Review of Literature on Chronic Obstructive Pulmonary Disease and Occupational Exposure to Silica

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Contents

Executive Summary

The Industrial Injuries Disablement Benefit (IIDB) Scheme provides benefits that can be paid to an employed earner because of an industrial accident or Prescribed Disease (PD; i.e. a disease listed in the terms of prescription for the purposes of IIDB). In the context of the IIDB scheme this review evaluates the evidence for an increased risk of chronic obstructive pulmonary disease (COPD), including chronic bronchitis and emphysema, in occupations and industries in which exposure to crystalline silica is the primary exposure. In particular, the review focuses on whether there is evidence to suggest that there is:

- a doubling of risk of COPD associated with exposure to silica
- a disabling loss of lung function (doubling of risk)
- a clear exposure-response relationship between silica exposure and loss of lung function, taking account of the effect of smoking
- clear evidence of an independent effect of silica on COPD in the absence of silicosis
- an indication of the level or accumulation of exposure (or a proxy measure for exposure such as duration of exposure) needed to cause COPD and a disabling loss of lung function.

Chronic Obstructive Pulmonary Disease (COPD) is characterised by a progressive, irreversible, decline in lung function and includes chronic bronchitis and emphysema, both of which can lead to the development of airways obstruction that may lead to impairment of lung function, disability and death. The most important causal factor of COPD, in particular CBE, is active smoking, but rates increase with age, are higher in males than females and are associated with low socioeconomic status.

Silica is a general term for a group of minerals composed of silicon and oxygen and is most commonly found in a crystalline form. Most processed minerals, from raw materials used in construction and industrial minerals to metallic ores and coal contain a proportion of silica which can vary considerably. Industries in which high levels of silica have been found include construction, iron and steel foundries, metal services, pottery, cut stone and stone products. Exposure is most often measured as concentration of total or respirable silica.

Prolonged exposure to high levels of silica has long been known to cause silicosis; silica exposure has also been associated with increased risk of other non-malignant respiratory disease, lung and renal cancers and autoimmune disease.

Construction industry, including tunnelling and exposure to cement and concrete

Many cross sectional studies show a significant difference in both prevalence of symptoms and lung function measurements between those exposed to silica dust experienced in the construction, cement and tunnelling industries and those not exposed. Although smoking tends to decrease the average values of lung function measurements, many studies of construction, tunnel and cement workers do not show a significant difference in, for example, FEV_1, between smokers and non-smokers in either silica dust exposed or control groups. Some of the longitudinal studies show an increased decline in lung function associated with silica dust exposure compared to those not exposed; this can occur at average levels of respirable dust concentrations below 1 mg/m^3, and several studies have found increasing decline with increasing exposures. Although several estimates of the annual decline in FEV_1 can be derived from these studies there is some evidence that a loss of 1 litre of lung function could occur after 20 or more years exposure.

Brick manufacturing industry
Although there appears to be consistent evidence of increased risk of COPD in brick workers, the nature and magnitude of the risk varies. For example a decline associated with exposure for most lung function measurements with the exception of FVC is found in one Taiwanese study but the opposite in a Croatian study. Although the risks of silica often increase with smoking, for most of the studies an increased risk remains with silica after adjustment for the effects of smoking. A study in the UK study found a low frequency of silicosis and predicted that 1.4% of non-smokers aged 40 exposed to an average dust concentration of 2.5 mg/m^3 for 20 years would be expected to have category ≥ 1/0 compared to 0.6% in the lowest dust concentration category. A small but consistent exposure response effect was found for chronic bronchitis with a significant Odds Ratio (OR) of 1.6 associated with cumulative dust exposure to ≥ 4.0 mg.y.m^3 in highly exposed jobs such as kiln demolition, where dust exposures of > 100 mg.y.m^3 (10 mg.m^3 for 10 years) might be expected.

Pottery and ceramic work
The studies show an increased risk of mortality from non-malignant respiratory disease (NMRD) (Standardised Mortality Ratio (SMR) 2.87 (95% Confidence Interval (CI) 2.17, 3.72)) in a UK pottery industry study. Prevalence of NMRD and reduced lung function related to dust exposure was also reported.

Silica sand industry
There is a clear relationship between excess mortality from NMRD and silicosis in studies from the USA but not in a UK study although exposure levels appear to be comparable. No studies of lung function decline have been carried out in this industry.

Granite industry
The mortality studies show a consistent excess of deaths from COPD and NMRD in granite workers with SMRs of about 1.2. Results for lung function in relation to exposure vary. Studies of granite workers in Vermont, USA, give conflicting results with early follow-ups finding a decline in lung function and later papers concluding that there is no significant decline in lung function. A study of Swedish granite crushers concludes that there is a moderate decline in lung function that is consistent with airway obstruction in the absence of silicosis (very few cases of silicosis occurred in this study). In one Singapore study no effect was found on lung function in the absence of small rounded opacities, with exposures being much higher for those with opacities than those without. In a Spanish study reduced lung function was associated with an interaction between smoking and dust exposure but not with the individual variables.

Iron, steel and foundry work
The studies have consistently shown increased risk for mortality from NMRD in steel workers, of between 1.3 and 1.8. A decline in FEV_1 has been found in several studies ranging from 1 to about 9-10 ml/year, after adjusting for smoking age and height, the latter in some of the studies associated with the dustiest jobs such as foundry work and moulding where silica is one of the main exposures.

Diatomaceous earth (DE)
The DE studies confirm the association between exposure to silica containing dust and increased mortality risk of silicosis and NMRD and have quantified the exposure-response relationship. Risks are clearly doubled and a relative risk of over 4 is found for exposures at the PEL level of 0.05 mg/m^3 experienced for 45 years (after adjusting for smoking).

Gold mining

Levels of exposure to silica in studies of gold miners in the US and South Africa are generally much higher than those experienced in other industries. Mortality studies consistently show increased risk from silicosis and NMRD. An estimate of loss of lung function over 5 years showed an average loss of 37 ml (controlling for age, original lung function and smoking) in those without initial silicosis rising to 128 ml for those with initial category 3 silicosis.

Slate workers

There is clear evidence of a relationship between exposure to slate dust, which contains a high percentage of silica, and increased respiratory symptoms and mortality, particularly from silicosis.

Discussion and conclusions

The studies reviewed for this report may have one or more of the general limitations inherent in epidemiological studies including loss to follow-up, healthy survivor and selection biases, inconsistencies in the diagnosis of COPD and definition of a case and inadequate or limited exposure estimation. Nevertheless the evidence from mortality studies and cross-sectional studies of respiratory symptoms suggests that there are consistent associations between the risk of COPD and all the occupations reviewed. Although risk estimates and prevalence rates vary, several show more than a doubling of risk, even after taking into account the effect of smoking.

In some of the occupations, for example tunnel working, in addition to concurrent exposure to cigarette smoke (direct or second hand) exposures to other work-place irritants (sometimes multiple) such as gases and fumes may occur. Factors influencing the variation from industry to industry in risks associated with exposure to silica-containing dusts include: the presence of other minerals in the dust, particularly when it is associated with clay minerals; the size of the particles and percentage of quartz; the physicochemical characteristics such as whether the dust is freshly fractured or not.

Average levels of total and respirable dust and crystalline silica vary between the studies and between industries as do the cumulative exposure levels. Average dust levels vary from about 0.5 mg/m^3 to over 10 mg/m^3 and average silica levels from 0.04 to over 5 mg/m^3. Levels reported in the studies are often well above any of the currents occupational standards, for example the UK MEL of 0.3 mg/m^3 and guidance OEL of 0.1 mg/m^3. In the UK there are a considerable number of workers potentially exposed to silica containing dusts although levels of exposure are known to have declined over recent decades in many industries.

A consistent finding in the studies reviewed is that, although smoking tends to decrease average values of lung function measurements, many studies do not show a significant different between smokers and non-smokers in the decline of lung function with exposure to silica.

It has been suggested that emphysema and airway obstruction in subjects exposed to silica seem to be independent of silicosis, and that silica exposure may cause obstructive lung function changes at lower concentrations and possible shorter latency time than is required for the induction of silicosis. The evidence from studies where radiological silicosis was absent suggest that loss of lung function occurs with exposure to silica dust and that the effect of cumulative silica dust exposure on airflow obstruction is independent of silicosis. Silica dust concentrations of between 0.1 and 0.2 mg/m^3 can cause this loss of lung function.

The results from longitudinal studies suggest that the annual loss of FEV_1 associated with exposure to silica varies between under 1ml to over 100ml depending on smoking status and presence of silicosis. In the absence of silicosis loss due to silica exposure appears to be <10 ml

per year. This indicates that a disabling loss of lung function of 1 litre would take at least 10 years if the same rate of lung function decline persisted and some of the studies indicate loss that would take over 20 years. There are unfortunately no very long term follow-up studies to address the latter issue.

1. Background

The Industrial Injuries Disablement Benefit (IIDB) Scheme provides benefits that can be paid to an employed earner because of an industrial accident or Prescribed Disease (PD; i.e. a disease listed in the terms of prescription for the purposes of IIDB). The Secretary of State for Social Security is advised on matters relating to the IIDB Scheme by the Industrial Injuries Advisory Council (IIAC).
Chronic bronchitis and emphysema (CBE) is listed in the Schedule as PD D12.

The current terms of prescription for PD D12 are listed in appendix 1. The current prescription was based on comprehensive evidence of the British workforce that exposure to the levels of coal dust underground in coal mines for a period or periods of 20 years doubled the risk of chronic bronchitis and emphysema [Department of Social Security, 1992]. The Council investigated the risk of chronic bronchitis and emphysema for coal miners working above ground in a subsequent review [Department of Social Security, 1996].

IIAC has identified the need to review the literature concerning chronic bronchitis and emphysema, specifically relating to the risks in particular occupations or occupational exposures. A previous review carried out by the MRC Institute for Environment and Health examined the evidence for extension of the scheme to coal surface workers and to other occupational exposures, excluding those in which silica is the main exposure of concern [Rushton, 2005]. This current review evaluates the evidence for an increased risk of chronic obstructive pulmonary disease (COPD), including chronic bronchitis and emphysema, in occupations and industries in which exposure to crystalline silica is the primary exposure. In particular, the review focuses on whether there is evidence to suggest that there is:

- a doubling of risk of COPD associated with exposure to silica
- a disabling loss of lung function (doubling of risk)
- a clear exposure-response relationship between silica exposure and loss of lung function
- account taken of the effect of smoking
- clear evidence of an independent effect of silica on COPD in the absence of silicosis
- an indication of the level or accumulation of exposure (or a proxy measure for exposure such as duration of exposure) needed to cause COPD and a disabling loss of lung function.

2. Methodology

Search terms to obtain relevant literature on CBE and, more generally, COPD in relation to exposure to silica were developed in collaboration with the IIAC librarian. Other relevant papers were identified from searching the reference lists and carrying out further searches on specific occupations, activities and materials. These included, among other terms:

- Industries: mining; quarrying; foundry work; pottery/ceramics; slate mining; construction; brick working; sand working; stone working; granite working; tunnel construction; cement and concrete working.
- Activities: breaking; grinding; crushing; blasting; building; construction.
- Materials: quartz; silica; flint; ceramics; sand; stone; glass.

The literature has been critically evaluated with regard to the quality of study design, implementation and analysis. The results from the literature are discussed taking into account the prescription requirements for a workable definition of the disease and a clear attribution to occupational exposure.

This report is structured as follows: Section 3 briefly describes the nature of CBE and COPD and the non-occupational factors which are related to its occurrence. Section 4 gives an overview of the nature of silica and the factors that need to be considered when estimating exposure to silica and its related adverse health effects. Section 5 reviews population studies of silica and COPD and discusses the complexities of the relationship between silica exposure, silicosis and other diseases such as COPD. Section 6 reviews the evidence from studies of individual occupations and agents. General limitations of the studies and overall conclusions are discussed in section 7.

3. The nature and aetiology of CBE and COPD

There appears to be no generally accepted definition of the term Chronic Obstructive Pulmonary Disease although over the years attempts have been made to standardise its use. There is general consensus however, that COPD is characterised by limitation of expiratory airflow [Rennard, 1998;Silverman and Speizer, 1996]. The two major components of COPD are chronic bronchitis and emphysema, both of which can lead to the development of airways obstruction [Snider, 1989]. The airways obstruction may be partially reversible and is often accompanied by airways hyper-reactivity, but it is the former that causes impairment of lung function, disability and death [Snider, 1989]. Asthma may also be included in the term COPD, if for example, subjects have chronic airflow obstruction, as may less common conditions, such as bronchiectasis and upper airway obstruction [Silverman and Speizer, 1996].

COPD is a leading cause of mortality and morbidity in both developed and developing countries and its natural history is mainly characterised by a progressive, irreversible, decline in lung function, as measured, for example, by forced expiratory volume in one second (FEV_1) [Anto et al., 2001]. The multifactorial aetiology and manifestation of COPD has led to the development of the 'Dutch hypothesis' of the natural history which holds that asthma, chronic bronchitis and emphysema are different expressions of one disease entity in which the tendency to develop allergy and airway hyperresponsiveness modulated by such factors as age and gender as well as extrinsic factors are implicated [Becklake, 1998].

The prevalence, incidence and mortality rates for COPD increase with age and are higher in males than females [Anto et al., 2001]. A consistent association with low socioeconomic status has been found, particularly with chronic bronchitis, in many populations [Anto et al., 2001]. The role of poor nutrition and increased susceptibility to infection has also been suggested [Silverman and Speizer, 1996]. The protective effect of some dietary components has been investigated with positive associations been reported for fish oil, vitamins C and E, and magnesium [Anto et al., 2001].

The most important causal factor of COPD, in particular CBE, is active smoking, although only a proportion of heavy smokers will develop the disease. Clear and consistent dose-response relationships have been shown from longitudinal studies of an accelerated decline in lung function associated with both the duration of smoking and the amount smoked. It has also been shown that after smoking cessation, FEV_1 decline levels off without returning to the base level. A systematic review of the effect of passive smoke (environmental tobacco smoke) has shown that it has a deleterious effect on the pulmonary function of children and also increases the risk of childhood respiratory infections [Cook and Strachan, 1999].

From studies of twins and families genetic susceptibility appears to play a role in the development of COPD [Silverman and Speizer, 1996], although it is increasingly recognised that the genetic determinants are likely to be complex. For example, individuals who are $alpha_1$-antitrypsin deficient may have a increased susceptibility to COPD [Sandford et al., 1997].

