = 1,177). 861 participants had other radiological abnormalities not thought to be PTB related, of which 44 were reported as have radiological signs of COPD.

**Table 8:** Radiological signs of PTB by category (n =9,598)

Previous PTB on CXR			Active PTB on CXR		
Category	Freq.	%	Category	Freq.	%
definite	834	8.69	definite	340	3.54
probable	68	0.71	probable	37	0.39
possible	275	2.87	possible	56	0.58
<b>Total</b>	<b>1,177</b>	<b>12.27</b>	<b>Total</b>	<b>433</b>	<b>4.51</b>

In total 5.9% (n = 571) had active PTB on CXR or history. On history, 11.3% (n = 1,083) of participants reported either current PTB on treatment or previous PTB treatment. A total of 20.4% (n = 1,958) of the participants had either radiological signs of PTB or a history of current or previous TB treatment. Interestingly, about 43% of this 20.4% had no history of TB treatment yet CXR signs of possible, probable or definite PTB, and about 24% had radiological signs of PTB yet no history of TB treatment.

**Table 9:** Silicosis by evidence of TB on CXR or history

ILO category	TB evidence on history* (Freq. / %)		PTB evidence on CXR† (Freq. / %)	
	Yes	No	Yes	No
<b>0/0 and 0/1</b>	981 10.8	8104 89.2	1,335 14.68	7,762 85.32
<b>1/0</b>	22 16.79	109 83.21	28 21.37	103 78.63
<b>1</b>	65 20.9	246 79.1	106 33.87	207 66.13
<b>2 &amp; 3</b>	15 25.86	43 74.14	21 36.21	37 63.79
<b>≥ 1/1</b>	80 21.68	289 78.32	127 34.23	244 65.77
<b>Total</b>	<b>1,083</b> <b>11.3</b>	<b>8,502</b> <b>88.7</b>	<b>1,490</b> <b>15.52</b>	<b>8,109</b> <b>84.48</b>

\*Includes history of previous or current TB

†Includes active and previous evidence of definite, probable and possible PTB on CXR

Table 9 above reports the prevalence of TB by ILO category, with an ordered rise in TB prevalence by increasing ILO category. For PTB evidence by CXR by ILO category the Chi-Squared Test is highly significant ( $\chi^2 = 107.4$ ,  $p < 0.001$ ), and the TB evidence by history is also highly significant ( $\chi^2 = 45.9$ ,  $p < 0.001$ ). The Chi-Squared test for trend was highly significant for evidence of TB on history ( $p < 0.0001$ ) and evidence of PTB on CXR ( $p < 0.0001$ ) by ordered ILO category.

**Table 10:** TB prevalence by cluster (n = 9,588)

Cluster	TB† (Freq. / %)		Silicosis* (Freq. / %)
	Yes	No	
GN MK	245 24.40	759 75.60	69 6.87
Kopanang	227 22.88	765 77.12	68 6.86
Cooke 3	197 21.74	709 78.26	49 5.40
Elandsrand	180 18.79	778 81.21	32 3.34
Mponeng	192 16.28	987 83.72	38 3.21
Tau Tona	215 18.04	977 81.96	37 3.10
Beatrix 1 2 3	188 20.28	739 79.72	27 2.91
Kloof 1 3 4	189 19.89	761 80.11	26 2.74
Beatrix 4	137 20.85	520 79.15	13 1.98
Kloof 7	188 22.84	635 77.16	12 1.46
<b>Total</b>	<b>1,958</b> <b>20.42</b>	<b>7,630</b> <b>79.58</b>	<b>371</b> <b>3.86</b>

\*ILO category  $\geq 1/1$  (n = 9,599)

†TB includes PTB on CXR and TB on history

Table 10 reports the variation in TB prevalence by cluster, with reference to silicosis prevalence. The prevalence of TB varies from 16.28% in Mponeng to 24.40% in GN MK. There is only 1.56% difference in TB prevalence between the cluster with the highest prevalence of silicosis (GN MK) and the cluster with the lowest prevalence of silicosis (Kloof 7).

#### 4.8 Prevalence of silicosis by cluster

Table 11 reports the prevalence of silicosis by cluster. There is considerable variation with 6.87% (n = 69) of participants read with silicosis for the GN MK cluster to 1.46% (n = 12) for Kloof 7. The chi-squared test for difference was highly significant ( $\chi^2 = 155.4$ ,  $p=0.000$ ).

**Table 11:** Silicosis prevalence by cluster (n = 9,599)

Cluster name	ILO Category (Freq. %)					Age & Years in industry (mean years)	95% CI† Age & Years in industry (mean years)	
	0/0 & 0/1	1/0	1*	2&3	≥ 1/1			
GN MK	924	11	50	19	69	40.0	39.5	40.6
	92.03	1.10	4.98	1.89	6.87	16.9	16.3	17.6
Kopanang	902	22	47	21	68	40.9	40.4	41.5
	90.93	2.22	4.74	2.12	6.86	17.7	17.0	18.3
Cooke 3	843	16	45	4	49	43.9	43.3	44.5
	92.84	1.76	4.96	0.44	5.40	20.8	20.1	21.5
Elandsrand	913	13	31	1	32	40.1	39.5	40.7
	95.30	1.36	3.24	0.10	3.34	16.5	15.8	17.3
Mponeng	1,118	27	33	5	38	39.9	39.4	40.3
	94.51	2.28	2.79	0.42	3.21	15.8	15.3	16.3
Tau Tona	1,145	11	31	6	37	40.6	40.2	41.1
	95.98	0.92	2.60	0.50	3.10	17.5	16.9	18.0
Beatrix 1 2 3	896	6	26	1	27	39.9	39.4	40.5
	96.45	0.65	2.80	0.11	2.91	16.5	15.8	17.2
Kloof 1 3 4	912	14	25	1	26	40.7	40.2	41.3
	95.80	1.47	2.63	0.11	2.74	16.7	16.0	17.4
Beatrix 4	641	3	13	0	13	41.4	40.7	42.1
	97.56	0.46	1.98	0.00	1.98	18.0	17.2	18.8
Kloof 7	803	8	12	0	12	41.6	40.9	42.2
	97.57	0.97	1.46	0.00	1.46	17.4	16.7	18.1
<b>Total</b>	<b>9,097</b>	<b>131</b>	<b>313</b>	<b>58</b>	<b>371</b>	<b>40.8</b>	<b>40.7</b>	<b>41.0</b>
	<b>94.77</b>	<b>1.36</b>	<b>3.26</b>	<b>0.60</b>	<b>3.86</b>	<b>17.3</b>	<b>17.1</b>	<b>17.5</b>

\*ILO category 1 excludes 1/0

†Confidence Interval

Table 11 reveals similar means for years in the industry and age by cluster, although there are significant differences when comparing 95% confidence intervals between certain clusters. Participants in GN MK are 3-times as likely to have silicosis,

(ILO category  $\geq 1/1$ ), as participants in Kloof 7 (prevalence OR 3.0, 95% CI 1.8 to 5.2,  $\chi^2 = 19.6$ ,  $p < 0.0001$ ).

#### 4.9 Prevalence of silicosis by company and region

This variation is evident not only at the shaft or cluster level but also at the company and regional level as reported in Table 12 and Table 13. Regarding company, Company A has a crude prevalence of silicosis of 4.85% to Company B of 2.32%.

**Table 12:** ILO category by company (n = 9,599), and comparing company by age, years in industry, and underground work

Company	ILO category (Freq. / %)					Age & Years in industry (mean years)	Underground work - ever & full-time† (%)
	0/0 & 0/1	1/0	1*	2 & 3	$\geq 1/1$		
Company A	4,089 93.53	71 1.62	161 3.68	51 1.17	212 4.85	40.36 16.94	97.07 92.40
Company B	3,252 96.76	31 0.92	76 2.26	2 0.06	78 2.32	40.85 17.06	97.92 94.63
Company C	1,756 94.11	29 1.55	76 4.07	5 0.27	81 4.34	41.98 18.62	98.02 93.44
<b>Total</b>	<b>9,097</b> <b>94.77</b>	<b>131</b> <b>1.36</b>	<b>313</b> <b>3.26</b>	<b>58</b> <b>0.60</b>	<b>371</b> <b>3.86</b>	<b>40.80</b> <b>17.30</b>	<b>97.55</b> <b>93.38</b>

\*ILO category 1 excludes 1/0

†Participants self reported work history - ever having worked underground and current full-time underground work

When stratifying the cluster, company and regional level variables by: 1) summary statistics for age and years in the industry; and 2) proportion that work underground, the means, inter-quartile range (IQR) and proportions are very similar. However, there is a significant difference in the mean age and mean years in the industry between Company A and Company C, confirmed by hypothesis testing using a two sample t-test for independent samples ( $p=0.000$ ). Regarding company, the 95% confidence intervals show overlap and therefore no significant differences for age and years in the industry between Company A and Company B, or Company B and Company C, or by region (not shown).