Studies comparing urban and rural populations have found increased frequency of respiratory symptoms and reduced levels of lung function in areas with high pollution. However, results are inconsistent with regard to specific pollutants and diagnoses, although it has been suggested that ambient air pollution may act indirectly by affecting lung function development and increasing childhood respiratory disease, which may consequently increase the risk of developing COPD [Anto et al., 2001;Silverman and Speizer, 1996].

4. The nature of silica

Silica is a general term for a group of minerals composed of silicon and oxygen. Silica is most commonly found in a crystalline state and less often in an amorphous state. It exists in nine different crystalline forms or polymorphs with the three main forms being quartz, tridymite and cristobalite. Most processed minerals, from raw materials used in construction and industrial minerals to metallic ores and coal also contain a proportion of silica which can vary considerably. Silica plays a major role in many industries as indicated in the search terms used for this review and is often both a key constituent and processing ingredient. Industries in which high levels of silica have been found include construction (masonry, heavy construction and painting), iron and steel foundries (casting), metal services (sandblasting, grinding or buffing of metal parts), painting and paper hanging, pottery, cut stone and stone products, glassware, and ship building and repair [Linch et al., 1998].

Regardless of the exact constituents of dust, the total surface area of silica containing dusts retained in the lungs of humans is an important determinant of toxicity. Surface area can be determined by both concentration of dust and particle size; smaller particles have a larger surface are per unit mass compared to larger sized particles. Very fine dusts of respirable crystalline silica may inflict different damage to the lungs than larger respirable size fractions. Probably the most important factor in the development of adverse health effects is the "dose" of respirable silica-containing dust in the workplace setting – that is, the product of the concentration of respirable dust containing silica in the workplace air and the percentage of silica in that dust. Other important factors are: (1) the range of particle sizes; (2) the crystalline or non-crystalline nature of the silica; (3) the cumulative duration of dust exposure; and (4) the varying time period from first exposure to diagnosis (from several months to more than 30 years)[American Thoracic Society, 1997;Banks, 1996;Hnizdo et al., 1993;Hnizdo and Sluis-Cremer, 1993;Kreiss and Zhen, 1996;Steenland and Brown, 1995b] The surface characteristics of silica particles have also been implicated in silica cytotoxicity. The physicochemical characteristics relevant to toxicity include:

- Freshly fractured versus aged surfaces
- Particle generated free radicals
- Iron ions as contaminants
- Association with clay
- Pure silica surface versus aluminium covered as in silica sands
- Polymer coating
- Hydrophobic versus hydrophilic surfaces
- H-bonding to membranes

5. Overview of the respiratory effects of silica exposure

Prolonged exposure to respirable crystalline silica has long been known to cause one of the oldest known industrial diseases, silicosis, and there is a large body of literature showing increased risk of silicosis in workers exposed to very fine particles of crystalline silica [Pilkington et al., 1996]. Silicosis is a prescribed disease under the IIDB scheme.

In addition to silicosis, respirable crystalline silica has been associated with autoimmune disease [Parks et al., 1999], non-malignant renal disease [Steenland et al., 2001], COPD [Hnizdo et al 2002] and lung cancer [IARC, 1997]. There remains controversy over the carcinogenicity of silica with regards to lung cancer, in particular the relationship between exposure, the development of silicosis and the risk of lung cancer.

Occupationally-related causes of COPD and CBE have been identified from a wide-range of industry based studies, including cohort and case-control designs, and from population or community-based studies and there have been several reviews of the topic [Balmes, 2002;Becklake, 1998;Garshick et al., 1996;Hendrick DJ, 1996;Viegi, 2001;Viegi and Di Pede, 2002]. Long-term exposure to fumes, chemical substances and dusts in the workplace have been implicated as risk factors for the development of COPD and include occupations in which silica is a major potential exposure. The literature from studies within specific silica based industries or occupations is reviewed in Section 6.

Population based studies

There have been a number of population-based studies of COPD that have identified occupations with high exposure to silica. In a longitudinal study of 878 men from Zutphen, Holland, increased risks of chronic non-specific lung disease were found for construction workers [Heederik et al., 1990]. Hospitalisations due to COPD were investigated in a Danish study in which occupation was obtained from three census returns 1981, 1986 and 1991. Standardised hospitalisation ratios for COPD were increased for workers in the iron and metal industry [Tuchsen and Hannerz, 2000].

A population-based case-control study compared COPD cases discharged from the Institute of Occupational Medicine in Padua, Italy [Mastrangelo et al., 2003]with a control group of patients without respiratory disease using a job-exposure matrix to define occupation and exposures. Elevated age-smoking adjusted ORs were found for welders (OR 6.4, 95% CI 1.6-25.5), painters (OR 4.7, 95% CI 1.3-16.4), foundry workers (OR 12.1, 95% CI 1.3-10.8), refractory brick workers (OR 4.7, 95% CI 1.14-37.0) and construction workers (OR 3.1, 95% CI 1.0-9.5). Adjusted ORs were 3.8 (1.21-12.0), 5.83 (1.82-18.6) and 8.86 (2.29-34.3) in workers exposed to high levels of mineral dust, gas/vapour/fume and biological dust respectively.

Exposure to silica has also been shown in population based studies to be associated with spirometric airflow limitation [Humerfelt et al., 1998]. All eligible men aged 30-46 years living in western Norway were invited to take part in a cross-sectional survey, including a self-administered respiratory questionnaire, spirometric measurements and chest x-ray. 26106 men took part. Occupational quartz exposure was reported by 13% (3445) with a mean duration of 7 years. The prevalence of wheezing was much higher (around 30%) in those exposed to quartz compared with those not exposed (14%). However, the proportion of those who were current smokers was also higher in those exposed (between 50 and 60%) than those not exposed (40%).

Analyses were carried out for FEV_1, FVC, standardised residuals of maximum FEV_1/height^2 ($SFEV_1/h^2$) and standardised residuals of FVC/height^2 (SFVC/height^2). The standardised residuals were calculated by estimating the predicted value of each measure from a reference population and then dividing the observed minus the predicted by the residual standard error from the prediction equation. These are dimensionless quantities. Crude values of $SFVC/h^2$ and $SFEV_1/h^2$ were higher in those exposed for less than 5 years compared to those not exposed but decreased thereafter with duration of exposure. The crude level of FVC was higher and the crude level of FEV_1 lower in those exposed compared with those not exposed. However, the difference in FVC increased after adjusting for age and smoking but disappeared for FEV_1. The ratio of FEV_1/FEC was slightly lower in those exposed to quartz (79.1%) than in those not exposed (79.6%) ($p < 0.01$) but decreased from 79.3% in subjects exposed for less than 5 years to 78.6% in those exposed for $\geq$ 15 years (test for trend $p<0.01$) with no difference between smokers and non-smokers. Multiple linear regression, adjusting for age, atopy, asthma, wheezing, marital status and other occupational exposure, showed that both $SFEV_1/h^2$ and $SFVC/h^2$ were dependent on smoking whereas only the former was dependent on duration of quartz exposure. For a man of 1.8 m the multiple regression equation estimated a reduction in FEV_1 of 4.3 ml for each year exposed to quartz and a reduction of 6.9 ml per year due to smoking 20 cigarettes daily.

Mechanisms involved in the develoment of COPD associated with silica exposure

The controversy that exists regarding the relationship of silicosis in the development of lung cancer also extends to COPD. Research that contributes to understanding of the latter and the potential mechanisms through which silica can cause pathological changes that may lead to the development of COPD has been reviewed[Gamble et al., 2004;Hnizdo and Vallyathan, 2002] Hnizdo and Vallyathan (2003) review the literature to address whether silica dust can cause pathological changes in the lungs leading to the development of COPD at exposure levels that may not cause silicosis. Current thinking is that chronic inflammation and remodelling of the small airways (neutrophils, macrophages, T lymphocytes) (bronchitis) and destruction of lung parenchyma (emphysema) occurs in response to inhalant oxidants from smoking and other environmental exposures and leads to COPD. Ways in which silica is suggested to cause COPD include: cytotoxicity by particles initiating toxic and inflammatory processes; epithelial cell injury that facilitates penetration of silica particles through the walls of small airways causing localised fibrosis. The paper reviews studies where radiological silicosis was present (mainly gold, hard rock and molybdenum miners) and cases where it was absent (granite, diatomaceous earth, concrete workers). In the latter, even in young workers without signs of silicosis there was a loss of lung function with increasing cumulative silica dust exposure in both smokers and non-smokers. However, the studies of hard rock miners showed that the lung function effects were different between smokers and non-smokers, with the former having significantly reduced FEV_1, FEV_1/FVC, FVC and maximal expiratory flow and increased residual lung capacity measurements and in the latter, decreases in residual lung capacity measurements were suggestive of restrictive impairment.

In gold miners, who have been studied in depth by the authors, silicosis was not associated with significant airflow obstruction, supporting the hypothesis of an independent effect of silica on COPD. The issue of undetected silicotic nodules in the lungs has been addressed by several CT studies – see below. CT scans were found to be more sensitive for detecting silicosis than the standard radiograph. The studies (mostly small) are reviewed by the authors who conclude that emphysema rather than silicosis correlates with airflow obstruction among silica dust exposed workers, including subjects with silicosis. These results are supported by evidence from post mortem studies. The authors suggest that the evidence points to silica exposure causing

emphysema in a similar pathological mechanism to smoking. They conclude that silica dust exposure increases the risk of chronic bronchitis even in the absence of emphysema. Their overall conclusion is that workers exposed to average respirable silica dust concentrations between 0.2 and 0.1 mg/m^3 shows a significant exposure response relationship for cumulative dust exposure and airflow obstruction that is independent of radiological signs of silicosis. However, in concrete workers a low level of 0.6 mg/m^3.year cumulative exposure was associated with a significant small loss of lung function (FEV_1/FVC) in the absence of silicosis, although there was no clear dose-response relationship with silica exposure [Meijer et al., 2001]. Smoking potentiates the effect of silica dust on airflow obstruction and death from COPD. Emphysema appears to be the predominant pathology associated with airflow obstruction in silica dust exposed workers.

The debate about whether changes in lung function among workers with a long history of silica exposure are due to the effect of dust exposure or silicosis or other factors is also discussed by Gamble et al (2004). They point out that the situation is complicated to evaluate because: silicosis and silica dust exposure are closely related; silicosis can be present in workers with no radiographic evidence; smoking is an important determinant of lung function and is often poorly quantified or not considered; studies have demonstrated a relationship between smoking and silicosis; the role of emphysema has often not been addressed; smoking, dust exposure and emphysema can all cause obstruction and restriction of lung function and reduce gas diffusion. The paper reviews studies of lung function and category of radiographic silicosis, including adjustment for smoking, dust exposure and emphysema. Graphs %predicted FEV_1 and FVC by category of silicosis for each study and includes studies of gold miners, firebrick workers, pottery workers, silica workers evaluated for compensation, diatomaceous earth workers and granite workers. The evidence is synthesised in two graphs of FVC % predicted and FEV_1 % predicted by category of silicosis and progressive massive fibrosis (PMF). As expected the general trend of nearly all the graphs is for both lung function measures to decrease as the severity of silicosis increases. The authors point out that reduction in lung function occurs most strongly at highest silicosis categories but that the studies that have adjusted for silicosis in their analysis show that emphysema is still related to reduction in lung function i.e. that emphysema associated with silicosis was likely to be responsible for the reduction in lung function. The authors do not present the data by levels of silica exposure and thus do not address the relationship between the levels of exposure at which silicosis and COPD occur.

Diagnosis of silicosis and the use of CT scans

Silicosis has been traditionally measured in terms of the presence of rounded opacities, but after the incorporation of the less discrete (irregular) opacities (associated with asbestos originally) into the ILO classification system in 1980 it was found that the presence of irregular opacities was associated with dust exposures traditionally associated with rounded opacities such as silicosis[Tjoe-Nij et al., 2003a]. Irregular opacities seem to be more prevalent when there is a high variability in quartz content of the dust and consequently to more mixed dust exposure (see refs in Tjoe). Irregular opacities can incorrectly be interpreted as the effect of asbestos exposure but apart from information on work history, the presence of diffuse pleural thickening which is commonly present when irregular opacities are the result of asbestos exposure, should be decisive on the nature of the opacities.

Emphysema with silicosis has been thought to be associated with progressive massive fibrosis (PMF), although other causative factors such as smoking and exposure to dust such as coal and asbestos often co-exist in those who have silicosis. Emphysema with silicosis has been found independently of smoking [American Thoracic Society, 1997]. Others have reported that silicosis *per se* without PMF does not contribute to emphysema. It has also been suggested that it is the

degree of emphysema with silicosis rather than the severity of silicotic nodule profusion that determines the level of lung function. Several studies have demonstrated the advantages of using computed tomography (CT) scans for diagnosis of emphysema and staging of silicosis and evaluating the results in relation to lung function.

In a study in Hong Kong this was addressed using visual scoring of emphysema at CT according to the extent of lung involvement [Ooi et al., 2003]. The study examined 76 men with silicosis. Nodular profusion (NP) at X-ray was graded using the ILO classification. NP and PMF at CT were visually graded. NP at x-ray correlated with all CT parameters of nodularity ($r>0.5$). NP at x-ray and all CT parameters were inversely related to lung function. CT PMF and emphysema index were independently associated with decreased FEV_1 and FVC and cigarette consumption and silica exposure had no independent effect on lung function.

A study of 207 Canadian coal workers being evaluated for pneumoconiosis who had a reading of category 0 (not detectable) or 1 (low grade) in the International Labour Office (ILO) scale was carried out together with 5 healthy volunteer controls and 96 with asbestos exposure[Begin et al., 1995]. CT scan emphysema was observed in 94 patients and the presence of emphysema was increased significantly with the presence of pneumoconiosis and confluent silicosis in the whole group and the lifetime non-smokers. In lifetime non-smokers emphysema was seen in 1 out of 20 patients without asbestosis or silicosis and in 8 out of 11 patients with one of these diseases. In smokers without asbestosis or silicosis the prevalence was 55% in patients with silica exposure and 29% of those with asbestos exposure suggesting that in smokers, exposure to silica has a synergistic effect on the prevalence and severity of emphysema. As expected, there was a significant association between emphysema and decreased lung function.

An Italian study compared CT scans with chest radiography in the diagnosis and assessment of severity of silicosis [Talini et al., 1995]. Two experienced readers evaluated CR and CT scans and concordance was higher for the latter (kappa = 0.49) than the former (kappa = 0.29). There was also poor concordance between CT and CR in the early stages of silicosis. The study showed increasing severity in CT categories of opacities was associated with decreasing expiratory flow and diffusion capacity whereas no relation could be found between CR categories. The authors suggest that the presence of similar percentages of smokers in the CT categories does not support the argument that parenchymal opacities found by CT are mainly due to smoking and concomitant chronic bronchitis which could explain the poor lung function test results. It should be noted that an autopsy study[Hnizdo et al., 1993] showed the degree of silicosis but not of emphysema at necropsy was associated with a significant impairment of lung function in non-smoking gold miners suggesting silicosis causes changes in lung function independently of the contribution of smoking and emphysema.