**Table 13:** ILO category by region (n = 9,599), and comparing region by mean age, mean years in industry, and history of underground work

Region	ILO category (Freq. / %)					Age & Years in industry (mean years)	Underground work - ever & full time† (%)
	0/0 & 0/1	1/0	1*	2 & 3	≥ 1/1		
Carletonville	5,734	89	177	17	194	41.05	98.14
	95.3	1.48	2.94	0.28	3.22	17.36	94.68
Orkney	1,826	33	97	40	137	40.47	96.94
	91.48	1.65	4.86	2.00	6.86	17.30	90.78
Welkom	1,537	9	39	1	40	40.55	96.09
	96.91	0.57	2.46	0.06	2.52	17.12	90.48
<b>Total</b>	<b>9,097</b>	<b>131</b>	<b>313</b>	<b>58</b>	<b>371</b>	<b>40.80</b>	<b>97.55</b>
	<b>94.77</b>	<b>1.36</b>	<b>3.26</b>	<b>0.60</b>	<b>3.86</b>	<b>17.30</b>	<b>93.38</b>

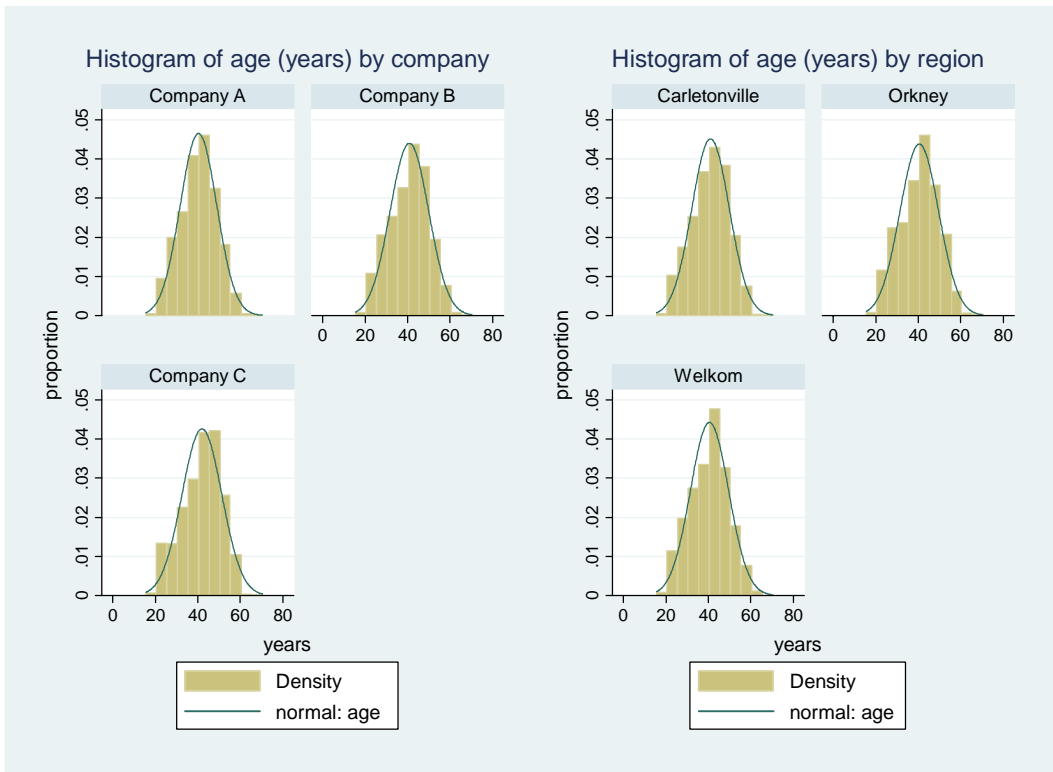
\*ILO category 1 excludes 1/0

†Participants self reported work history - ever having worked underground and current full time underground work

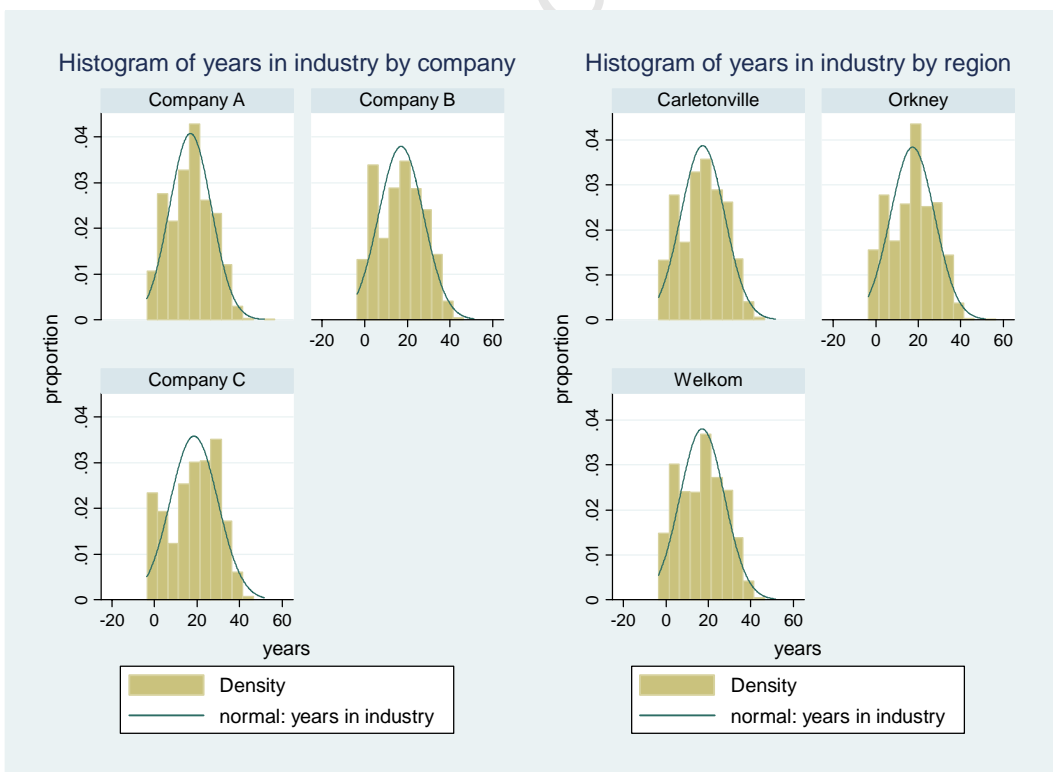
Regarding region, the Orkney region has a much higher crude prevalence of 6.86% compared to Welkom at 2.52%.

The crude prevalence odds ratio reported for silicosis (ILO category  $\geq 1/1$ ) variation between Orkney and Welkom was highly significant in that a miner was 2.8 times as likely to have silicosis in Orkney as compared to Welkom (95% CI = 1.97 – 4.19;  $\chi^2 = 35.5$ ,  $p < 0.0001$ ).

Regarding the distribution of data for age and years in industry, the Shapiro-Wilk test on age and years in industry had p-values of 0.000, and therefore indicated normally-distributed data. Histograms of age show a smooth normally-distributed range of ages across both company and region as shown below in Figure 3. However, the histograms of years in the industry by region or company show a double peak, with a drop-off in the proportion of participants having served 5-10 years in the industry across both region and company as shown below in Figure 4.



**Figure 3:** Histograms of age by company and region



**Figure 4:** Histograms of years in industry by company and region

#### 4.10 Comparison with Cowie's study

The prevalence of silicosis when compared to Cowie's 1987 thesis where the prevalence was stratified by age group is reported in Table 14.<sup>21</sup> The same age groups were analysed and compared with Cowie. However, as Cowie did not base his definition of silicosis on the ILO categories, for this study both ILO category  $\geq 1/1$  and  $\geq 1/0$  were reported. Cowie should at least have been able to detect 1/1 profusion nodules. This study generally found a lower prevalence for both definitions used, compared to the Cowie study for the groups above the age of 30 years. Of note is that Cowie studied a much younger workforce with almost 50% being below the age of 26 years, and this is why his overall prevalence was much lower.

**Table 14:** Silicosis prevalence by age group compared to Cowie's thesis (1987)<sup>21</sup>

Age group (years)	Cowie thesis (1987)			Knight thesis (2009)			
	No of cases of silicosis	% of population in age group	Prevalence of silicosis (%)	No of cases of silicosis*	% of population in age group	Prevalence of silicosis >1/1 (%)	Prevalence of silicosis >1/0 (%)
<26	0	48.88	0.00	1	5.67	0.19	0.38
26-30	10	17.36	0.04	4	9.42	0.45	0.56
31-35	105	13.34	0.59	6	12.64	0.50	0.58
36-40	312	9.08	2.59	15	17.87	0.88	1.82
41-45	582	5.52	7.94	67	22.20	3.17	4.64
46-50	402	3.36	9.01	140	18.17	8.09	10.58
51-55	274	1.36	15.17	87	10.03	9.11	11.94
>55	125	1.10	8.56	48	4.00	12.60	14.7
<b>Total</b>	<b>1810</b>	<b>100.00</b>	<b>1.36</b>	<b>368</b>	<b>100.00</b>	<b>3.87</b>	<b>5.21</b>

\*silicosis defined as ILO score  $\geq 1/1$

#### 4.11 Comparison with Churchyard's study

The 40+ year age group for the GN MK cluster is reported in Table 15 so as to compare with the previous Churchyard study, which was conducted in the same cluster about 8 years previously.<sup>2</sup> The Chi-Squared Test was significant (p=0.001).

**Table 15:** Silicosis prevalence in GN MK shaft for the 40+ years in industry group (n = 536): comparison with Churchyard study (n = 510)

Years in industry (years)	Churchyard study (2004)		Knight thesis (2009)	
	Radiographic silicosis (Freq. / %)		Radiographic silicosis (Freq. / %)	
	nil	silicosis*	nil	silicosis*
<15	58	1	41	1
	98.31	1.69	97.62	2.38
15-19	107	13	93	6
	89.17	10.83	93.94	6.06
20-24	153	42	113	10
	78.46	21.54	91.87	8.13
25-29	78	27	113	15
	74.29	25.71	88.28	11.72
30+	21	10	113	31
	67.74	32.26	78.47	21.53
<b>Total</b>	<b>417</b>	<b>93</b>	<b>473</b>	<b>63</b>
	<b>81.76</b>	<b>18.24</b>	<b>88.25</b>	<b>11.75</b>

\*silicosis defined as ILO score  $\geq 1/1$

## 5 Discussion

### 5.1 General

Silicosis and tuberculosis have blighted the South African gold mining industry since its inception in 1887, despite gold mining being the largest single contributor to South Africa's gross domestic product and foreign exchange earnings for over a century.

#### 5.1.1 *General strengths of the study*

This study, a sub-study of the Thibela-TB project, is the largest conducted to date on in-service miners investigating the prevalence of silicosis (and tuberculosis). It enables a review of secular trends in prevalence, and provides important information for future research. It is the first industry-wide study and therefore the first to compare prevalence across multiple mine shafts or clusters. Following this, it is able to comment to some extent on the variation in prevalence between shafts, and at a company and regional level. Risk factor analysis as part of an ecological study using regression modelling of prevalence was not possible owing to having only 10 clusters. However, as successive clusters are captured over the next five years, this may become possible (20 clusters in total will be captured with over 80,000 miners).

#### 5.1.2 *General limitations of the study*

Cross-sectional studies by design are prone to length-biased sampling (also known as cross-sectional bias). This results in an underestimation of the burden of disease, particularly for acute diseases where death or cure occurs within a short space of time. As silicosis is a chronic disease with no cure, the potential for underestimation of disease burden is reduced, although not completely. Silicosis is a risk factor for PTB, and the combination of silicosis and HIV has a multiplicative effect on the risk of PTB.<sup>57</sup> Death of miners with silicosis or HIV-related TB could produce a healthy worker effect that would lead to underestimation of the true burden of silicosis in black South African miners. This is likely to have occurred in this study. Limitations are addressed more specifically below.

## 5.2 Crude prevalence and covariates

### 5.2.1 *Crude prevalence*

The estimated crude prevalence of silicosis for ILO category 1/0 and above is 5.22%, and 3.86% for ILO category 1/1 and above. This cross-sectional study estimated silicosis prevalence in a working population of predominantly black Southern African gold miners. The overall estimate of silicosis prevalence is industry wide in that it covers 10 clusters in three companies and in three gold mining regions of South Africa. Silicosis prevalence varies considerably when stratified by certain covariates. This will be discussed in detail below.

### 5.2.2 *Validity of crude and stratified silicosis prevalence*

Regarding the crude and stratified prevalence of silicosis, the findings could be spurious or real. Bias as a potential cause of a spurious result could come in two forms in the context of this study: 1) selection bias in selecting participants, and/or 2) information bias in measuring silicosis cases or determinants of silicosis.

As selection was random, selection bias in sampling is unlikely. However, there is the likelihood of a healthy worker survivor effect, with out-selection of silicosis cases as discussed previously. This would lead to an underestimate of the true prevalence of silicosis. This type of bias is quite likely, and may be possible to estimate more accurately in the cohort component of the Thibela-TB project.

With regard to information bias, there is no reason to suspect that age would have been measured differently in silicotics when compared to non-silicotics, and likewise with duration of service. In terms of confounding, the potential confounding by age has been cancelled by stratification.

Finally, the possibility of the findings being due to chance is reduced as a result of the large sample size and highly significant hypothesis tests.

### 5.2.3 *Service duration*

Duration of exposure to respirable crystalline silica is one part of the equation that determines risk of the developing silicosis (and tuberculosis) along with intensity of exposure and latency, (and possibly other factors affecting toxicity of the crystalline silica particles in the lung).

The average length of service of black miners has increased substantially since gold mining first started, with the stabilisation in service ramping up particularly during the 1970s and increasing continuously since. However, there are reports in the last few years that miners are becoming more mobile and moving into other industries such as construction.<sup>73</sup>

This study found a mean of 17.3 years for time in the industry compared to 14.6 years in the study by Steen<sup>19</sup> and 12.2 years in the study by Trapido.<sup>18</sup> Both Steen and Trapido studied an ex-workforce that would have originally worked from around the early 1960s to the early 1980s. Unfortunately there are few reliable data on duration of service among black miners prior to this.

This study relied on self-reported years in the industry. There is, therefore, the potential for imprecision in this study as this variable was not independently verified. However, from personal experience most miners tend to recall quite accurately their age at or year of first exposure to mining work.

This study did not measure breaks in mining service or record mixed service and this could also have led to overestimation of the mean length of service. However, personal communication with Churchyard and others seems to indicate that mixed service in miners over the last 20-30 years is not common. Most tend to be career miners, with little opportunity for employment outside of the industry due to low levels of education and high unemployment rates, along with lack of opportunities in other sectors in South Africa, (until recently).

The reason for the smaller proportion of category 2 and 3 profusion nodules in the 30+ year service group compared to other strata could be a result of a healthy worker effect, with more severe silicotic cases exiting the workforce with age and pulmonary disability.

The fact that the increase in ILO category severity is ordered with increasing service duration, (apart from the trimming off as above), suggests that this variable is a reliable proxy for cumulative respirable crystalline silica exposure in this sample (see Table 14).

There are only nine cases recorded of radiographic silicosis, (ILO category 1/1 and above), in miners with fewer than 10 years in the industry. This is worth commenting on as acute and accelerated silicosis is now a rare disease in modern

mining, as dust exposures should rarely grossly exceed the exposure limit on repeated occasions.<sup>c</sup> These nine cases had a mean age of 34 years (range 25 to 44 years), and mean service duration of 5.6 years (range 3 to 9 years). Three had evidence of PTB, and all were graded as ILO category 1/1. There is the possibility that some may have unrecorded past exposure to silica dust that they did not indicate when interviewed. All worked underground.

#### 5.2.4 Age

Age acts as a confounder in the causal relationship between cumulative respirable crystalline silica dust exposure and silicosis. Age is related to cumulative dust exposure and is associated with silicosis. To explain further, the older a miner, the greater the probability that they have been exposed to a cumulative dust dose sufficient to cause silicosis. Furthermore, there is a greater probability of an increased latency period or “dust residence time in the lung” as compared to a younger miner.