Summary

The evidence from studies of gold miners and other occupational groups where radiological silicosis was absent suggests that significant loss of lung function occurs with exposure to silica dust and that the effect of cumulative silica dust exposure on airflow obstruction is independent of silicosis. Smoking has been shown to potentiate these effects but not always significantly. Silica dust concentrations between 0.1 and 0.2 mg/m^3 appear to cause this loss of lung function, and this occurs also in groups of relatively young silica dust exposed workers without radiological signs of silicosis. A clear dose-response relationship between COPD and silica exposure has not been shown consistently, although in large studies where trends have been found, the relationship, for example between FEV_1 and duration of silica dust exposure, is similar

among non-smokers, ex-smokers and smokers [Humerfelt et al., 1998]. The excess loss of lung function varies but appears to be about 5-10 ml per year. An estimated 10-20 years duration of work at these exposure levels would cause an excess loss of 1 litre due to silica exposure.

6. Review of COPD in specific industries and occupations with exposure to silica

6.1 Construction industry, including tunnelling and exposure to cement and concrete

6.1.1 Construction industry

Nature of the industry and exposures

Exposure to silica within the construction industry and studies of ill-health among the sector workforce has been extensively reviewed [Lumens and Spee, 2001;Meldrum, 2005]. A key element of the construction industry is that there is a diverse set of trades involved and the nature of the work and thus the exposures vary widely. Dust is omnipresent at construction sites and exposure can occur in almost all activities. The nature of the dust varies depending on the materials being used and can contain a considerable amount of silica and other substances that can potentially affect respiratory health. Other concomitant exposures can include fumes, diesel exhaust, asbestos, chemicals such as chromates and cadmium. Given the dynamic environment of the construction industry, exposure is likely to be intermittent and varying levels may be experienced for different periods of time. The measurement of exposure, including to silica, and the relationship of this to adverse health effects is thus challenging. Exposure to silica occurs during processing of materials containing sand and stone (e.g. brick, concrete, granite, mortar, tiles) particularly during demolition, cleanup, blasting, drilling, grinding, concrete mixing and other activities where large amounts of respirable dust are generated. It has been pointed out that materials containing silica do not have a homogeneous composition and the dust may thus have different characteristics resulting in different biological activity [Meldrum, 2005].

In a study of 30 construction sites, geometric means and standard deviations, GM (GSD) in mg/m^3 for total dust were 5.2 (3.8) for all surveyed, 3.1 (2.7) for recess millers (making recesses for concealing utility lines and pipes), 2.1 (2.9) for inner wall constructors and 10.8 (3.5) for demolition workers [Lumens and Spee, 2001]. Comparative figures for quartz dust concentrations were 0.5 (5.6), 0.7 (3.3), 0.04 (2.6) and 1.1 (4.0). The average level of respirable quartz was higher than the Dutch limit value of 0.075 mg/m^3. As expected, exposure to quartz increased with increased quartz content, dusty working methods, little use of local exhaust ventilation, increasing numbers of workers present, low level of house keeping and limited use of PPE. Others have also found high proportions of measurements above limit values, for example, in a Swiss study nearly 80% of measurements were above the Swiss limit of 0.15 mg/m^3 with the highest levels being encountered when renovating a sandstone wall and during the milling of recesses within a building (reviewed by Lumens).

Mortality studies

Several proportional mortality (PMR) studies have been carried out of construction workers (reviewed by Meldrum) showing increased mortality for respiratory diseases including emphysema, COPD, pneumonoconioses in various trades such as carpenters, ironworkers, painters and plasterers, bricklayers etc. PMRs were generally less than 2 with typical results being, for example, 115 (95% CI 102, 130) for emphysema in a US study of members of the US Carpenters' Union; 122 (95% CI 104, 120) for emphysema in a US study of members of the International Union of construction iron workers; 133 (95% CI 111, 157) for emphysema and 119 (95% CI 110, 129) for other non-malignant respiratory diseases including COPD in a study of members of US International Union of bricklayers and allied craft workers. The disadvantage of this type of study design is that no comparison has been made with an external non-exposed population and excesses could have occurred partly because of deficits in other disease groups.

A follow-up study was carried out of German employees aged 40-65 years working as plumbers, carpenters, painters or varnishers, plasterers, bricklayers, unskilled workers or as office workers, engineers or architects, who had undergone occupational health examinations by the health service of the German Workman's Compensation Board between 1986 and 1988 [Rothenbacher et al., 1997]. 87% of those invited agreed to participate and were followed up between 1992 and 1994. Three different measures were used to characterise the respiratory disease morbidity: 1) the presence of clinical findings on lung auscultation (rales, rhonchi or crackling or prolonged duration of expiration); 2) FEV_1 <70% predicted; and 3) medical diagnosis of chronic respiratory disease (ICD 9 490-496, COPD). An active follow-up of all employees was conducted to ascertain whether early retirement due to permanent disability or death had occurred after the initial examination. Life status and employment status at follow-up could be ascertained for 96% and 92% of participants respectively. In total, during the period of follow-up (4-5 years), 340 employees were granted a disability pension for health related reasons and 141 employees died. The relative risk (RR) for mortality from COPD was 2.0 (1.3, 3.1). The RR for all causes of death was 2.9 (1.0, 4.2) for workers with $FEV_1 \leq 69\%$ predicted and for workers with pathological findings on lung auscultation after adjustment for age, occupation, nationality and company size. However, smoking status was not adjusted for in these models. Atopy was also not recorded although the authors acknowledge this might be relevant, particularly for painters.

A cohort of over 300,000 Swedish male construction workers was followed from 1971 to 1999 [Bergdahl et al., 2004]. Exposure to four major groups of exposure i) inorganic dust (asbestos, man-made mineral fibres, dust from cement, concrete and quartz), ii) gases and irritants (epoxy resins, isocyanates and organic solvents), iii) fumes (asphalt fumes, diesel exhaust and metal fumes) and iv) wood dust was estimated based on a job exposure matrix. There was considerable overlap of exposures particularly the first three broad groupings. Smoking habits were obtained from the first voluntary health examination; 80% of workers had had at least one examination. An internal group of unexposed workers was used as a comparison group. After adjusting for smoking and age there was a slight but significant increase in risk from mortality from COPD (RR = 1.12 (95% CI 1.03, 1.22)) and in those exposed to inorganic dusts (RR = 1.16 (95% CI 1.05, 1.28)), gases and irritants (RR = 1.18 (95% CI 0.98 – 1.41)) and fumes (RR = 1.22 (95% CI 1.04, 1.42)). For never smokers the mortality from COPD overall increased to 2.11 (95% CI 1.43, 3.00) and the RRs for specific exposure groups also increased significantly; inorganic dusts (RR = 2.38 (95% CI 1.59, 3.44)); gases and irritants (RR = 2.92 (95% CI 1.46, 5.22)); fumes (RR = 2.72 (1.31, 3.68)). The fraction of work attributable to work among the exposed was estimated as 10.7% overall and 52.6% among the never smokers.

Cross-sectional and longitudinal studies of COPD prevalence and lung function

In an early study of 200 French construction workers first investigated in 1971 88% admitted to smoking and the prevalence of chronic bronchitis was 21% [Pham et al., 1977]. After follow-up of three and a half years, (32 could not be located) 25% of the initially asymptomatic workers had become bronchitic although 22% of the initially bronchitic workers claimed an improvement in their symptoms. The authors suggest that seasonal variation in the prevalence of respiratory symptoms may have contributed to this; the initial examination was carried out in winter and the second in spring. The authors report a significant decline in lung function over the follow-up period at all ages although the actual lung function results are not clearly reported in the paper.

In the German follow-up study described above[Rothenbacher et al., 1997] prevalence at occupational health examination at the start of follow-up of a reduced FEV_1 ranged from 4.5% (white-collar employees) to 12.9% (unskilled workers). A diagnosis of chronic respiratory disease

in the health record of employees was between 3.0% for white collar employees to 9.1% for unskilled workers. In general, in most occupational groups measurement of a reduced FEV_1 <70% predicted was more common than recording of pathological findings on lung auscultation or a medical diagnosis related to chronic respiratory disease. The crude prevalence of all 3 morbidity measures was highest in current smokers. For example, for current smokers, the prevalence of COPD and FEV_1<70% predicted was 3.3 and 2.2 respectively for white collar workers compared to 9.2 and 8.6 for plumbers, 11.5 and 12.7 for carpenters, 7.8 and 12.4 for painters/varnishers, 13.0 and 11.6 for plasterers, 12.6 and 13.7 for unskilled workers and 7.9 and 10.7 for bricklayers. Prevalences increased as age increased for all levels of smoking status.
A cross-sectional study of the respiratory health effects associated with quartz dust exposure was carried out using a Dutch construction worker database [Tjoe-Nij et al., 2003b]. Only currently working employees were included working in tuck pointing (1270), demolition (1130), concrete (816), natural stone (640), pile-top crushing (26), terrazzo (291), road construction (15) and unknown job (19). 32% (1335) of those invited were enrolled for lung function and chest X-ray measurements and to complete a respiratory symptom questionnaire. A semi-quantitative exposure index was derived using available exposure measurement data and expert judgement. 55% of the full-shift respirable quartz dust measurements were above the Dutch OEL of 0.075 mg/m^3. Concrete driller and grinders, tuck pointers and demolition workers had the highest exposure levels. Exposure was highly variable and repeated measurements showed highly variable day-to-day values. After correction for smoking FEV_1, FVC and PEF were respectively 120 ml/s, 130 ml and 225 ml lower in construction workers compared to values expected in the ERS reference figures. Excluding construction workers with pneumoconiosis (profusion category > 1/1) (3% of workers), the difference was about 10% lower than the reference values. Low FEV_1 and FVC values were more prevalent among those with radiographic evidence of pneumoconiosis (reduction of 267 ml/s and 181 ml respectively). Lung function was not associated with the exposure index except for a reduction in FVC of 5 ml per year after correction for pack year smoked. The authors suggest that this general lack of association with cumulative exposure could be the result of non-response bias. It should be noted that only construction workers with a current contract at the time of the study were included. The exclusion of retired workers and leavers could thus have caused bias.

Another Dutch cross-sectional study investigated radiographic abnormalities indicative of pneumoconiosis among 1339 construction workers involved in grinding, jack-hammering, drilling, cutting, sawing and polishing [Tjoe-Nij et al., 2003a]. The average quartz content of the dust was 12% (range 0.4 – 40%). There was also a range of mean 8-hour time weighted average respirable dust levels among jobs, from 0.99 mg/m3 (range 0.1 – 2.5) for site cleaners to 2.8 mg/m3 (range 0.2 – 11.5) for concrete drillers and grinders including recess milling) and 3.5 mg/m3 (range 0.6 – 8.0) for tuck pointers. Exposures of respirable quartz were 0.032 mg/m3 (0.002 – 0.1) for site cleaners, 0.84 mg/m3 (0.03 – 3.8) for concrete drillers and 0.56 mg/m3 (0.09 – 1.7). A prevalence of 10.2% of profusion category >1/0 and 2.9% of profusion category >1/1, irrespective of the shape of the opacities was found. The average duration of exposure of this group was 19 years and the average age was 42 years. The predominant type of opacities were small irregularly shaped which the authors suggest is indicative of mixed dust pneumoconiosis. The prevalence of early signs of nodular silicosis (small rounded opacities of category 1/0 or greater) was low (0.8%).

The prevalence of small irregular opacities of PC>1/0 was highest among workers who had ever been a pile-top crusher (17%), natural stone worker (13%), demolition worker (11%), tuck pointer (11%) or concrete worker drilling holes (9%). The prevalence of small rounded opacities was high among those who had ever been a pile-top crusher (17%), recess miller (11%), rubble clearer (9%), cutter and grinder (5%) or demolition worker (2%). The authors point out that many

workers had complex work histories. Individuals with rounded opacities had an average higher cumulative exposure index than individuals without radiographic abnormalities. The risk of opacities increased with increasing exposure after adjustment for age and smoking pack years, and significantly for profusion category 1/1 or greater. The presence of small rounded opacities was not significantly related to either age or smoking. The authors suggest that in their study workers were unlikely to have been exposed to sufficient asbestos exposure to influence the results.

An unpublished case-control study of 96 workers after 4.5 years with different stages of pneumoconiosis at baseline showed that rounded opacities in both X rays and CT scans were present in lungs of a larger number of workers (13 out of 79 CT scans and 11 out of 93 x-rays) than at baseline (5 x-rays). The authors suggest that the use of techniques with higher resolution could have caused this. They estimate that the prevalence in the whole population of rounded opacities would have been 14% if CT scans had been used initially [Tjoe-Nij and Heederik, 2005].

A cross-sectional study in the US investigated the prevalence of asthma and CB with workplace exposures in heavy and highway (HH), construction and tunnel workers (TW) and included operating engineers (OE) and labourers who were recruited from union members (359 in total) [Oliver et al., 2001]. The prevalence of asthma was 13% for labourers including TW, and 11.4% for OEs and of CB was 6.5% and 1.9% respectively; the latter gave a significant OR of 3.59 (1.02, 12.60) but this became non-significant after adjusting for duration in the union, age, gender, race, BMI, health care use in the last year and smoking status (OR = 3.07, 0.75,12.58). Increasing age and smoking was associated with an increased risk. Length of time in the union was used as a surrogate for duration of work. There was a significant decrease in risk for CB with increasing time in the union for both OEs and labourers, probably due to a health worker survival effect.