The ordered increase in proportion of cases with radiographic silicosis by increasing age group is expected from the dose-response relationship of crystalline silica. The longer the silica residency time in the lung, the greater the profusion of nodules for a fixed dose, and the longer the duration of exposure at a fixed concentration, the greater the total cumulative dust load and thus the greater the profusion of nodules. The ordered increase is not as smooth as when stratified by years in the industry and thus age might be a less reliable indicator of cumulative respirable crystalline silica exposure than service duration for this sample. There is a flattening in the proportion of cases read with ILO category 2 and 3 profusion nodules in the 55+ years age group. This could be due to proportionately more miners with more severe silicosis exiting employment before reaching 55 years of age, (or possibly not partaking in the study for fear of being found unfit to work underground and hence retrenched).

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<sup>c</sup> This is in contrast to the latency period between first exposure to mining and diagnosis of silicosis in European miners in South Africa in the early 1900s, with for example, the average duration of service being just 109 months in 1917/1918.<sup>71</sup>

#### 5.2.5 *Country of origin*

The reasons for the variation in radiographic silicosis prevalence by country of origin are not known. One possibility is that miners from Botswana and particularly Lesotho tend to be employed in dustier jobs such as stope development work, (G. Churchyard, personal communication). This can be confirmed once the occupation variable has been grouped and analysed, (not in this report). The other possibility is that workers from Lesotho and Botswana are older and have longer service durations than South African miners for example. Participants from Botswana are, in fact, older and have longer service duration than participants from other countries, except for Mozambican participants. Mozambicans have similar service duration and age as participants from Lesotho, yet have a much lower prevalence of radiographic silicosis. The answer may therefore lie partially in the distribution of types of job by country of origin, or distribution of country of origin by company, region or cluster, which themselves have varying rates of silicosis.

#### 5.2.6 *Ethnic group and underground work*

As expected the overwhelming majority of the sample are black African miners. Compared to white miners, black miners typically are of lower socio-economic status, are migrant workers, are exposed to dustier work, and are less likely to be compensated and less likely to find alternative employment on exiting the mining industry. They are also currently at much greater risk of HIV infection and hence active PTB. The black underground mining workforce is therefore likely to be at higher risk of silicosis than the white workforce. Comparisons were not made in the analysis between different ethnic/socioeconomic groups due to the lack of heterogeneity.

The finding that over 90% were permanently employed underground means that more than 90% of the sample population was exposed to dusty work and at risk of silicosis.

#### 5.2.7 *Tuberculosis*

PTB on CXR and TB on history is strongly associated with silicosis. There is an ordered increase in TB prevalence by increasing category of ILO nodule profusion. This is in keeping with previous studies.<sup>59-61</sup>

Regarding the interaction between HIV, silicosis and TB, Corbett reported a multiplicative interaction between HIV and silicosis on PTB rates.<sup>57</sup> Although HIV status was not reliably measured in our baseline study, HIV prevalences are in the order of 20-35% in gold miners in South Africa. Girdler-Brown found an HIV prevalence of 22% in a sample of former Basotho mine workers.<sup>17</sup> AngloGold Ashanti estimated an HIV prevalence in their workforce of around 30% in 2007,<sup>73</sup> and Goldfields estimated 33.5% in its 2008 Occupational Health and Safety Report.

The overall prevalence of past or present TB in this sample of 20.4% is thus not surprising. It is slightly lower, but of the same order of magnitude, as the prevalence of past and current TB reported in former black migrant mineworkers: 24%,<sup>19</sup> 26%<sup>17</sup> and 33%.<sup>18</sup>

### 5.3 Comparison with previous in-service miner prevalence studies

#### 5.3.1 *Comparison with Cowie study*

This study found a decreased prevalence of silicosis (ILO category  $\geq 1/1$ ) by age stratum compared to the 1987 Cowie study.<sup>21</sup> Specifically, this was for all age strata between 30 and 55 years. For the over 55 years stratum, a health worker survivor effect may explain the lower prevalence in the Cowie study.

The Cowie study is not easily comparable, as the definition of silicosis may differ as discussed previously.<sup>d</sup> However, even though the definition is uncertain in Cowie's study, there was a reported agreement between MMR and large film CXR of kappa = 0.89 in his validation study. He was therefore most likely to have had the sensitivity to report at least ILO category 1/1 or greater. There is also a decrease between studies for most age groups over 30 years using a more sensitive silicosis definition of ILO category  $\geq 1/0$ .

Regarding crude prevalence, this study reported 3.86% for ILO category 1/1 and above, and 5.22% for ILO category 1/0 and above in the 10 clusters studied. The crude prevalence is considerably higher than the crude prevalence first reported by Cowie<sup>1</sup> in the 1984 workforce of between 0.87-1.38%. However, once stratified by age, there is a striking difference between the two studies. Cowie was studying a

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<sup>d</sup> See section 2.8 Prevalence in in-service black miners, page 17

much younger workforce, with almost 50% of participants under than 26 years of age, as compared to this study with only 6% younger than 26 years old.

The South African gold mining workforce has generally become more stable with less mixed service over the last 30 years, with a greater propensity to retain older workers. Taking this into account, the fall in age-stratified prevalence is significant.

### 5.3.2 *Comparison with Churchyard (2004) study*

This study also found a decreased prevalence of silicosis in older black miners compared to the Churchyard study<sup>2</sup> conducted in the same shaft about eight years earlier, controlled for age. Specifically, this study has found a lower prevalence of silicosis of 11.6% in the 40+ year age group compared to the Churchyard study's silicosis prevalence of between 18.3-19.9%. The mean length of service of 23.9 years in this study is similar to that of 21.8 years in the Churchyard study. The results from the Churchyard study are easily comparable as silicosis was defined as ILO category  $\geq 1/1$ .

Stratified by length of service the prevalence of silicosis is lower in all length of service groups, barring the less than 15-year length of service group for which there are insufficient numbers of cases to be meaningful. It therefore seems, at least for the GN MK shaft, that the prevalence of silicosis has fallen by about 40% over approximately eight years.

This fall could be due to a number of reasons. The respirable crystalline silica levels could have fallen over the last 20-30 years, (the mean duration of service of silicotics in the 40+ year age group is 30 years for this study). The healthy worker survivor effect could be more pronounced in this study than in the Churchyard study. The toxicity of the rock mined could have changed with changing seams mined in the GN MK shaft. And finally, there could be detection bias owing to the use of different readers for the chest radiographs in the two studies.

Detection bias, although likely to account for some differential bias between the two studies, is unlikely to account significantly for the 40% fall in prevalence. The reader in this study is highly experienced as discussed in Section 3.5, and the Churchyard study was validated. Although there has been no validation study on the

results of the one reader who read all the radiographs for this study, a validation study is currently underway and should resolve this issue.

With regards to a possible difference in healthy worker effect, the issue is uncertain. Although policies regarding medical separation of workers with silicosis shifted towards retaining miners with silicosis or TB in employment since the 1980s, the maturing of the HIV epidemic over the last decade may have led to the increased medical separation of workers with HIV-related TB. This could have selected silicotic cases out of the workforce, as HIV and silicosis augment the incidence of active TB. Finally, recent downsizing of the mining industry in South Africa could possibly have led to more pressure on silicotic workers to exit employment.

Possible ways to resolve whether the declining prevalence is spurious or real would be: 1) to record *accurate* respirable crystalline silica dust measurements year on year (which currently has not been the case to date); 2) to review medical separation data; 3) to perform a silicosis prevalence study on HIV-negative miners; and 4) to analyse autopsy data restricted to those who died by accident or injury, (this is currently under way, J Murray, personal communication). Selecting only those miners that died by accident or injury provides a more random selection of autopsy specimens compared to selecting all autopsy specimens, where many would have died of HIV-related TB.

#### 5.4 Variation between cluster and region

##### 5.4.1 *Prevalence odds ratios*

This study found a significant three-fold difference in silicosis prevalence between the highest prevalence (GN MK) and lowest prevalence (Kloof 7) clusters, (prevalence odds ratio 3.0, 95% C.I. 1.8 to 5.2,  $\chi^2 = 19.6$ ,  $p < 0.0001$ ). At a regional level this study found a significant 2.8-fold difference in silicosis prevalence between the highest prevalence (Orkney) and the lowest prevalence (Welkom) regions, (prevalence odds ratio 2.8, 95% CI = 1.97 – 4.19,  $\chi^2 = 35.5$ ,  $p < 0.0001$ ).

#### 5.4.2 Validity of the prevalence odds ratios

The variation seen at cluster, company and regional level is interesting and lends itself to further research. The variation could be spurious due to bias, or the variation could be real.