6.1.2 Concrete and cement workers

A cross-sectional study of 144 workers at 2 concrete materials-producing factories in the Netherlands exposed to respirable dust containing silica and 110 controls used respiratory questionnaires and lung function tests and carried out exposure assessment using personal air sampling and categorisation into occupational groups by department and job title [Meijer et al., 2001]. Overall average respirable dust concentration was 0.77 mg/m^3 (range 0.08 – 2.67 mg/m^3) and average respirable silica concentration was 0.059 mg/m^3 (range 0.0003 – 0.186). Average silica content of respirable concrete dust was 9.3% (range 4.4 – 11.3%). Average cumulative dust exposure was 7.0 mg/m^3 year and average cumulative silica exposure was 0.6 mg/m^3 year. Concrete workers had a lower FEV_1/FVC ratio than controls (98% (sd 8.1) versus 100.2% (sd 6.9), p = 0.02) and maximal mid expiratory flow (MMEF) (93.2% (sd 26.2) versus 98.6% (sd 25.8), p = 0.10). In multiple regression modelling, exposure to concrete dust adjusted for smoking and a history of allergy showed negative associations with FEV_1, FEV_1/FVC and MMEF, the last 2 significantly. COPD was defined as standardised FEV_1/FVC < -1.64, and was found in 10 concrete workers and 3 controls. A history of allergy, chronic obstructive pulmonary symptoms (COPS) and work-related lower respiratory symptoms (WRLRS) were significantly associated with COPD. There was no interaction between smoking and these variables. The authors conclude that concrete workers with COPS and/or WRLRS are at risk of reduced FEV_1/FVC ratio outside the 5th percentile of the external reference population and therefore of mild COPD at respirable concrete dust levels below 1 mg/m^3 with a respirable crystalline silica content of 10%.

No dose-response relationship and no cases of silicosis were found between cumulative exposure and loss of lung function at the levels experienced in this study. This is in contrast to other studies of granite workers and gold miners where exposures were similar, i.e. between 0.5 and 1.00 mg/m^3 year [Ng et al., 1992;Steenland and Brown, 1995b].

There have been a number of studies of workers in Portland cement factories, most being cross-sectional in design and many carried out in non-UK countries. The main constitutents of Portland cement are tricalcium silicon oxide and dicalcium silicate, with varying amounts of calcium oxide, silicon oxide, aluminium trioxide, ferric oxide, magnesium oxide, alkali oxides, selenium and thallium, and often low concentrations of hexavalent chromium. Several studies have reported significant across-shift reduction in PEF and in FEV_1. Significantly lower ventilatory function has been found compared with controls.

In a study in Malaysia [Noor et al., 2000] of workers exposed to total dust concentrations of 10.18 mg/m^3 significantly lowered FEV_1% (92.1 litres controls, 84.2 litres non-smoking exposed, 82.09 litres smoking exposed) and FEF 25-75% (4.57 l/s controls, 3.71 l/s non-smoking exposed, 3.33 l/s smoking exposed) and a higher prevalence of respiratory symptoms were found compared to controls.
Higher prevalence of respiratory symptoms and lower ventilatory function indices were also found in a Canadian study with 36% of the exposed workers having mild respiratory impairment compared to those not exposed [Al-Neaimi et al., 2001]. Although there were significant differences between exposed and unexposed workers, differences between smokers and non-smokers were not substantial e.g. for FEV_1 mean (standard error) l/s values were 2.57 (0.10) for exposed smokers, 2.60 (0.09) for exposed non-smokers, 3.05(0.06) for unexposed smokers and 2.89(0.05) for unexposed non-smokers.

A Tawainese study found geometric mean respirable dust concentrations of 3.58 (sd 4.89) mg/m^3 in exposed workers compared with controls (0.41 (sd 0.98) mg/m^3) [Yang et al., 1996]. The risk of cough, phlegm, wheezing and dyspnea was significantly raised in those exposed, but not for bronchitis (OR 1.10, 0.96, 1.27) after adjustment for age, smoking status, duration of employment and plant. There was also significantly lower lung function in those exposed (FVC, FEV_1, FEF_{50}, FEF_{75}) after adjusting for the same variables, e.g. adjusted mean FEV_1 was 2.73 l/s for exposed workers compared 2.98 l/s for controls.

The evidence for an exposure-response relationship between cement dust exposure and respiratory health effects is not consistent with some studies finding lower FVC and/or FEV_1 with increasing dust exposure [Noor et al., 2000;Yang et al., 1996] and others finding no relationship between levels of exposure e.g. Siracusa 1988 and Abrons 1988. However, a lack of an exposure-response relationship could be due to loss of follow-up, insufficient contrast in exposure between groups of workers the use of surrogate exposures such as duration of exposure and exposure misclassification.

A cross-sectional study of 119 Norwegian men who had worked at a Norwegian cement plant were identified and compared with a control group of 50 workers from an ammonia producing plant[Fell et al., 2003]. Mean concentration of total dust was 7.4 mg/m^3 (SD 12.9) and for respirable dust was 0.91 mg/m^3 (SD 0.55). Only three symptoms (cough during the day, breathlessness when resting, symptoms during work) were non-significantly associated with exposure. A semi-quantitative index of 4 exposure levels of cement dust was derived for each worker using expert judgement. Crude mean FEV_1(%) was 2.78 l/s for exposed workers compared with 2.74 l/s for the controls, giving a positive regression coefficient of 0.0014 (95% CI -0.01, 0.003) for exposed versus controls, adjusted for age, height, tobacco and asbestos

exposure. Crude mean FVC% and FEV_1/FVC were also slightly higher in the exposed than the controls. There was a slight tendency toward a lower FEV_1% in the highest semi-quantitative exposure group compared with the lowest level of exposure with a regression coefficient of -0.04 (95% CI -0.07, 0.01). This study does not support the hypothesis that cement dust exposure has a negative impact on lung function.

Another cross sectional study, this time in the US, that compared 2736 Portland cement plant workers with 755 controls from various non-cement industries such as machinery manufacturing plants or a dairy also found similar prevalences of symptoms between the two groups[Abrons et al., 1988]. The exception was dyspnoea which was found in 5.4% of the cement workers compared to 2.7% of the controls (OR =1.60 p=0.05). None of the mean lung function measures differed significantly between the cement workers and the controls. However, the prevalence and risk of chronic phlegm increased with increasing tenure with a significant trend up to an OR of 2.02 for over 30 years tenure. The geometric mean concentration of respirable dust for the cement workers was 0.57 mg/m^3 and for total dust was 2.90 mg/m^3 .

A cross-sectional study of 126 production workers at a Tanzanian Portland cement factory and 120 controls found significantly low FVC, FEV_1, PEF, FEV_1/FVC, FVC%, FEV_1% and FEF% in those exposed, adjusted for age, duration of employment, height and pack-years. Exposed workers had higher current dust exposure than controls (GM 10.6 versus 0.7 mg/m^3) and cumulative total dust exposure (GM 69.1 versus 10.8 mg/m^3 year) [Mwaiselage et al., 2004]. Significantly lower values of FVC, FEV_1, PEF, FEV_1/FVC, FVC%, FEV_1% and PEF% were found in exposed workers compared to controls after adjusting for age, height, duration of employment and pack years e.g. mean (SD) l/s values for FEV_1 were 79.2 (15.5) for exposed ever smokers, 83.0 (14.4) for exposed never-smokers, 99.4 (10.2) for control ever smokers and 99.3 (13.0) for controls never smokers. In multiple regression analyses both current and cumulative dust exposure were negatively associated with FVC (-14.4 $mL/mg/m^3$ and -0.8 $ml/mg/m^3$ year), FEV_1 (-28.3 $mL/mg/m^3$ and -1.7 $ml/mg/m^3$ year) and PEF (-17.6 $mL/mg/m^3$ and -1.5 $ml/mg/m^3$ year). Overall 14.7% of the total workforce had airflow limitation (FEV_1/FVC < 0.70) with more in the exposed group, 22.6%, than controls, 5.9%. Cumulative dust exposure greater than 300 mg/m^3 year versus < 100 mg/m^3 was significantly associated with increased risk of developing airflow limitation (OR = 9.9, 3.5, 27.6). Their model predicts that an average worker in their total population, aged 38, a non-smoker, 170 cm tall and exposed to a total cumulative dust level of 28.9 mg/m^3 would experience a decline in FEV_1 of 49.1 ml/s per year. They also suggest that exposure continuously for 30 years at say, 10 mg/m^3, giving 300 mg/m^3 year cumulative exposure will produce a decline of 500 ml for 30 years of aging. Their results contrast with those from studies such as Abrons et al and Fell et al but average dust levels in these were generally much lower i.e. around 3 or 4 mg/m^3.

6.1.3 Tunnel construction

There have been a large number of studies investigating the respiratory health of workers involved in tunnel and underground tunnel construction, particularly in Norway. The exact nature of the work varies depending on the project but generally includes excavation, rock support and various finishing works, including installation of electricity and paving [Bakke et al., 2001]. Excavation methods are by drilling and blasting or by the use of a full-face tunnel-boring machine (TBM). The latter is often used in heavily populated areas where the use of blasting is considered inappropriate because of the release of blasting fumes and noise to the surroundings. A detailed description of the processes is given by Bakke et al 2001. The main jobs can be grouped as: drilling and blasting; shaft drilling; TBM drilling; protection and securing, including shotcreting (applying shotcrete on the tunnel walls for rock support); support work, including

installation and maintenance of ventilation ducting, compressed air, cables and pipes and transport of material; finishing, including concrete workers doing iron/welding and carpentry work; electricians. All workers are potentially exposed to dust, respirable dust and α-quartz. Diesel exhaust, oil mist and vapour, nitrogen dioxide and carbon monoxide are also exposures of concern for all job groups except TBM workers.

A large study carried out in Norway [Bakke et al., 2001]of the exposure of over 200 workers found the following results:

Agent	Arithmetic Mean	Geometric mean (GSD)	Range
Total dust ($mg.m^{3)}$	5.5	3.5 (2.6)	0.2-56
Respirable dust ($mg.m^3$)	1.7	1.2 (2.4)	0.03-9.3
α-quartz ($mg.m^3$)	0.13	0.035 (5.0)	0.001-2.0
VOC ($mg.m^3$)	4.0	1.8 (5.7)	0.004-26
Oil mist ($mg.m^3$)	0.47	0.33 (2.2)	0.02-4.4
Oil Vapour ($mg.m^3$)	4.0	2.6 (2.6)	0.11-49
Formaldehyde (ppm)	0.020	0.018 (1.6)	0.005-0.04
Nitrogen dioxide (ppm)	0.8	0.6 (2.6)	0.03-2.9
Carbon monoxide (ppm)	8.6	5.7(2.5)	0.8-40
Carbon dioxide (ppm)	1100	1000 (1.7)	87-3100
Ammonia (ppm)	6.0	-	<2.5-60
Elemental carbon ($\mu g.m^3$)	220	160 (2.2)	63-580

The highest GM exposure to total dust (> 6 $mg.m^3$) and respirable dust (≥2 $mg.m^3$) were found in shotcreters, shaft drillers and TBM workers and for α-quartz were found for shaft drillers (0.33 $mg.m^3$) and, TBM workers (0.39 $mg.m^3$). The GMs for nitrogen dioxide did not vary substantially between jobs. However, the drill and blast workers were exposed to high peaks of nitrogen dioxide when passing through the blasting fume during transportation of the blasted rock out of the tunnel. The authors comment that the exposures were substantial when compared to Norwegian Occupational Exposure Limits e.g. 10, 5, 0.1 $mg.m^3$ respectively for total dust, respirable dust and α-quartz.

An early study in Germany investigated exposure and lung function of 30 German workers involved in shotcreting [Kessel et al., 1989]. The total dust concentration measured by personal sampler ranged from 3.2 to 62.1 $mg.m^3$. Lung function measurements at the beginning and end of a shift showed a significant decrease in FVC, FEV_1, PEF and MEF_{75} of 3%, 4%, 6%, and 8% respectively. The change was more marked in non-smokers than smokers. Long-term effects were examined by comparing initial lung function data with data after about 2 years and comparing the group with 21 non-exposed individuals. After 2 years across shift changes showed a further decrease in MEF_{50} and MEF_{25} in the exposed group although there was no difference between exposed and non-exposed in VC and FEV_1.

A cross sectional study was carried out of 212 tunnel workers and a reference group of 205 other outdoor heavy construction workers employed at 15 sites in Norway, all of whom worked 10 hour shifts for 2 weeks and then had 1 week's break. Assessment of respiratory health effects was by questionnaire, spirometric tests and chest x-ray [Ulvestad et al., 2000]. The tunnel workers reported a statistically significantly higher prevalence of cough during the day (17%), shortness of breath on exercise (23%) and chest tightness and wheezing (26%) than the control group (11%, 10%, 13% respectively). Morning cough was associated with smoking in both groups. Compared with the control group the tunnel workers had a significant decrease in FVC % predicted and

FEV_1 % predicted after 10 years employment. After adjusting for pack years of smoking and atopy, FEV_1 decreased by 17 ml for each year of tunnel work compared with 0.5 ml for outdoor heavy construction work. The prevalence of COPD was 14% in the tunnel workers and 8% in the construction workers giving an odds ratio of 2.50 (1.31, 4.96) after adjusting for smoking, years employed and atopy. The authors point out that the annual decline in FEV_1 was much higher than other studies of Norwegian men exposed to α-quartz (4.3 ml/year) [Humerfelt et al., 1998], British coal miners (7 ml/year) [Marine et al., 1988] and South African gold miners (9ml/year) [Cowie and Mabena, 1991]. They suggest that the combined exposures to dust, quartz, diesel exhaust, nitrogen oxide and other substances may have an increased effect on the airways.

In a much smaller study a group of 29 non-smoking underground tunnel and concrete workers and a reference group of 26 outdoor concrete workers were examined at the end of the excavation phase for signs of upper and lower airway inflammation [Ulvestad et al., 2001b]. The underground workers had significantly higher exposure to total dust (GM 5.4 versus 1.0 $mg.m^3$), respirable dust (1.61 versus 0.21 $mg.m^3$), α-quartz (0.087 versus 0.003 $mg.m^3$) and nitrogen dioxide (.90 versus non-detectable ppm) than the outdoor workers. The occurrence of respiratory symptoms was also higher in the underground workers than the outdoor workers: congested nose (76% versus 42%); sore throat (65% versus 23%); cough with phlegm (38% versus 0); chest tightness and wheeze (38% versus 0), all of these difference being statistically significant. There was no difference in spirometry measures between the two groups. Exhaled nitric oxide was significantly higher in the underground workers (GM 8.4 versus 5.6 ppb) and they also had smaller nasal cross-sectional area and volume and more pronounced increase after decongestion than the control group ($p<0.001$). The authors comment that uncertainty in the biological significance of the nitric oxide result although they suggest that it might reflect early signs of airway inflammation.