Regarding bias, a differential healthy worker effect could be an important source of bias that could increase or decrease the prevalence odds ratio between Orkney and Welkom or between Kloof 7 and GN MK clusters. The Orkney mines are both operated by Company A whereas the Welkom mines are operated by Company B. If Company B had a policy or practice of retrenching miners with occupational lung disease at lower levels of impairment than Company A, this would result in Company B having a healthier workforce.

Although legislation prohibits the continued employment of miners certified with both silicosis and tuberculosis, there is anecdotal evidence that some companies have stopped submitting miners for compensation during service as they conclude that it is more equitable to keep them employed than consign them to unemployment and poverty. In Cowie's thesis, for example, he notes that since 1983 the AngloAmerican company stopped submitting black miners with silicosis for compensation while they were still in active service for this very reason.<sup>21</sup> The finding of only two workers with a score of Category 3/3 is probably due to workers with more severe grades of silicosis having been selected out through medical surveillance and medically separated. This would result in a healthier pool of current workers and an underestimate of the true prevalence of more severe grades of silicosis. While this could have biased the crude and stratified prevalences, it is unlikely to have biased the prevalence odds ratios. This is because there is anecdotal evidence to suggest that there was, and currently is, no *difference* between the three companies regarding medical separation policy and procedures. This is supported by company annual reports that state identical annual medical separation rates of 25 per 1000 employees in 2007 for Company A and in 2008 for Company B.<sup>e</sup>

There is the potential for differential misclassification bias in classifying silicosis between cluster, region or company. However, as only one experienced

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<sup>e</sup> These reports are freely accessible on their respective websites.

reader read all the CXRs, it is highly unlikely that there was *differential* misclassification of cases at shaft, company or regional level.

Other forms of bias that could be operating include differential selection bias in selecting participants who were more (or less) likely to have silicosis in certain clusters. This is also highly unlikely owing to the methodology used (random selection), and the finding that there were no significant differences between those participants who had a CXR reported and those who did not (see Sections 3.2 and 4.1).

Differential detection bias in measuring length of service could be an issue if certain companies or clusters were more likely to have broken service employees – i.e. employees who moved out of the industry for a period and then returned to underground mining. There is anecdotal evidence that the three companies have very similar service records amongst their respective workforce. In addition, differential detection bias is unlikely as the same standardised and validated interview method was used at all clusters to capture data, and participants were selected randomly.

Mixed service could be a source of measurement bias in calculating the prevalence differences or odds ratios if miners from some clusters were more likely to have been employed in multiple companies or clusters over time – i.e. they moved between mines. It could be that there are more mixed service miners in a particular cluster owing to human resource policies employed, or a greater proportion of contract miners (who tend to be more mobile). Mixed service could thus bias the prevalence differences at cluster level. This is possible, as from personal experience with submitting miners for compensation, they typically have worked at more than one mine over the course of their career. However, the view of a mine doctor interviewed was that, for the past 20 years, most employees have tended to stay with one company for the duration of their mining career and rather get moved between the various company shafts as operational demands require, (D Barnes, personal communication). This would not bias prevalence differences, as the two clusters compared (NG MK and Kloof 7) are from different companies. The AngloGold Ashanti company estimated for 2007 that employee turnover rates which varied by operation and occupation had increased and ranged from 10%-55%.<sup>73</sup> This source of bias could be defined and potentially controlled for by

examining the labour recruiting office records for the study participants at The Employment Bureau of Africa (TEBA) Limited, (which has been operating since 1902), and which tends to be a reliable source of data.

The presence of a third variable could confound a real result, if the third variable differs significantly between cluster and region. As the result is likely to be real and not spurious, one needs to consider age, socioeconomic status and TB as potential confounders of the prevalence differences.

Socioeconomic status is unlikely to confound the differences as there is no reason for participants from one shaft or region to be of lower socioeconomic status than participants from another shaft or region.

Regarding age, the three-fold difference in silicosis prevalence between the highest and lowest prevalence clusters cannot be explained by differences in mean age or mean years in the industry, as Kloof 7 has a slighter higher mean age and mean years in industry, with data that are normally distributed. The 2.8-fold difference at a regional level between the Welkom and Orkney regions also cannot be explained by differences in mean age or mean years in the industry.

TB as a confounder is unlikely in that silica dust exposure is robustly demonstrated in the literature to be a risk factor for TB in the absence of silicosis, and there is good biological evidence to support this through the impaired functioning of silica dust-laden lung macrophages (as explained in Section 2.1).

Finally, a real result regarding prevalence differences could potentially be due to chance. This is not likely as the Chi-Squared Test for difference was highly significant between the Welkom and Orkney regions and between GN MK and Kloof 7 clusters. Likewise, the confidence intervals for the odds ratios did not cross the null.

#### *5.4.3 Speculation on risk factors for variation*

The result seems to be valid, and confounding is not likely to be a significant factor. Therefore, the potential risk factors explaining prevalence differences at the cluster and regional level could be one or a combination of: 1) differences in cumulative exposure to respirable crystalline silica dust; 2) differences in the toxicity of the dust in various clusters and by region; and 3)

differences in host factors in various clusters and by region. These will be explored separately below.

#### 5.4.4 *Variation in dust exposure*

Variation in dust exposures is in all likelihood the major risk factor explaining the variation.

Underground work is a crude proxy for dust exposure, as miners that work underground tend to have higher dust exposures compared to miners working on the surface. There are similar proportions of participants who have either ever worked underground, or have full-time underground work, across all the clusters (not shown) and across the three regions.

Exposure assessment was not possible as part of this study. However, it might be possible to analyse company data submitted by law to the South African Department of Minerals and Energy (DME) and/or to use job title as a proxy for dust exposure using the Safety in Mines Research Advisory Committee 606 Report to average dust exposures for each main job group.<sup>22</sup>

There are some data to suggest that historical routine company records of dust exposure measurements, at least in the last 10 years, are fairly accurate in so far as the mean, median and range are concerned for one shaft where research dust measurements were compared to routine measurements.<sup>2</sup> However, there is also a lot of debate and controversy, (mainly outside of the published literature), as to the methodology and accuracy of routine dust measurements on South African gold mines in general<sup>52, 96</sup>, and how to link these to medical surveillance systems and operational control of dust. For example, there are reports that the silica quartz proportion of total respirable dust varies even at the stope level and temporally due to new stope development. Despite this, the quartz proportion is often determined at the mine/shaft level and sub-shaft level measurements inherit this proportion for the purposes of determining respirable quartz concentrations, without regular updating.

There is also the problem concerning requirements by law to place miners into three basic homogenous exposure groups for dust, and to base exposure assessment on group averages. This may result in some high risk dust exposure occupations having their exposure assessments diluted by being grouped with lower dust exposure occupations.

Ideally, exposure assessment should be conducted down to the individual, task, or job title level, and not reported only at a group level. This is especially so when considering that the industry has such high rates of dust-related lung disease. In addition, it may be problematic to place recent exposure measurements into a job exposure matrix for the purposes of calculating long-term cumulative exposure indices. Recent exposures may not reflect exposures a decade or two earlier, and in addition miners may change jobs and hence exposure profiles. Changing jobs can potentially be accounted for by examining labour records, but determining past exposures can be very difficult in the absence of reliable routine dust measurements from the various clusters.

Exposure assessment should be further investigated. Policies and procedures should be implemented forthwith to ensure that future respirable crystalline silica data are accurate and reliable. This could require independent measurement of dust in gold mines as suggested at the International Congress of Occupational Health in 2009 (R. Ehrlich, conference discussion).

#### 5.4.5 *Variation in silica toxicity*

Differences in toxicity of silica dust are a potential partial determinant of variability. M Gulumian and others have found considerable variation between South African gold mines in dust particle surface area, percentage quartz content, proportion of co-contaminants in dust samples, and the level of hydroxyl radicals generated by alveolar macrophages in the presence of bulk dust.<sup>97</sup> Guthrie<sup>98, 99</sup> and Gulumian<sup>47</sup> provide a good discussion of the toxicity issues regarding silica containing dust. For example, there is now considerable evidence to point to the increased toxicity of freshly fractured silica and silica surfaces contaminated with iron as detailed in Section 2.9. There is current research being conducted into relative toxicity of quartz polymorphs and co-contaminants by V Vallyathan and V Castranova's group at the National Institute of Occupational Safety and Health in America (NIOSH), and M Gulumian at the National Institute of Occupational Health in South Africa (NIOH), amongst others. Geological maps of South African mineral deposits show that the Welkom area belongs to a different geological group from that of the Klerksdorp (Orkney region) and Carletonville areas. This could

result in a different dust toxicity profile between Orkney and Welkom, but requires further research.

#### 5.4.6 *Host factor variation*

Differences in host factor responses to silica dust are not going to play a role in explaining variation as there is no reason for genetic bias at cluster, company or regional level. This might be a factor in explaining a difference between (say) a black African workforce and an Asian workforce if there were some subtle associations between single nucleotide polymorphisms (SNPs) in the gene coding for TNF- $\alpha$  expression and SNPs associated with continental ancestry, (SNPs in the promoter region for TNF- $\alpha$  have been posited as an explanation for severe silicosis in black South African miners<sup>76</sup>). However, this cannot explain the prevalence differences between cluster-, regional- or company-level in South Africa as the ethnic breakdown is very similar, and mostly all are of the same continental ancestry.

Differences in HIV infection prevalence at the cluster-, regional- or company-level could also provide a possible explanation for varying silicosis rates. As alluded to in section 5.2.7 and 5.3.2, HIV infection is associated with PTB, and PTB can lead to lung fibrosis and nodule formation, either mimicking silicosis or even promoting silica nodule formation. It is uncertain whether HIV is associated with lung fibrosis directly in the absence of PTB through other infections.. Moreover, the possibility arises that HIV could *inhibit* lung fibrosis through disabling the immune response, and therefore slow down silicosis progression or post-tuberculous fibrosis. Hence, although HIV infection is potentially a confounder in the relationship between silica dust exposure and nodule formation, it is difficult to predict the net effect on silicosis prevalence in working miners.

However, HIV may drive a healthy worker survivor effect. Selecting out HIV infected workers from the workforce could have a number of effects. Firstly, if TB promotes silica nodule formation then silicotics would also be selected out if workers with HIV related TB leave for health reasons. Secondly, both silicosis and HIV increase the risk of TB, and consequently the risk of being found unfit to work owing to second degree compensable lung disease (see Section 2.5).

However, Company A and Company B report very similar HIV prevalence in their respective workforce, and there is no reason to suspect that Company C is significantly different. Therefore, it seems unlikely that the difference in silicosis prevalence, at least at the company-level, can be explained by HIV prevalence variation.

## 5.5 Conclusions

This study has found an estimated *crude* prevalence of silicosis (for ILO category 1/0 and above) in an industry-wide sample of South African gold miners of 5.22%. This is probably an underestimate due to a healthy worker survivor effect. The maturing HIV epidemic in Southern African may possibly be selecting silicotic workers out of the workforce via the greatly enhanced risk of pulmonary TB.

Furthermore, this study has found that there is significant variation in silicosis prevalence between gold mining clusters (shafts) and between mining regions that requires further research. This variation is probably real and not due to confounding or chance, and various explanations for this variation have been suggested. The reason(s) for this variation is probably differences in respirable crystalline silica exposures, and possibly differences in respirable dust toxicity between the clusters and regions. These are two key areas that require further research.

This study has also found that the *crude* silicosis prevalence has fallen since Cowie's original study performed in 1984. In addition, prevalence among older, longer service gold miners has fallen quite significantly in the one shaft examined by Churchyard in 2000 and included in this study again in 2007/8.

This study does appear to show that recent progress has been made in combating the scourge of silicosis that has afflicted the South African mining industry. However, there is still an unacceptable high prevalence of silicosis. In addition, there are 15 cases in this sample of miners who have developed silicosis, (ILO category 1/0 and above), with fewer than 10 years of exposure to dust. This would suggest that there are still jobs and tasks in the industry where very high silica dust exposures are occurring.

As explained in Section 1.1, the South African government and mining industry have set a target of no new cases of silicosis in miners exposed to dust after 2008. This seems unachievable.

## 6 References

1. Cowie RL, van Schalkwyk MG. The prevalence of silicosis in Orange Free State gold miners. *J Occup Med* 1987; Jan;29(1):44-6.
2. Churchyard GJ, Ehrlich R, teWaterNaude JM, Pemba L, Dekker K, Vermeijs M, et al. Silicosis prevalence and exposure-response relations in South African goldminers. *Occup Environ Med* 2004; Oct;61(10):811-6.
3. Gochfeld M. Chronologic history of occupational medicine. *J Occup Environ Med* 2005; Feb;47(2):96-114.
4. Bisetti AA. Bernardino Ramazzini and occupational lung medicine. *Ann N Y Acad Sci* 1988;534:1029-37.
5. Ramazzini B. *De Morbis artificum diatriba. 1700-1713*. Chicago: University of Chicago Press; 1713.
6. Gerhardsson G. The end of silicosis in Sweden - a triumph for occupational hygiene engineering. *OSH & Development* 2002;(May):13-25.
7. Rees D, Murray J. Silica, silicosis and tuberculosis. *Int J Tuberc Lung Dis* 2007; May;11(5):474-84.
8. Chen W, Zhuang Z, Attfield MD, Chen BT, Gao P, Harrison JC, et al. Exposure to silica and silicosis among tin miners in China: exposure-response analyses and risk assessment. *Occup Environ Med* 2001; Jan;58(1):31-7.
9. National Institute of Occupational Safety and Health (NIOSH). Hazard review: health effects of occupational exposure to respirable crystalline silica; 2002.
10. Katz E. *The White Death: Silicosis on the Witwatersrand Gold Mines 1886-1910*. Johannesburg, South Africa: Witwatersrand University Press; 1994.
11. Meiklejohn A. The development of compensation for occupational diseases of the lungs in Great Britain. *Br J Ind Med* 1954; Jul;11(3):198-212.

12. Chamber of Mines of South Africa. Estimated Western World gold production (1887 - 2002). Available at: <http://www.bullion.org.za/>. Accessed 18 April, 2009.
13. Leger JP. Occupational diseases in South African mines--a neglected epidemic?. *S Afr Med J* 1992; Feb 15;81(4):197-201.
14. White NW, Steen TW, Trapido AS, Davies JC, Mabongo NM, Monare N, et al. Occupational lung diseases among former goldminers in two labour sending areas. *S Afr Med J* 2001; Jul;91(7):599-604.
15. South African Department of Minerals and Energy. Commission of Enquiry into Safety and Health in the Mining Industry (Leon Commission); 1994.
16. Stanton DW, Belle BK, Dekker KJJ, Du Plessis JJJ. South African Mining Industry Best Practice on Prevention of Silicosis. Braamfontein, South Africa: Mines Health and Safety Council, Safety in Mines Research Advisory Committee (SIMRAC); 2006.
17. Girdler-Brown BV, White NW, Ehrlich RI, Churchyard GJ. The burden of silicosis, pulmonary tuberculosis and COPD among former Basotho goldminers. *Am J Ind Med* 2008; Sep;51(9):640-7.
18. Trapido AS, Mqoqi NP, Williams BG, White NW, Solomon A, Goode RH, et al. Prevalence of occupational lung disease in a random sample of former mineworkers, Libode District, Eastern Cape Province, South Africa. *Am J Ind Med* 1998; Oct;34(4):305-13.
19. Steen TW, Gyi KM, White NW, Gabosianelwe T, Ludick S, Mazonde GN, et al. Prevalence of occupational lung disease among Botswana men formerly employed in the South African mining industry. *Occup Environ Med* 1997; Jan;54(1):19-26.
20. Cowie RL. Silica-dust-exposed mine workers with scleroderma (systemic sclerosis). *Chest* 1987; Aug;92(2):260-2.
21. Cowie RL. Silicosis, Pulmonary Dysfunction and Respiratory Symptoms in South African Gold Miners [dissertation]. University of Cape Town; 1987.

22. Safety in Mines Research Advisory Committee (SIMRAC). Silicosis prevalence and exposure response relationships in older black mineworkers on a South African goldmine. Johannesburg, South Africa: SIMRAC; 2003. Report No.: Health 606.
23. Lippman M. Respiratory system - structure and function. In: International Labour Organisation, editor. Encyclopaedia of Occupational Health. 4th Edition ed. Geneva: International Labour Office; 1998.
24. James AC, Stahlhofen W, Rudolf G, Köbrich R, Briant JK, Egan MJ, et al. Annexe D. deposition of inhaled particles. *Annals of the ICRP* 1994;24(1-3):231-99.
25. Gulumian M. An update on the detoxification processes for silica particles and asbestos fibers: success and limitations. *J Toxicol Environ Health B Crit Rev* 2005; Nov-Dec;8(6):453-83.
26. Li N, Xia T, Nel AE. The role of oxidative stress in ambient particulate matter-induced lung diseases and its implications in the toxicity of engineered nanoparticles. *Free Radic Biol Med* 2008; May 1;44(9):1689-99.
27. Albrecht C, Knaapen AM, Becker A, Hohr D, Haberzettl P, van Schooten FJ, et al. The crucial role of particle surface reactivity in respirable quartz-induced reactive oxygen/nitrogen species formation and APE/Ref-1 induction in rat lung. *Respir Res* 2005; Nov 2;6:129.
28. Ayres JG, Borm P, Cassee FR, Castranova V, Donaldson K, Ghio A, et al. Evaluating the toxicity of airborne particulate matter and nanoparticles by measuring oxidative stress potential--a workshop report and consensus statement. *Inhal Toxicol* 2008; Jan;20(1):75-99.
29. Vallyathan V, Castranova V, Pack D, Leonard S, Shumaker J, Hubbs AF, et al. Freshly fractured quartz inhalation leads to enhanced lung injury and inflammation. Potential role of free radicals. *Am J Respir Crit Care Med* 1995; Sep;152(3):1003-9.
30. Gulumian M. The role of oxidative stress in diseases caused by mineral dusts and fibres: current status and future of prophylaxis and treatment. *Mol Cell Biochem* 1999; Jun;196(1-2):69-77.