A follow-up study of 96 Norwegian tunnel workers (drillers and shotcreters) and 249 other workers (outdoor heavy construction workers and white collar workers) was carried out over 8 years from 1991 to 1999[Ulvestad et al., 2001a]. Subjects were aged less than 55 and did not have COPD in 1991. In 1991 there was no significant difference in lung function across the 4 job groups and mean values for FVC and FEV_1 were above 100% predicted for all groups. Compared with the reference group and adjusting for age and smoking (pack years) the drillers had a significantly larger decrease in FEV_1 between 1991 and 1999 and the shotcreters a larger decrease in both FEV_1 and $FEF_{25-75\%}$, with the changes being associated with cumulative exposure to respirable dust and α-quartz. Regression modelling predicted that in a worker aged 40 years the annual decline in FEV_1 in a non-exposed non-smoker would be 25ml (corresponding to that predicted), in a non-exposed smoker would be 35ml, in a non-smoking driller 50 ml, and in a non-smoking shotcreter 63ml. Compared with the reference group, after adjusting for age and current smoking the OR for any new respiratory symptoms was 3.8 (2.3, 6.4) and the OR for any new respiratory symptom associated with cumulative exposure to respirable dust was 2.9 (1.9, 4.5) (ORs were greater than 2 for all individual symptoms). None of the tunnel workers had radiographic signs of pneumoconiosis and at the start of the study only 1 worker had signs of pleural plaques, excluding the possibility that the decline in lung function could be due to silicosis.

A much larger similar follow-up study from 1989 to 2002 was carried out by the same investigators of 651 male construction workers and 542 control workers [Bakke et al., 2004]. Exposure was assessed for all the agents highlighted in the table above. Similar results for respiratory health as in the previous follow-up study were found with no major changes in lung function variables between periods for the control group and a decrease for the tunnel workers. This decrease was associated with all the exposures after adjustment for age and years observed

and for both smokers and non-smokers. The authors carried out multiple regression modelling including all the exposure variables and nitrogen dioxide showed the strongest association of all the agents with a decrease in FEV_1. Reduction in FVC was associated with cumulative exposure to α-quartz in both smokers and non-smokers. However, a correlation matrix presented in the paper shows that the exposures were fairly strongly correlated, for example between nitrogen dioxide and dust. It is not clear whether the analysis carried out was able to take account of these correlations sufficiently to evaluate the relationship between lung function and the separate exposures and also whether investigation of any possible interactions between exposures was carried out.

Summary

Many of the cross sectional studies show a significant differences in both prevalence of symptoms and lung function measurements between those exposed to silica dust experienced in the construction, cement and tunnelling industries and those not exposed. Although smoking tends to decrease the average values of lung function measurements, many studies of construction, tunnel and cement workers do not show a significant difference in, for example, FEV_1, between smokers and non-smokers in either silica dust exposed or control groups. Some of the longitudinal studies show an increased decline in lung function associated with silica dust exposure compared to those not exposed; this can occur at average levels of respirable dust concentrations below 1 mg/m^3, and several studies have found increasing decline with increasing exposures. Although several estimates of the annual decline in FEV_1can be derived from these studies there is some evidence e.g. from Ulverstad 2001 that a loss of 1 litre of lung function could occur after 20 or more years exposure.

6.2 Brick manufacturing industry

Nature of the industry and exposures

Refactories or firebricks are widely used in the heating processes of many industries e.g. lining furnaces and kilns. Raw materials used for the bricks include silica, fire clay, rock high alumina, chrome, magnesite, chrome and zirconium [Liou et al., 1996].

Mortality studies

A cohort study of 231 male workers employed on 1.1.1960 at a refactory plant situated in Genoa was followed up for mortality until the end of 1979 [Puntoni et al., 1988]. An increased risk was observed for non malignant respiratory diseases (SMR 3.04, 95% CI 1.77, 4.86) together with respiratory tract cancer (SMR 2.08, 95% CI 0.30, 9.24). For those workers receiving workmen's compensation for silicosis (136 men) greater than expected mortality was found for all causes of death (SMR 1.63, 95% CI 1.23, 2.11)), cancer of the larynx (SMR 6.82, 95% CI 1.40, 19.91), cancer of the colon excluding rectum (SMR 4.41, 95% CI 0.90, 12.87), respiratory tract cancer (SMR 2.23, 95% CI 1.02, 4.20), cardiovascular disease (SMR 1.73, 95% CI 1.04, 2.69) and non-malignant respiratory diseases (SMR 5.00, 95% CI 2.86, 8.10). Although there was reduced mortality overall for the non silicotics (95 men), there was an increase in lung cancer mortality (SMR 2.08, 95% CI 0.67, 4.84). Information obtained from the relatives on smoking habits of the 14 respiratory cancer deaths found that at least 4 of these occurred to non smokers.

Cross-sectional and longitudinal studies of COPD prevalence and lung function

A Taiwanese cross-sectional study compared respiratory symptoms, X rays and lung function of 526 workers employed in the firebrick manufacturing processes at 34 factories with 164 control workers who were office and administrative personnel[Liou et al., 1996]. The silica content of the clay varied from 0 – 50% depending on the source. The mean age of the exposed group (42.7 years) was significantly different from that of the controls (36.1 years), as was the proportion of smokers (45.6% exposed, 34.1% controls). The prevalence of pneumonoconiotic abnormalities in the chest x-rays was 6.9% in the exposed group, all being round opacities in profusion category 1. Only 1 control had an abnormality (category 2 profusion). Both prevalence of pneumoconiosis and severity increased as length of employment increased. No differences in FVC were founded between the exposed and control groups. However, in both smokers and non-smokers of the exposed group FEV_1/FVC, mean maximal expiratory flow, $FEF_{50\%}$ and $FEF_{75\%}$ were significantly lower than in the control groups. Pulmonary function, adjusted for smoking, decreased as duration of exposure increased with significant trends for FEV_1/FVC% (control 88.4±7.3, exposed ≤ 5 years 87.3 ± 8.1, exposed 5-10years 85.9±7.6, exposed > 10years 82.3±7.2), MMEF (control 103.3±31.0, exposed ≤ 5 years 98.3 ± 29.4, exposed 5-10years 97.2±30.5, exposed > 10years 86.7±29.4), $FEF_{50\%}$ (control 97.7±29.0, exposed ≤ 5 years 91.9 ± 26.9, exposed 5-10years 89.4±28.5, exposed > 10years 82.2±29.1), and $FEF_{75\%}$ (control 82.8±33.5, exposed ≤ 5 years 77.7±30.1, exposed 5-10years 75.4±30.2, exposed > 10years 62.9±25.2). There were no differences between the exposed and control groups with respect to cough, phlegm and shortness of breath, although the prevalence of wheezing was significantly higher in the exposed group. Similar results were found when stratifying for smoking with no differences between the groups except for wheezing which occurred significantly more in the exposed workers who were non smokers (8.9%) compared with the non smoking control group (1.1%). The study is limited by the lack of dust or silica measurements but the presence of pneumoconiosis implies that levels must be relatively high.

A 2 year follow-up study of the same population was carried out [Chen et al., 2001]. 291 exposed workers and 72 controls were included in the follow-up, with the others being untraceable

because of factory closure of because of transfer to other industries. A comparison of those lost to follow-up with those included showed no difference with regard to prevalence of respiratory symptoms or radiological abnormalities found at baseline. Over the 2 year follow-up period there was no difference in decline in FVC and FEV_1 between exposed and control workers after adjustment for age, sex, height and smoking status. However, decline in PEFR, MMF and $FEF_{50\%}$ was significantly greater in the exposed than the control workers after adjustment for age, sex, height and smoking status and the decline of FEV_1/FVC% was significantly higher in the exposed group (6.3%) than the control group (5.5%) after adjustment for smoking. The authors comment that their results suggest that the lung function damage was predominantly obstruction of the large and medium airways.

A Croatian study of 233 male workers employed in 2 brick manufacturing plants and 149 matched controls employed in packing food products in the food industry found significantly higher prevalence of chronic cough (31.8% exposed, 20.1% controls), chronic phlegm (26.2% exposed, 18.1% controls) and chest tightness (24.0% exposed, 0% controls) in the exposed group compared to the controls, prevalence being higher among smokers compared with non smokers and in workers with over 10 years duration of work compared with those with less than 10 year. No cases of pneumoconiosis were diagnosed and mean ILO scores of chest x rays did not differ between exposed workers and controls. Significantly lower FVC and FEV_1 compared with that predicted were recorded in exposed workers compared with controls. Multiple regression analyses of lung function (FVC, FVC_1, FEF_{50}, FEF_{25} respectively) against age, exposure and years smoking showed a significant effect of age and no effect of smoking for all measures but a significant effect of exposure only for FVC. Dust measurements showed a high mean total dust concentration of 10 mg/m^3 (range for most workers 8 to 12 mg/m^3) and a mean respirable fraction of 2 mg/m^3.

A Chinese study of refactory workers was designed to investigate the contribution of silicosis and emphysema (using hyperinflation on a radiograph) to pulmonary dysfunction [Wang and Yano, 1999]. The plant used silica sand consisting of more than 80% quartz to produce firebricks and concentrations of respirable dust exceeded 2 mg/m^3 by 1991, the time of the study. The study included 220 workers exposed to silica with (112) or without (108) silicosis. The prevalence of radiographic hyperinflation and respiratory symptoms (dyspnea, chronic cough and chronic phlegm) increased significantly with progression of silicosis category. Multiple logistic regression models including age, silica exposure, presence of silicosis, ex smoking, current smoking and pack years of smoking, found that the presence of silicosis was significantly associated with radiographic hyperinflation (OR 5.3 95% CI 1.58, 19.30) and being an ex smoker (OR 5.0, 95% CI 1.50, 18.76) but the OR for age, pack years and silica exposure were 1.0. Models of the association with lung function showed silicosis presence was associated with reduced lung function but when radiographic hyperinflation was included the association with silicosis disappeared. Radiographic hyperinflation was significantly associated with a decrease in FEV_1 and FEV_1/FVC with the workers with hyperinflation having a lower mean value for each lung function parameter than those without it, regardless of silicosis. The authors suggest that their study provides evidence that pulmonary dysfunction, particularly obstructive airways and decreased diffusing capacity may be attributed to emphysema associated with silicosis and/or silica exposure. The authors also draw attention to the heavy exposures experienced by the workers and the lack of preventive measures.

A UK cross sectional study of workers in the heavy clay industry included 18 brick and tile works that had been in continuous operation for at least 20 years[Love et al., 199]. Mean dust concentrations ranged from 0.4 to 10.0 mg/m^3 with the highest exposures being in sand users, the clean up squad and in kiln demolition. Mean quartz concentrations ranged from 0.04 to 0.62

mg/m^3. 1925 workers, the majority men, attended for medical examination, and x rays were available for 1831. The prevalence of small opacities increased with age from 0% at age ≤ 24 to 8.5% for those aged ≥ 55 years. Prevalence also increased from 1% among men exposed to <0.5 mg.y.m^3 to 10% for those exposed to ≥ 4.0 mg.y.m^3. The relationship between radiographic abnormality and cumulative exposure to dust adjusted for age, smoking and factory site showed that the risk of having a category ≥ 1/0 radiograph increased significantly with age and exposure and differed between sites even after allowance for exposure. There was a non significant increased effect of smoking. Prevalence of respiratory symptoms increased with age and with smoking and in those employees most exposed to dust. From logistic regression analysis there was a significant effect associated with cumulative dust exposure to ≥ 4.0 mg.y.m^3 of the presence of chronic bronchitis for all clay workers (OR 1.5, 95% CI 1.1, 2.0) and for kiln demolition workers alone (OR 1.6, 95%CI 1.1, 2.7), adjusting for smoking, site and time worked in other industries. Similar ORs were found for breathlessness.

Summary

Although there appears to be consistent evidence of increased risk of COPD in brick workers, the nature and magnitude of the risk varies. For example a decline associated with exposure for most lung function measurements with the exception of FVC is found in one Taiwanese study but the opposite in a Croatian study. Although the risks of silica often increase with smoking, for most of the studies an increased risk remains with silica after adjustment for the effects of smoking. The UK study found a low frequency of silicosis. The study predicts that 1.4% of non-smokers aged 40 exposed to an average dust concentration of 2.5 mg/m^3 for 20 years would be expected to have category ≥ 1/0 compared to 0.6% in the lowest dust concentration category. A small but consistent exposure response effect was found for chronic bronchitis with a significant OR of 1.6 associated with cumulative dust exposure to ≥ 4.0 mg.y.m^3 in highly exposed jobs such as kiln demolition, where dust exposures of > 100 mg.y.m^3 (10 mg.m^3 for 10 years) might be expected.

6.3 Pottery and ceramic work

Nature of the industry and exposures

The effects of silica containing dusts on the respiratory health of workers in the china clay industry and in the pottery industry have been studied in several countries including the UK, although the emphasis of the research has mainly been on the occurrence of silicosis and lung cancer.

A detailed study of the exposures experienced in different jobs and time period has been carried out in the UK pottery industry [Burgess, 1998]. For the period 1990-1995, daily 8-hour time weighted average airborne concentrations of respirable silica were estimated to range from 2 μg/m^3 for pottery support activities to 50 μg/m^3 for tile making and jobs working in body preparation and primary shaping production. Very much higher exposures were estimated for previous periods with a clear downward trend. For example estimates for firing were: 1930-39 800 μg/m^3; 1940-49 650 μg/m^3; 1950-59 500 μg/m^3; 1960-69 220 μg/m^3; 1970-79 24 μg/m^3; 1980-89 20 μg/m^3; 1990-95 20 μg/m^3.

Several studies of the effects of silica have been carried out in China. These tend to include pottery factories and tungsten, copper and iron, and tin mines but have the advantage that results can be compared between the difference sources of silica. Estimation of historical levels of silica in 9 Chinese pottery factories found that the percentage of crystalline silica varied over time, but that there was a tendency for an increase from 28% in 1959 to 53% in 1993[Zhuang et al., 2001]. A sampling survey carried out in 1988/89 reported by Zhuang (2001) found an overall average respirable crystalline silica concentration of 0.116 mg/m^3 and average total dust concentration of

5.1 mg/m^3 for the pottery factories and these were estimated to have remained fairly constant from the 1950s to 1993. These levels are higher than those estimated in the UK pottery industry from 1970 onwards but lower before that time.

Mortality studies

In the UK a cohort study of 5115 men born between 1916 and 1945 and employed in the pottery, refactory and sandstone industries of Stoke-on-Trent was followed up to 1992 for mortality[Cherry et al., 1998]; exposure estimates for this population are those published in the paper by Burgess et al 1998. The SMR for all causes of death, lung cancer and for non-malignant respiratory disease were significantly raised when compared to England and Wales population (all cause SMR, 1.46 95% CI 1.33, 1.60; lung cancer SMR 1.91, 95% CI 1.48, 2.42; non-malignant respiratory disease SMR 2.87, 95% CI 2.17,3.72). The results were reduced slightly when the rates for Stoke on Trent were used. However, care must be taken when using too small an area/population for comparison if the rates of disease in the local population are influenced by the occupational causes.

Cross-sectional and longitudinal studies of COPD prevalence and lung function

In a subcohort of 1080 men with at least 10 years work in the UK potteries since 1960, 64 (5.9%) had at least one radiograph read as ≥ 1/0 for small opacities, and 21 had a reading ≥ 2/1. The prevalence of small opacities increased with cumulative exposure. The risk of small opacities in relation to cumulative exposure (as a continuous variable), duration of exposure, average concentration and smoking was examined by modelling. Adjusting for smoking (itself an associated with small opacities OR 2.28, 95% CI 1.02, 5.10) results were: cumulative exposure/1000 (μg/m^3.y) OR 1.37, 95% CI 1.24, 1.53; mean concentration/100 (μg/m^3) OR 2.66 95% CI 1.94,3.66; Duration/10 (year) OR 1.08 95% CI 0.83,1.40. Although results for a nested case referent study of lung cancer cases are reported no further results are given for non-malignant respiratory disease.

An assessment of the relationship between exposure to silica dust and chronic airflow limitation was carried out in a pottery factory in France and in a comparison plant in which pipelines were made[Neukirch et al., 1994]. Irritant fumes and gases were not present in either factory. No significant difference was found between the two groups in the prevalence of respiratory conditions, perceived hyper-responsiveness and allergy. However, the prevalence rates for men were higher in the pottery workers than among controls for runny nose (19% versus 13.6%, p=0.07), itching throat (22.0% versus 9.0%, p<0.001) and wheezing (12.6% versus 6.8%, p=0.04). Standardised FVC and FEV_1 were significantly lower for the exposed workers overall compared to the controls and particularly for those defined as directly exposed to silica. Unfortunately these results are presented in graphs and it is difficult to estimate the actual loss of lung function from these.

Employees in the china clay industry in the south west of England have been studied with regard to the development of radiographic abnormalities [Ogle et al., 1989]. Average concentrations of dust in 1984-86 were found to vary from 0.5 mg/m^3 for work using tube presses to 2.5 mg/m^3 for calciners and 2.7 mg/m^3 for working using altritor mills. The study included 3689 workers of whom 1146 were non-smokers, 1061 were ex-smokers and 1482 were smokers. 16 workers were found to have large opacities on reading the radiographs. Pleural thickening was recorded in 87 radiographs with significantly more occurring in smokers. Small opacities were found for 315 workers with the majority, 271 being in category 1/0.1/1 or 1/2. Regression analyses were carried out of the radiographic score against duration of employment, separately for dryers, work in attritor mills, non-dusty jobs and work in china stone mills. Exploratory analyses showed similar results by category of smoking. Results showed that rate of development of pneumoconiosis for

workers exposed before 1971 were about double those of workers exposed after 1971. The results are not presented in a form in which actual figures can be derived. Lung function variables were strongly related to age and radiological score but not to duration of employment.

Summary
The studies show an increased risk of mortality from and prevalence of NMRD and reduced lung function related to dust exposure. However, none of the papers report the exposure response results in sufficient detail to assess the magnitude of the loss of lung function by exposure level.

6.4 Silica sand industry

Nature of the industry and exposures
There is a relatively large industrial sand industry in the UK with many quarries. The sandstone is either extracted by blasting sandstone rock and then crushing it before processing or dug from unconsolidated deposits. A study including 7 UK quarries collated 2429 personal and 583 static measurements of respirable crystalline silica (RCS) measured between 1978 and 2000 [Brown and Rushton, 2005]. The overall geometric (GM) mean RCS concentration was 0.09 mg/m^3 (geometric standard deviation 3.9). Mean values varied depending on the job with 'dry' jobs and work with silica flour having the highest average values. For example the arithmetic mean total respirable dust for a dry bagger was 0.81 mg/m^3 (SD 2.96) (GM 0.46 (0.02)), and for total respirable crystalline silica was 0.18 (SD 0.75) (GM 0.06 (0.005)). For all jobs total respirable dust and total crystalline silica exposure levels decreased over the 20 years, with levels for dry process workers starting at about 0.2 mg/m^3 in 1978 decreasing by about 0.006 mg/m^3 per year.

Mortality studies
The main studies of the health of workers in the industrial sand industry have been mortality studies with a focus on lung cancer.

A companion paper to the one reporting exposures in UK sand quarries gives results of a retrospective mortality study of a cohort of 2703 workers at 7 UK quarries followed up from 1950 to 2001[Brown and Rushton, 2007]. Mortality overall was significantly lower than that expected using the UK national population as a comparison (SMR for men 90.0, 95% CI 83.6, 96.8). A slight reduction in respiratory disease overall was seen in men (SMR 90.8, 95% CI 72.8, 112.0) and also for COPD (SMR 80.6, 95% CI 49.9, 123.2). A non significant excess was found for pneumoconiosis (SMR 148.2, 95% CI 17.9, 535.4) based on only 2 deaths, both occurring in workers in dry jobs where silica exposure would be greatest. There was no trend in risk of NMRD across increasing categories of cumulative exposure, (adjusted for age, period from first employment, employment status, year of starting employment and quarry).

A mortality study of 2452 men in 8 US sand plants followed up from 1940 to 2000 found significantly increased deaths from all causes compared with the US national rates (SMR 122 $p < 0.001$) 20 or more years after hire[McDonald et al., 2005]. Deaths were also significantly raised from TB (SMR 434 $p < 0.007$), all malignancies (SMR 118 $p < 0.007$), lung cancer (SMR 147 $p < 0.001$), kidney cancer (SMR 202 $p = 0.03$), NMRD (SMR 164 $p < 0.001$) and nephritis/nephrosis (SMR 280 $p < 0.001$).

Another US mortality study of 4626 industrial sand workers followed up from 1960 to 1996 also found excess mortality from silicosis/pneumoconiosis (SMR 18.2, 95% CI 10.6, 29.1)[Steenland and Sanderson, 2001]. The SMR for lung cancer was 1.60 (95% CI 1.31, 1.93) and a multiple cause analysis (as opposed to only using the underlying cause of death on the death certificate) for other respiratory disease (included pneumoconiosis and non specific COPD) gave an SMR of

2.37 (95% CI 2.03, 2.68). Estimated average (GM) exposure was 0.05 mg/m^3 but ranged from 0.09 mg/m^3 for quarry workers to 0.6 mg/m^3 for baggers. Standardised risk ratios (SRR) for lung cancer, silicosis/pneumoconiosis and other respiratory disease (multiple cause) all showed positive trends with increasing quartile of exposure to silica, with the SRR for other respiratory disease being 2.40 for respirable silica greater than 1.28 mg/m^3. There were only limited data on smoking for this cohort.

Summary
There is a clear relationship between excess mortality from NMRD and silicosis in the US studies but not in the UK study although exposure levels appear to be comparable. No studies of lung function decline have been carried out in this industry.

6.5 Granite industry

Nature of the industry and exposures
Information on the effect of silica on respiratory ill health and in particular on longitudinal lung function losses is available from studies of workers in the granite industry. The Vermont granite workers in the US have been studies for over 50 years. In 1974 [Theriault et al., 1974a] the average dust concentrations was found to be 523 μg/m^3 and the average concentration of quartz was 50 μg/m^3.

Mortality studies
All workers (5414) employed in the Vermont granite manufacturing plants or quarries during 1950 and 1982 and who had had at least one X ray (implying that a work history would be available) were followed up for mortality[Costello and Graham, 1988]. Mortality from all causes of death was significantly less than that expected using the population of the US as a comparison population (SMR 0.91, 95% CI 0.87, 0.95). Raised mortality was found for TB (SMR 5.86, 95% CI 4.87- 69.9), cancer of the lung (SMR 1.16, 95% CI 0.96, 1.39), all respiratory disease (SMR 1.21, 95% CI 1.01, 1.43) and silicosis (SMR 6.35, 95% CI 4.56, 8.62). Mortality for these diseases was much higher for workers in the granite shed than those in the quarries. Analyses taking into account tenure showed that most of the excess occurred in men who had worked for over 30 years.

A recent follow-up for mortality of the Vermont granite workers focuses on lung cancer and reports elevated mortality from lung cancer (SMR 1.18, 95% CI 1.03, 1.35), TB (SMR 11.77, 95% CI 9.82, 13.99), silicosis (SMR 20.54, 95% CI 15.39, 26.87), and non malignant respiratory disease (SMR 1.47, 95% CI 1.30, 1.66)[Graham et al., 2004]. Non malignant respiratory disease was significantly elevated in those hired before 1940 (levels of exposure gradually reduced after this date) (SMR 1.81, 95% CI 1.55, 2.11) but is also high in those hired after 1940 (SMR 1.10, 95% CI 0.88, 1.35). When silicosis (50 deaths) was excluded from total non malignant respiratory disease (168 deaths) for the pre 1940 data the SMR became non significantly elevated. Only 3 silicosis deaths occurred in those hired after 1940 out of a total of 91 non malignant respiratory deaths.

A mortality study of 3246 workers employed in the US crushed stone industry, including granite, between 1940 and 1980 found 4 deaths attributed to pneumoconiosis [Costello et al., 1995]. Mortality attributed to pneumoconiosis and other non-malignant respiratory diseases, including COPD, was significantly increased overall (SMR 1.98, 95% CI 1.21, 3.05) and particularly for a subcohort of crushed stone workers that processed granite (SMR 7.26, 95% CI 1.97, 18.59).

Cross-sectional and longitudinal studies of COPD prevalence and lung function

A companion paper to the exposure monitoring paper in 1974 suggested that quartz dust exposure was producing an excessive loss of lung function independent of aging or smoking history and that a 2 ml loss in FVC occurred annually in relation to average year of dust exposure (estimated to be 526 μg/m^3 and 9% quartz), in contrast to a 9 ml loss per year due to smoking and a 30 ml loss per year due to aging [Theriault et al., 1974b]. A later subsequent article detailing longitudinal losses suggested that far greater losses of 50 – 70 ml annually for FEV_1 and 70 – 80 ml loss for FVC were occurring. However, a relationship between dust exposure and lung function loss could not be demonstrated [Musk et al., 1977]. However, in 1981, retesting of a sample of workers revealed that losses of lung function had not occurred as predicted in the 1970s and that FVC values had increased and FEV_1 values had remained about the same[Graham et al., 1981]. A further follow-up reported the results of biennial lung function tests carried out between 1979 and 1987[Graham et al., 1994]. 711 workers were tested three times or more. Linear regression suggested annual losses of 0.018 l for FVC, 0.03 l for FEV_1 and 0.37% for FEV_1/FVC, with a gradation from smoking to non smokers. These values are far lower than those reported in the earlier papers. Analysis of covariance was carried out to examine the separate effects of age, smoking history and granite working history. For FVC and FEV_1 height, age, initial FEV_1 and FVC values, and smoking all individually had significant effects on lung function changes. Years employed in the granite industry had no significant effect. Office, shed and quarry workers did not have significantly different lung function decrements. In 1983 and 1984 a large number of dust measurements were made in the stone sheds. The mean (± SD) concentration was 601(± 368) μg/m^3, similar to that reported previously in 1974. Using an estimate of 10% quartz content the average quartz dust level was estimated to be 60μg/m^3. The authors suggest that earlier spirometry tests had not been carried out correctly leading to spuriously high results and that workers in the granite industry do not experience excessive loss of lung function compared to other populations of non-dust exposed workers.

In Sweden there have been a series of studies of granite stone crushers [Malmberg et al., 1993]. A follow up study of participants in a case-control study carried out in 1976 were invited back in 1988 for a chest radiograph and lung function tests. The 1976 study consisted of 62 male granite crushers and 263 male referents selected from a general population health survey in Sweden. The follow-up study consisted of 45 granite crushers (6 of the original granites crushers had died, 5 refused and 6 were too ill to attend) and 45 controls. Dust exposure was assessed for each individual based on yearly dust measurements. In 1988 the granite crushers had on average worked for 22 years and inhaled 136mg of granite dust and 7mg of silica. Average concentrations of respirable dust were 0.87 mg/m^3 before 1976 and 0.83 mg/m^3 between 1976 and 1988 and for respirable silica were 0.21 mg/m^3 before 1976 and 0.18 mg/m^3 between 1976-1988. Two of the granite crushers had evidence of silicosis on the chest radiograph. Five granite crushers but none of the referents had FEV_1 values < 80% predicted and respiratory symptoms were more common among the granite crushers. Granite crushers had significantly lower mean FEV_1/VC and FEF_{50} than the referents. Over the 12 years FEV_1 had decreased 4.6%, FEV_1/VC 5.4%, MEF 8.0% and FEF_{50} 13.7% more than in referents ($p<0.01$ for all variables). The authors suggest that, although the changes in lung function over the 12 years are moderately higher in the granite crushers, they are consistent with airway obstruction, uneven gas distribution and decrease in elastic recoil. They suggest that the lack of radiographic evidence of silicosis, even though the exposures were generally twice that of the TLV, is consistent with other findings implying that airway obstructive changes may occur independently and precede silicosis.

Two studies of workers employed in granite quarries have been carried out in Singapore. One paper compares lung function data and respiratory symptoms of a cohort of 239 quarry workers with 148 postal delivery workers. The quarry workers were divided into high and low exposed groups, although no details are given in the paper for the basis of this categorisation. Highly

exposed workers showed a greater prevalence of chronic bronchitis (defined as cough and phlegm for as much as 3 months of the year for the last three years) (11%) compared with 2% of the low exposed quarry workers and 3% of the postmen. Higher prevalence of respiratory symptoms was related to smoking although the dust-related differences were apparent for both current smokers and non-smokers. Multiple regression showed that, after adjusting for age, height, race and smoking, the highly exposed worked showed an average 5% lower FEV_1, FVC and $\%FEV_1/FVC$ when compared with the low exposed group and postmen. The results were similar for smokers and non smokers. The authors suggest that dust particles in the respirable size range (<10 microns aerodynamic equivalent diameter) may be responsible for development of silicosis and larger size particle ('inspirable' dust) may give rise to large airways diseases such as chronic bronchitis and obstructive airways disease.