31. Phagocytosis of apoptotic neutrophils by crystalline silica treated U937 macrophages. The 9th International Conference on Particles: Risks and opportunities; 2008; Cape Town, South Africa. p. 68.
32. Schins RP, Knaapen AM. Genotoxicity of poorly soluble particles. *Inhal Toxicol* 2007;19 Suppl 1:189-98.
33. Schins RP, Duffin R, Hohr D, Knaapen AM, Shi T, Weishaupt C, et al. Surface modification of quartz inhibits toxicity, particle uptake, and oxidative DNA damage in human lung epithelial cells. *Chem Res Toxicol* 2002; Sep;15(9):1166-73.
34. Geh S, Shi T, Shokouhi B, Schins RP, Armbruster L, Rettenmeier AW, et al. Genotoxic potential of respirable bentonite particles with different quartz contents and chemical modifications in human lung fibroblasts. *Inhal Toxicol* 2006; May;18(6):405-12.
35. Cakmak GD, Schins RP, Shi T, Fenoglio I, Fubini B, Borm PJ. In vitro genotoxicity assessment of commercial quartz flours in comparison to standard DQ12 quartz. *Int J Hyg Environ Health* 2004; Feb;207(2):105-13.
36. 't Mannetje A, Steenland K, Attfield M, Boffetta P, Checkoway H, DeKlerk N, et al. Exposure-response analysis and risk assessment for silica and silicosis mortality in a pooled analysis of six cohorts. *Occup Environ Med* 2002; Nov;59(11):723-8.
37. Steenland K, Brown D. Silicosis among gold miners: exposure--response analyses and risk assessment. *Am J Public Health* 1995; Oct;85(10):1372-7.
38. Murray J, Kielkowski D, Reid P. Occupational disease trends in black South African gold miners. An autopsy-based study. *Am J Respir Crit Care Med* 1996; Feb;153(2):706-10.
39. Hnizdo E, Sluis-Cremer GK. Risk of silicosis in a cohort of white South African gold miners. *Am J Ind Med* 1993; Oct;24(4):447-57.
40. Chen W, Hnizdo E, Chen JQ, Attfield MD, Gao P, Hearl F, et al. Risk of silicosis in cohorts of Chinese tin and tungsten miners, and pottery workers (I): an epidemiological study. *Am J Ind Med* 2005; Jul;48(1):1-9.

41. Cowie RL. The influence of silicosis on deteriorating lung function in gold miners. *Chest* 1998; Feb;113(2):340-3.
42. Cowie RL, Mabena SK. Silicosis, chronic airflow limitation, and chronic bronchitis in South African gold miners. *Am Rev Respir Dis* 1991; Jan;143(1):80-4.
43. Gamble JF, Hessel PA, Nicolich M. Relationship between silicosis and lung function. *Scand J Work Environ Health* 2004; Feb;30(1):5-20.
44. Hnizdo E, Vallyathan V. Chronic obstructive pulmonary disease due to occupational exposure to silica dust: a review of epidemiological and pathological evidence. *Occup Environ Med* 2003; Apr;60(4):237-43.
45. Ng TP, Chan SL. Lung function in relation to silicosis and silica exposure in granite workers. *Eur Respir J* 1992; Sep;5(8):986-91.
46. Wang X, Yano E. Pulmonary dysfunction in silica-exposed workers: a relationship to radiographic signs of silicosis and emphysema. *Am J Ind Med* 1999; Aug;36(2):299-306.
47. Gulumian M. Elimination of silicosis: to eliminate which silica?. *Occupational Health Southern Africa* 2007; March/April;13(2):6-11.
48. Verma DK, Ritchie AC, Muir DC. Dust content of lungs and its relationships to pathology, radiology and occupational exposure in Ontario hardrock miners. *Am J Ind Med* 2008; Jul;51(7):524-31.
49. Steenland K, Mannetje A, Boffetta P, Stayner L, Attfield M, Chen J, et al. Pooled exposure-response analyses and risk assessment for lung cancer in 10 cohorts of silica-exposed workers: an IARC multicentre study. *Cancer Causes Control* 2001; Nov;12(9):773-84.
50. Baur X, Latza U, Jockel KH. Silica dust and lung cancer. *Thorax* 2000; Feb;55(2):172-3.
51. Chen W, Bochmann F, Sun Y. Effects of work related confounders on the association between silica exposure and lung cancer: a nested case-control study

among Chinese miners and pottery workers. *Int Arch Occup Environ Health* 2007; Feb;80(4):320-6.

52. Dahmann D, Taeger D, Kappler M, Buchte S, Morfeld P, Bruning T, et al. Assessment of exposure in epidemiological studies: the example of silica dust. *J Expo Sci Environ Epidemiol* 2007; Dec 5;.

53. Sluis-Cremer GK, Hessel PA, Hnizdo E, Churchill AR. Relationship between silicosis and rheumatoid arthritis. *Thorax* 1986; Aug;41(8):596-601.

54. Steenland K, Rosenman K, Socie E, Valiante D. Silicosis and end-stage renal disease. *Scand J Work Environ Health* 2002; Dec;28(6):439-42.

55. Steenland K. One agent, many diseases: exposure-response data and comparative risks of different outcomes following silica exposure. *Am J Ind Med* 2005; Jul;48(1):16-23.

56. Sluis-Cremer GK, Hessel PA, Nizdo EH, Churchill AR, Zeiss EA. Silica, silicosis, and progressive systemic sclerosis. *Br J Ind Med* 1985; Dec;42(12):838-43.

57. Corbett EL, Churchyard GJ, Clayton TC, Williams BG, Mulder D, Hayes RJ, et al. HIV infection and silicosis: the impact of two potent risk factors on the incidence of mycobacterial disease in South African miners. *AIDS* 2000; Dec 1;14(17):2759-68.

58. Cowie RL, Langton ME, Becklake MR. Pulmonary tuberculosis in South African gold miners. *Am Rev Respir Dis* 1989; May;139(5):1086-9.

59. Cowie RL. The epidemiology of tuberculosis in gold miners with silicosis. *Am J Respir Crit Care Med* 1994; Nov;150(5 Pt 1):1460-2.

60. Hnizdo E, Murray J. Risk of pulmonary tuberculosis relative to silicosis and exposure to silica dust in South African gold miners. *Occup Environ Med* 1998; Jul;55(7):496-502.

61. teWaternaude JM, Ehrlich RI, Churchyard GJ, Pemba L, Dekker K, Vermeis M, et al. Tuberculosis and silica exposure in South African gold miners. *Occup Environ Med* 2006; Mar;63(3):187-92.