A related paper reports results from lung function tests and chest X-rays of 206 actively employed and 132 previously employed granite workers from two quarries. Cumulative exposure to total dust and respirable quartz was estimated using work histories and dust measurement data. Irregular and rounded small opacities with a minimum radiological profusion of 0/1 were present in 79 (25%) and 60 (19%) of subjects respectively and large opacities were present in 10 (3%). Compared to subjects without any radiological opacities (0/0), no significant differences in FEV_1 and FVC were found for subjects with irregular opacities, after adjusting for age, height, cigarette-years and cumulative silica exposure. However, subjects with rounded opacities had statistically significantly lower values for FEV_1 (mean (sd) 2.5 (0.48)) and FVC (3.2 (0.53) than those with no opacities (FEV_1 2.7 (0.48), FVC 3.3 (0.55)). The differences increased for those with higher profusion categories 2 and 3. The difference was much more marked when comparing those with no opacities with those who had large opacities for which mean adjusted FEV_1 was 1.8 (0.48) and mean adjusted FVC was 2.4 (0.54). In multiple regression analyses in which cumulative respirable silica exposure or profusion of small opacities were entered separately as explanatory variables, each were individually significantly associated with decrements of FEV_1 and FVC. However, no additional effect of cumulative silica exposure was shown when simultaneously allowing for profusion of rounded opacities (and adjustment for age, height and cigarette-years). The multiple regression analyses are carried out separately for the results for 3 different readers of the radiographs and also for the median reading. The results for small opacities appear to be similar between readers but differ for multiple regressions carried out on the data for subjects with profusion score $\leq$ 0/1. Generally respirable silica exposure was not significantly related to lung function in these subjects with the exception for the data for one reader in which there is a borderline significant association, particularly for FEV_1/FVC. Subjects without radiological opacities (either profusion 0/0 or 0/0-0/1) were exposed to average cumulative silica exposure of 0.69 $mg.m^3$.yr, 3 to 4 times lower than those with radiological opacities.

Further investigation of small airways obstruction in those without radiographic evidence of silicosis or physiological evidence of obstruction to the large airways was carried out by the same researchers[Chia et al., 1992] using time domain indices. They postulate that small airways obstruction may be present for years before it becomes evident. They selected the volume-time spirograms of 153 currently employed quarry workers (no details given of how these were selected) and digitized these data. These data were used to derive the mean transit time (an index of the average rate of emptying the vital capacity), coefficient of skewness of transit times (the amount of variation between the initial and the terminal slower portion of the VC) and the index of transit times (a measure of the 'slow finish' at the terminal end of expiration. The workers were divided into three dust exposure groups (low administrative staff, moderate transport and maintenance staff, high past or current drillers and crushers for most working life) based on occupational history and environmental assessment of personal dust exposure by job categories.

The average quartz content in the respirable dust was 28%. With adjustment for age, height and smoking status, all the time domain indices showed significant difference between the three exposure groups. $FEF_{75\%}$ and $FEF_{75\text{-}85\%}$ were also significantly lower in the high exposure group, although FEV_1 and FVC were not significantly different. Separate analyses for smokers and non-smokers showed a greater degree of airways obstruction than non-smokers, except for FEV_1 and FVC, although the trend for greater small airways obstruction in the higher exposure group was seen in both groups. The authors feel that their results suggest that small airways obstruction is present among silica-exposed workers in the absence of radiological evidence of silicosis and large airways obstruction, with this increasing as exposure increased. They suggest that time domain indices are more sensitive indicators of small airways obstruction as these give more emphasis to the end of the forced expiratory manoeuvre.

A recent study has investigated the respiratory health of workers in 24 aggregate quarries (mostly limestone) in Spain[Montes et al., 2004]. 378 workers took part and personal monitoring of respirable dust was carried out for each of them. Serum levels of alpha-1 antitrypsin (AAT) and protease inhibitor (Pi) phenotype were also determined. There was a significant association between AAT and smoking but no relationship with age or dust exposure. The AAT values were significant different between phenotypes MM, (MS, MZ), and (SS, SZ, ZZ). Multivariate analyses showed a significant relationship between the presence of both round and irregular opacities with smoking, cumulative exposure and age. There was also a significant relationship between rounded opacities and AAT, even after excluding smokers. In univariate analyses FEV_1 decreased significantly in relation to exposure to respirable dust, smoking and serum AAT but no association with Pi phenotype was detected. However, in multivariate analyses FEV_1 was negatively associated with the interaction between cigarette pack years and dust but not with these factors individually, after controlling for age (not significant) and the presence of radiologic opacities (highly significant). This study confirms the interaction or synergistic effect of dust and smoking.

Summary

The mortality studies show a consistent excess of deaths from COPD and NMRD in granite workers. Results for lung function in relation to exposure vary. The Vermont papers conclude there is no significant decline in lung function. The study of Swedish granite crushers concludes that there is a moderate decline in lung function that is consistent with airway obstruction in the absence of silicosis (very few cases occurred in this study). In one of the Singapore studies no effect is found on lung function in the absence of small rounded opacities, with exposures being much higher for those with opacities than those without. In a Spanish study reduced lung function was associated with an interaction between smoking and dust exposure but not with the individual variables.

6.6 Iron, steel and foundry work

Nature of the industry and exposures

Workers in the iron and steel industry are exposed to a variety of gases, fumes and dusts that may adversely affect the respiratory system. The dusts are often potentially fibrogenic containing various levels of asbestos and/or crystalline silica. A general review of the literature of this industry was given in the previous review of chronic bronchitis and emphysema and occupational exposure [Rushton, 2005]. However, the contribution of exposure to silica to the occurrence of COPD as opposed to mixed exposures or exposures to gases and fumes was not specifically addressed in that review. The findings from key papers previously reviewed are given below together with details of any findings relating only to silica exposure.

Mortality Studies

The European Coal and Steel Community (ECCS) have over many years, carried out research on respiratory diseases among workers in the steel industry including prevalence of functional impairment and respiratory disease. Studies from the 1970s and 1980s suggest a high prevalence of symptoms of bronchitis in jobs classified as dusty and excess mortality from non-malignant respiratory disease, particularly pneumonia. A mortality study of 278 foundry workers found a statistically significant excess proportional mortality due to non-malignant respiratory disease (Standardised Proportional mortality ratio (SPMR) = 1.77), in particularly in among finishers (SPMR = 2.79) and in the core room (SPMR = 3.21) [Silverstein et al., 1986]. In this study the finishers were assumed to have substantial exposures to respirable silica dust, but also smaller exposures to metal dust and possibly polycyclic aromatic hydrocarbons. However, in this study none of the death certificates mentioned silicosis.

A significantly raised SMR of 1.53 (95% CI 1.41, 1.66) was found for non-malignant diseases of the respiratory system in a mortality study of UK steel foundry workers, with a positive dose-response trend by duration of employment. However, dust or fume exposure did not appear to be highly related to mortality [Sorahan et al., 1994]. In a study of approximately 3000 Danish foundry workers there was an extremely high risk of dying from pneumoconiosis (SMR = 73.68, 95% CI 40.29, 12.36) and a non significant excess from CBE (SMR = 1.32, 95% CI 0.98, 1.85) [Hansen, 1997].

In a study of workers in Norwegian ferroalloy plants mortality from CBE (including asthma) was raised in employees employed in ferrosilicon/silicon-metal plants (SMR = 1.24, 95% CI 0.93, 1.61) and particularly for the furnace workers in these plants who had worked for more than 3 years (SMR = 1.82, 95% CI 1.04, 2.95) [Hobbesland et al., 1997]. Dust measurements suggested that about 50% of the dust consisted of amorphous silica and 4-6% was crystalline silica. A Poisson regression analysis showed a significant increase of 0.06 per unit of amorphous silica exposure observed 10-20 years after the exposure.

A mortality and morbidity cohort study of foundry, metal product and electrical workers in Finland found excess mortality from respiratory diseases in the foundry workers compared to the Finnish national population (SMR = 1.52, 95% CI 1.08, 2.06) [Koskela, 1997].

Cross-sectional and longitudinal studies of COPD prevalence and lung function

In the Finnish study current foundry, workers had over twice the age standardised prevalence of chronic bronchitis (15%) than electrical workers (6%) regardless of their smoking habits. However chronic bronchitis was much more prevalent among smokers, particularly in former foundry workers.

As part of the ECSC research programme a study was carried out of the prevalence of chronic bronchitis and lung function impairment in iron and steel workers compared to a control group [Scotti et al., 1989]. The prevalence of chronic bronchitis was 38% in those exposed (worked) more than 19 years, 15% in those exposed less than 10 years and about 13% in new workers and the control group. The odds ratios, adjusted for age and smoking, compared to controls were 1.8 (95% CI 1.4, 2.4) for the new workers, 1.5 (95% CI 1.2, 1.9) for those exposed less than 10 years and 1.7 (95% CI 1.4, 2.16) for those exposed greater than 10 years. High prevalence and significant odds ratios were also found for obstructive syndrome in both exposed groups but there was no relationship with small airways impairment. Mean FVC, standardised for age, smoking and height was significantly reduced in both exposure groups compared with those newly hired and controls. However, standardised mean FEV_1 was only significantly reduced in those exposed for <10 years with the values of newly hired and exposed >10 years being the same. The authors

suggest that this is due to attrition with those exposed more than 10 years, with greater functional impairment leaving the industry

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In a study of 475 steel workers who had at least 3 spirometry tests over a 5 year period, aging, being overweight, excessive weight gain, smoking status and dust exposure were related to a lower level and a steeper slope of decline of pulmonary function [Wang et al., 1996]. Estimated loss at baseline of FEV_1, FVC and FEV_1/FVC% was 9.3, 64ml and 0.1% per year of employment in a dusty area, respectively. Of the 475, 121 were categorised as rapid decliners (an annual rate of decline in FEV_1 exceeding the 75% percentile of the slope distribution). The prevalence of pneumonia was significantly greater in the rapid decliners than the other workers.

In a related study by the same authors the influence of weight gain was further investigated in a subgroup of 541 male steel workers (95% white) with at least two valid spirometry tests between 1982 and 1991 and a follow-up interval of 4 or more years [Wang et al., 1997]. The average number of tests per worker was 4.5. Dust exposure estimates were derived from a detailed job history and dust levels for each job location. FEV_1 and FVC declined an average of 44 and 50 ml/year respectively overall, with results for current smokers, ex-smokers and non-smokers being 52 and 54 ml/year, 43 and 53 ml/year and 36 and 43 ml/year respectively. Increasing weight (also measured at each time of spirometry testing) was highly correlated with accelerated decline in lung function ($p < 0.0001$).

A matched analysis was also carried out for 75 pairs of steel workers matched by age, height, initial FEV_1 and smoking status, but whose FEV_1 declines differed by 60 ml//year. Workers with the greater annual FEV_1 decline were defined as rapid decliners. The mean regression slopes of FVC, FEV_1 and FEV_1 /FVC ratio were – 96 ml/year, -95 ml/year and –0.40%/year respectively for rapid decliners and +5ml/year, +10ml/year and +0.10%/year respectively for the comparison workers. On average the rapid decliners gained 4.3kg while the comparison workers gained 1.04kg over the follow up period. The authors suggest that weight gain may be relevant in understanding airways obstruction in rapid decliners in dust-exposed populations.

A total of 583 male workers in 50 iron foundries in Taiwan were investigated with regard to respiratory symptoms, lung function and radiographic changes [Kuo et al., 1999]. Total airborne dust concentrations were highest in the moulding area (5.96 mg/m^3) followed by the furnace (3.74 mg/m^3) and after-processing (1.61 mg/m^3). The average respirable dust concentration was 1.89 $mg.m^3$ for the moulding group, 2.76 mg/m^3 for the furnace group and 2.07 $mg.m^3$ for the after-processing group. Furnace workers were found to have the highest prevalence of chronic phlegm, thoracic disorders and chronic bronchitis. However over 60% of this group were smokers and in general smokers had a higher prevalence of respiratory symptoms than non-smokers. Pulmonary function abnormalities and pneumoconiosis were also closely linked to smoking habits. After adjusting for age, height and smoking there was a significant decrease in FVC and FEV_1 for furnace and moulding workers -9.74 ml/year and -9.29 ml/year respectively, compared with the after-processing (-3.12 ml/year and -3.04 respectively) and administrative workers (-2.59 ml/year and -3.46 ml/year respectively). The overall prevalence of pneumoconiosis was 8.8%, and was highest among furnace (16.3%) and after-processing workers (11.4%) and lowest among administrative workers (2.5%).

A more recent study of employees of US foundry included 1072 current and former hourly wage employees who had been employed before 1986[Hertzberg et al., 2002] and analysed annual lung function tests in relation to exposure to silica. 36 individuals with radiographic findings of parenchymal changes consistent with asbestosis (8) or silicosis (28) were excluded. Exposure measurements were found for 26 years of the 30 years covered by the study and were used to

calculate time-weighted average exposures for various jobs in the foundry. Employment in other foundries or silica-related industries was determined form personnel record and questionnaire. Cumulative exposure was calculated as the product of exposure intensity and duration at each job. Nearly 700 individuals had one or more tests for FEV_1 and 523 had one or more tests for FVC. There was no association overall between increasing cumulative exposure to silica and FEV_1 or FVC for non-smokers. In smokers, there was a statistically significant trend of an increasing percentage of individuals with a decreased FVC, decreasing percent-predicted FVC, and decreasing percent-predicted FEV_1 with increasing cumulative silica exposure. However, multiple regression models including cumulative silica exposure, pack years of cigarette smoking, ethnicity, age, height and exposure to silica at another height showed a significant relationship between decreasing lung function and increasing cumulative silica exposure. In addition, longitudinal analysis of FEV_1 and FVC, after adjusting for ethnicity and pack-years smoked, showed a decline of 1.1 ml/year and 1.6 ml/year respectively. The authors conclude that their results are consistent with the hypothesis that silica exposure is associated with restrictive lung disease as well as the occurrence of obstructive changes, although the latter only occurred with silica exposure in smokers.

Summary

The studies have consistently shown an increased risk from COPD in steel workers, although this has not always been doubled. A decline in FEV_1 has been found in several studies ranging from 1 to about 9-10 ml/year, after adjusting for smoking age and height, the latter in some of the studies associated with the dustiest jobs such as foundry work and moulding where silica is one of the main exposures. This would indicate that between 10 and 40 years work is required to give a loss of over 1 litre in FEV_1.

6.7 Diatomaceous Earth

Nature of the industry and exposures

There have been a series of papers reporting investigations of the relationship between respirable dust and crystalline silica exposure and silicosis and NMRD in the diatomaceous earth (DE) mining and process industry in California. DE is extracted by open pit or quarry mining. The raw material, containing mainly amorphous silica, is then crushed, dried and air classified to remove contaminants. Calcining then takes place and exposures to crystalline silica (mainly cristobalite) can occur; silica content of calcined DE ranges from 10 – 25%. DE is used as a filtration aid for water, foods and beverages, as a filler in construction materials, paints and insulation, and as a carrier or anticaking agent for agricultural chemicals.