62. Charalambous S, Churchyard GJ, Murray J, De Cock KM, Corbett EL. Persistent radiological changes following miliary tuberculosis in miners exposed to silica dust. *Int J Tuberc Lung Dis* 2001; Nov;5(11):1044-50.
63. National Institute of Occupational Health (NIOH). Pathology Division Surveillance Report, 2007. Johannesburg, South Africa: NIOH; 2007. Report No.: 14/2008.
64. Churchyard GJ, Kleinschmidt I, Corbett EL, Murray J, Smit J, De Cock KM. Factors associated with an increased case-fatality rate in HIV-infected and non-infected South African gold miners with pulmonary tuberculosis. *Int J Tuberc Lung Dis* 2000; Aug;4(8):705-12.
65. Kreiss K, Zhen B. Risk of silicosis in a Colorado mining community. *Am J Ind Med* 1996; Nov;30(5):529-39.
66. Verma DK, Sebestyen A, Julian JA, Muir DC, Schmidt H, Bernholz CD, et al. Silica exposure and silicosis among Ontario hardrock miners: II. Exposure estimates. *Am J Ind Med* 1989;16(1):13-8.
67. Muir DC, Shannon HS, Julian JA, Verma DK, Sebestyen A, Bernholz CD. Silica exposure and silicosis among Ontario hardrock miners: I. Methodology. *Am J Ind Med* 1989;16(1):5-11.
68. Muir DC, Julian JA, Shannon HS, Verma DK, Sebestyen A, Bernholz CD. Silica exposure and silicosis among Ontario hardrock miners: III. Analysis and risk estimates. *Am J Ind Med* 1989;16(1):29-43.
69. De Klerk NH, Ambrosini GL, Pang SC, Musk AW. Silicosis compensation in Western Australian gold miners since the introduction of an occupational exposure standard for crystalline silica. *Ann Occup Hyg* 2002; Nov;46(8):687-92.
70. De Klerk NH, Musk AW. Silica, compensated silicosis, and lung cancer in Western Australian goldminers. *Occup Environ Med* 1998; Apr;55(4):243-8.

71. Watkins-Pitchford W. The Silicosis of South African Gold Mines, and the Changes Produced in it by Legislative and Administrative Efforts. *The Journal of Industrial Hygiene and Toxicology* 1927;9(4):109-39.
72. Du Toit RSJ. Period of Service Before Certification for Pneumoconiosis on South African Gold Mines. Proceedings of the International Conference Johannesburg, Symposium on Silicosis; 1970 1969; Johannesburg. Oxford University Press; p. 470-2.
73. AngloGold Ashanti. Country Report South Africa, Vaal River Operations, 2007. AngloGold Ashanti; 2007.
74. Beadle DG. The relationship between the amount of dust breathed and the incidence of silicosis: An epidemiological study of South Africa European gold miners. Proceedings of the International Conference Johannesburg, 1969; 1970; Johannesburg, South Africa. Johannesburg: Oxford University Press.
75. Gulumian M. An update on the detoxification processes for silica particles and asbestos fibers: success and limitations. *J Toxicol Environ Health B Crit Rev* 2005; Nov-Dec;8(6):453-83.
76. Corbett EL, Mozzato-Chamay N, Butterworth AE, De Cock KM, Williams BG, Churchyard GJ, et al. Polymorphisms in the tumor necrosis factor-alpha gene promoter may predispose to severe silicosis in black South African miners. *Am J Respir Crit Care Med* 2002; Mar 1;165(5):690-3.
77. Qu Y, Tang Y, Cao D, Wu F, Liu J, Lu G, et al. Genetic polymorphisms in alveolar macrophage response-related genes, and risk of silicosis and pulmonary tuberculosis in Chinese iron miners. *Int J Hyg Environ Health* 2007; Dec;210(6):679-89.
78. Bruch J, Rehn S, Rehn B, Borm PJ, Fubini B. Variation of biological responses to different respirable quartz flours determined by a vector model. *Int J Hyg Environ Health* 2004; Jul;207(3):203-16.

79. Donaldson K, Stone V, Duffin R, Clouter A, Schins R, Borm P. The quartz hazard: effects of surface and matrix on inflammogenic activity. *J Environ Pathol Toxicol Oncol* 2001;20 Suppl 1:109-18.
80. Elias Z, Poirot O, Daniere MC, Terzetti F, Marande AM, Dzwigaj S, et al. Cytotoxic and transforming effects of silica particles with different surface properties in Syrian hamster embryo (SHE) cells. *Toxicol in Vitro* 2000; Oct;14(5):409-22.
81. Fenoglio I, Fonsato S, Fubini B. Reaction of cysteine and glutathione (GSH) at the freshly fractured quartz surface: a possible role in silica-related diseases?. *Free Radic Biol Med* 2003; Oct 1;35(7):752-62.
82. Fenoglio I, Prandi L, Tomatis M, Fubini B. Free radical generation in the toxicity of inhaled mineral particles: the role of iron speciation at the surface of asbestos and silica. *Redox Rep* 2001;6(4):235-41.
83. Fubini B, Fenoglio I, Ceschino R, Ghiazza M, Martra G, Tomatis M, et al. Relationship between the state of the surface of four commercial quartz flours and their biological activity in vitro and in vivo. *Int J Hyg Environ Health* 2004; Feb;207(2):89-104.
84. Fubini B, Fenoglio I, Elias Z, Poirot O. Variability of biological responses to silicas: effect of origin, crystallinity, and state of surface on generation of reactive oxygen species and morphological transformation of mammalian cells. *J Environ Pathol Toxicol Oncol* 2001;20 Suppl 1:95-108.
85. Fubini B, Hubbard A. Reactive oxygen species (ROS) and reactive nitrogen species (RNS) generation by silica in inflammation and fibrosis. *Free Radic Biol Med* 2003; Jun 15;34(12):1507-16.
86. Gulumian M, Borm PJ, Vallyathan V, Castranova V, Donaldson K, Nelson G, et al. Mechanistically identified suitable biomarkers of exposure, effect, and susceptibility for silicosis and coal-worker's pneumoconiosis: a comprehensive review. *J Toxicol Environ Health B Crit Rev* 2006; Sep-Oct;9(5):357-95.

87. Shoemaker DA, Pretty JR, Ramsey DM, McLaurin JL, Khan A, Teass AW, et al. Particle activity and in vivo pulmonary response to freshly milled and aged alpha-quartz. *Scand J Work Environ Health* 1995;21 Suppl 2:15-8.
88. Harrison J, Chen JQ, Miller W, Chen W, Hnizdo E, Lu J, et al. Risk of silicosis in cohorts of Chinese tin and tungsten miners and pottery workers (II): Workplace-specific silica particle surface composition. *Am J Ind Med* 2005; Jul;48(1):10-5.
89. Duffin R, Gilmour PS, Schins RP, Clouter A, Guy K, Brown DM, et al. Aluminium lactate treatment of DQ12 quartz inhibits its ability to cause inflammation, chemokine expression, and nuclear factor-kappaB activation. *Toxicol Appl Pharmacol* 2001; Oct 1;176(1):10-7.
90. Castranova V, Vallyathan V, Ramsey DM, McLaurin JL, Pack D, Leonard S, et al. Augmentation of pulmonary reactions to quartz inhalation by trace amounts of iron-containing particles. *Environ Health Perspect* 1997; Sep;105 Suppl 5:1319-24.
91. Corbett EL, Murray J, Churchyard GJ, Herselman PC, Clayton TC, De Cock KM, et al. Use of miniradiographs to detect silicosis. Comparison of radiological with autopsy findings. *Am J Respir Crit Care Med* 1999; Dec;160(6):2012-7.
92. Corbett EL, Churchyard GJ, Hay M, Herselman P, Clayton T, Williams B, et al. The impact of HIV infection on Mycobacterium kansasii disease in South African gold miners. *Am J Respir Crit Care Med* 1999; Jul;160(1):10-4.
93. Corbett EL, Hay M, Churchyard GJ, Herselman P, Clayton T, Williams BG, et al. Mycobacterium kansasii and M. scrofulaceum isolates from HIV-negative South African gold miners: incidence, clinical significance and radiology. *Int J Tuberc Lung Dis* 1999; Jun;3(6):501-7.
94. Corbett EL, Churchyard GJ, Clayton T, Herselman P, Williams B, Hayes R, et al. Risk factors for pulmonary mycobacterial disease in South African gold miners. A case-control study. *Am J Respir Crit Care Med* 1999; Jan;159(1):94-9.
95. Hnizdo E, Murray J, Sluis-Cremer GK, Thomas RG. Correlation between radiological and pathological diagnosis of silicosis: an autopsy population based study. *Am J Ind Med* 1993; Oct;24(4):427-45.

96. Gibbs GW, Du Toit RS. Estimating the quartz exposure of South African gold miners. *Ann Occup Hyg* 2002; Oct;46(7):597-607.
97. Gulumian M. Surface activity of silica dusts collected from different mines in South Africa. International Occupational Hygiene Association 2005 Pilansberg; 2005; South Africa. International Occupational Hygiene Association; p. 1-5.
98. Guthrie GD,Jr, Heaney PJ. Mineralogical characteristics of silica polymorphs in relation to their biological activities. *Scand J Work Environ Health* 1995;21 Suppl 2:5-8.
99. Guthrie GD,Jr. Mineral properties and their contributions to particle toxicity. *Environ Health Perspect* 1997; Sep;105 Suppl 5:1003-11.

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