Mortality studies

A mortality study of 2570 workers employed for at least one year overall and at least one day between 1942 and 1987 found a slightly increased all cause SMR or 1.12 (95% CI 1.03, 1.21) using the US white male population as a comparison[Checkoway et al., 1993]. There was a statistically significant excess from lung cancer (SMR 1.43, 95% CI 1.09, 1.84) and NMRD (excluding infectious diseases and pneumonia) (SMR 2.59, 95% CI 1.96, 3.3.6). A semi-quantitative index of crystalline silica exposure was derived by combining information on duration of exposure, differences in exposure intensity between jobs and calendar periods, the crystalline content of the various product mixes and the use of respiratory protection devices. Poisson regression modelling, adjusting for age, calendar year, duration of follow up and ethnicity), showed a weak trend for increased risk of NMRD with increasing duration of employment but a clear monotonic increase with respect to cumulative crystalline silica index (cumulative intensity x year) (< 50 RR 1.00; 50 – 99 RR 1.29, 95% CI 0.52, 3.22; 100 – 199 RR

2.19, 95% CI 1.00, 4.79; >200 RR 2.91, 95% CI 1.41, 6.00). Workers who had possible previous exposure to asbestos in any early DE and asbestos mining operation were omitted from this analysis. However, there was no adjustment for smoking as this information was limited.

A follow up to 1997 and quantitative dose-response analysis of this cohort included 2343 white males (317 workers from a small plant were excluded because of inadequate exposure data and 89 previously excluded workers were included as quantitation of their asbestos exposures was now possible)[Checkoway et al., 1997]. Exposure assessment was carried out using job specific monitoring data for exposure intensities and associated duration of in jobs obtained from work histories. Excess mortality was again found for NMRD (SMR 2.01, 95% CI 1.56, 2.55) and lung cancer (SMR 1.29, 95% CI). There were strong mortality gradients for NMRD with respect to cumulative exposure to respirable dust and especially to respirable crystalline silica, adjusted for age, calendar year, duration of follow-up and ethnicity; cumulative exposure mg/m^3.years <0.05 RR 1.00; 0.5 - < 1.1 RR 1.52, 95% CI 0.55, 4.20; 1.1 - <2.1 RR 1.98, 95% CI 0.75, 5.22; 2.1 - <5.00 RR 2.24, 95% CI 0.91, 6.0; ≥ 5.0 RR 4.79, 95% CI 2.01, 11.9. Smoking data were available for 50% of the cohort. Using this and assuming a 20-fold increased risk for NMRD related to smoking, the rate ratios for NMRD mortality lagged for 15 years were estimated to decrease from 4.79 to 2.62 for the highest exposure of respirable dust and from 5.35 to 4.15 for the highest exposure strata of crystalline silica. These results are in line with those of the risk estimates of 2.5 – 9.00 found in the most heavily exposed segments of the US crushed stone industry, Italian brick workers and South African and US gold miners.

A related paper reports radiographic findings in relations to crystalline silica exposure[Hughes et al., 1998]. On the basis of the median of three independent readings, 81 (45%) workers were judged to have opacities on chest radiographs (small opacities, profusion ≥ 1/0, and/or large opacities). Age-adjusted relative risk of opacities increased significantly with cumulative exposure to crystalline silica: cumulative exposure mg/m^3.year ≤ 1 RR 1.00; >1 - ≤3 RR 4.35, 95% CI 1.7, 11.06; >3 - ≤6 RR 20.13, 95% CI 8.2, 49.7; >6 RR 40.37, 95% CI 16.1, 101.3. The concentration of respirable silica to which workers were exposed was highly correlated with period of hire and was an important determinant of risk after accounting for cumulative exposure. For workers with an average exposure to crystalline silica of ≤0.50 mg/m^3 (or hired ≥ 1950), the cumulative risk of opacities for a cumulative exposure to crystalline silica of 2.0 mg/m3.year was approximately 1.1%; for an average exposure >0.50 mg/m^3 (or hired < 1950), the corresponding cumulative risk was 3.7%. The authors suggest that these findings indicate an exposure-response relationship between cumulative exposure to crystalline silica and radiographic opacities; in addition the relationship is substantially steeper among workers exposed at the highest average concentrations of crystalline silica.

A more recent related paper explores the use of various models (including log linear, log quadratic, log square root, linear relative rate etc) of exposure-response in order to estimate excess lifetime risk for different exposures [Park et al., 2002]. Because there were no deaths for NMRD with cumulative exposure > 3.2 mg/m^3.years the exposure-response diminished at high cumulative exposures. A similar finding occurred for models with presence and severity of radiographic silicosis. The authors suggest this may indicate some form of survivor selection. Refitting the models excluding observation time with cumulative exposure >10 mg/m^3.years (corresponding to 45 years of exposures at 4 times the PEL of 0.05 mg/m^3), the best fitting, linear relative rate model predicted a RR of 4.2 after adjusting for smoking at the mean cumulative exposure experienced by the NMRD cases (5.8 mg/m^3.years). The excess lifetime risk for white men exposed to respirable cristobalite dust for 45 years at the PEL was 54/1000 (95% CI 17, 150), i.e. 54 out of 1000 workers would die from silica related NMRD when exposed to respirable crystalline silica for their working life at the PEL. At a higher concentration of 0.20

mg/m^3 the excess lifetime risk was 140/1000 for all workers and 190/1000 i.e. nearly 20% if the highest cumulative exposures were excluded.

The authors conclude that current occupational health standards in the US for crystalline silica do not prevent a considerable amount of respiratory ill health.

Summary
The DE studies confirm the association between exposure to silica containing dust and increased risk of silicosis and NMRD and have quantified the exposure-response relationship. Risks are clearly doubled and a relative risk of over 4 is found for exposures at the PEL level of 0.05 mg/m^3 experienced for 45 years (after adjusting for smoking).

6.8 Gold mining

Although the UK does not have a large gold mining industry, there have been many studies of gold miners in the US and South Africa investigating the relationship between exposure to silica and the development of silicosis and deterioration of lung function.

Mortality studies
Mortality studies have consistently shown increased mortality from silicosis and NMRD. For example, in a study of 3328 gold miners who had worked underground for at least 1 year between 1940 and 1965 in South Dakota and followed up to 1990, the SMR for lung cancer was 1.13 (95% CI 0.94, 1.36, for pneumoconioses the SMR was 2.61 (95% CI 1.09, 5.61) and for NMRD overall was 1.86 (95% CI 1.58, 2.16)[Steenland and Brown, 1995a]. The levels of exposure to crystalline silica in this cohort were high, particularly before 1950 when exposure was approximately 10-30 mppcf (millions of particles per cubic foot), with the dust composed of about 13% free silica; exposures were under 10 mppcf after 1950.

In a related paper reporting nested case-control study of the 170 cases of silicosis, the overall risk of silicosis was found to be <1% with a cumulative silica exposure of <0.5 mg/m^3.years increasing to 84% for the cumulative exposure > 4 mg/m^3.years [Steenland and Brown, 1995b]. The authors conclude that, after adjusting for competing risks of death, a 45 year exposure at the OSHA standard of 0.09 mg/m^3 would lead to a lifetime risk of silicosis of 35 - 47%.

There have been many papers written by Eva Hnizdo investigating COPD mortality and morbidity in South African gold miners. A review published in 1992 of the evidence relating to the mortality of 2209 white gold miners who were studied in 1968-1970 for respiratory impairment and followed up to 1986 for mortality [Hnizdo, 1992a]. Those with the most marked obstructive profile with restriction in 1968 had the lowest survival rate and the survival was worst in smokers. Although miners in the lowest dust quartile had the highest survival, there was no difference in survival patterns for the other three quartiles.

Cross-sectional and longitudinal studies of COPD prevalence and lung function
Another paper by Hnizdo investigated the evidence for decline in FEV_1 (standardised to a height of 173cm)[Hnizdo, 1992b]. From linear regression, a 50 year old gold miner exposed for 24 years to an average respirable dust level of 0.30 mg/m^3 (14.4 gh/m^3) would lose, on average, 236 ml (85% CI 136, 337) due to the effect of dust. In comparison the loss of FEV_1 attributable to being a current smoker for a 50 year old miner with a smoking history of 1 pack per day for 30 years was 552 ml (95% CI 461-664). Statistical tests showed that the effects of silica dust and smoking on loss of FEV_1 were additive.

A 5 year follow-up study of 242 South African gold miners investigated the progression of lung dysfunction in those with (78 with category 1 nodule profusion, 73 with category 2, 32 with category 3) and without (59) an initial diagnosis of silicosis [Cowie, 1998]. Radiological features of silicosis had progressed on average on one subcategory in the follow-up period. FEV_1 had deteriorated more rapidly in the men with silicosis (57ml in category 1, 100 ml with category 2, 128 ml with category 3) than those with out initial silicosis (37ml). These changes remained significant after controlling for age, original lung function and smoking.

Summary

The studies of gold miners confirm the association of exposure to silica and the development of silicosis. However, levels of exposure are much higher than those experienced in other industries and the studies are thus limited in their ability to investigate loss of lung function in the absence of silicosis.

6.9 Slate workers

Nature of the industry and exposures

Slate rock originates from sedimentary marine deposits that have been moulded by pressure and heat over many years. The capacity to fissure along cleavage planes has led to its importance industrially. In north Norway the silica content of the slate is 60-70% and after processing up to 83%[Bang and Suhr, 1998]. In North Wales the slate contains 30-40% quartz [McConnochie et al., 1988]. In Norway the average concentration of total quartz in the slate factory was 0.27 mg/m^3 and the average concentration of respirable quartz was 0.12 mg/m^3. Outdoors in the quarries the average levels were 0.58 and 0.13 mg/m^3 for total and respirable quartz respectively.

Mortality studies

In North Wales a cohort of 726 slate workers and 529 controls was established in 1975 and followed up for mortality to 1998 [Campbell et al., 2005]. A survey in 1975 of the cohort collected information on smoking history, dust exposure history, pneumoconiosis grade and lung function. The hazard ratio (HR) for all mortality for slate exposure (relative risk compared with controls) was 1.17 (95% CI 0.99, 1.38). This reduced very slightly when adjusted for smoking habit and FEV_1 in 1975 (adjusted for age and height). The latter was itself a highly significant predictor of mortality. On average, slate workers had a mean FEV_1 of 0.151 lower compared with controls ($p<0.001$) adjusted for age and height. In the slate workers increased pneumoconiosis score in 1975 was a strong predictor for mortality (controls were not graded for pneumoconiosis). There was a suggestion of a relationship between lung cancer and slate work, adjusted for smoking, and clear evidence of a link with NMRD (which include pneumoconiosis), with both slate work and smoking being highly significant predictors of NMRD.

Cross-sectional and longitudinal studies of COPD prevalence and lung function

A study of 108 slate workers and 127 controls were studied in Norway for lung function and prevalence of respiratory symptoms [Suhr et al., 2003]. There were significantly more smokers among slate workers than controls. The slate workers had a significantly higher occurrence of many respiratory symptoms, including: respiratory symptoms at work than controls (30.9% versus 11.9%, OR 3.08, 95% CI 1.54, 6.17); cough with phlegm (38.0% versus 17.5%, OR 2.69 95% CI 1.44, 5.04)); breathlessness walking uphill (28.2% versus 11.5, OR 2.74, 95% CI 1.34, 5.63); breathlessness walking on level ground (7.6% versus 2.4%, OR 3.11 95% CI 0.76, 12.72); all ORs adjusted for smoking. PEF was significantly lower among slate workers than controls (figures not given). The prevalence of silicosis was 1.9% or 6.5% depending on the interpretation

of two radiologists. No significant difference was found between the groups regarding the occurrence of COPD.

Summary

There is clear evidence of a relationship between exposure to slate dust, which contains a high percentage of silica, and increased respiratory symptoms and mortality, particularly from silicosis. The available studies are small however, with none reporting longitudinal results for lung function.

7. Discussion and conclusions

There is a considerable literature on the relationship between exposure to silica and the adverse effects on respiratory health. No attempt has been made here to carry out a formal systematic review of this literature. The review has, instead, focused on those papers that address the key issues regarding prescription for benefits, including:

- Estimation of the magnitude of the risk relating to occupational circumstances
- Assessment of the exposures necessary for development and severity of the disease
- Evaluating evidence regarding the relationship between silica exposure and the development of silicosis and COPD.

The studies reviewed for this report may have one or more of the general limitations inherent in epidemiological studies including loss to follow-up, healthy survivor and selection biases, inconsistencies in the diagnosis of COPD and definition of a case and inadequate or limited exposure estimation. Nevertheless the evidence from mortality studies and cross-sectional studies of respiratory symptoms suggests that there are consistent associations between the risk of COPD and all the occupations reviewed. Although risk estimates and prevalence rates vary, several show more than a doubling of risk, even after taking into account the effect of smoking.

In some of the occupations, for example tunnel working, in addition to concurrent exposure to cigarette smoke (direct or second hand) exposures to other work-place irritants (sometimes multiple) such as gases and fumes may occur. Factors influencing the variation from industry to industry in risks associated with exposure to silica-containing dusts include: the presence of other minerals in the dust, particularly when it is associated with clay minerals (Love 1999); the size of the particles and percentage of quartz; the physicochemical characteristics such as whether the dust is freshly fractured or not.

Average levels of total and respirable dust and crystalline silica vary between the studies and between industries as do the cumulative exposure levels. Average dust levels vary from about 0.5 mg/m^3 to over 10 mg/m^3 and average silica levels from 0.04 to over 5 mg/m^3. Levels reported in the studies are often well above any of the currents occupational standards, for example the UK MEL of 0.3 mg/m^3 and guidance OEL of 0.1 mg/m^3.

In the UK there are a considerable number of workers exposed to silica containing dusts. Table 1 gives the numbers of workers exposed to crystalline silica by industry according to Carex for 1990-1993. [The **CAREX** database is an international information system on occupational exposure to 139 known and suspected carcinogens evaluated by IARC (all agents in Groups 1 and 2A, and selected agents in Group 2B) (Kauppinen et al. 1998). Estimates were generated by the CAREX system on the basis of national workforce data and exposure prevalence estimates from two reference countries (Finland and USA). These estimates were then adjusted for the economic structure (workforce distribution) of each country individually, but did not take into account country-specific exposure patterns that may have been different from those of the reference countries. For selected countries, these estimates were further refined by national experts in view of the similarity/dissimilarity to the perceived exposure patterns in their own countries, for the UK this was carried out by Pannett et al (1998).]

Table 1 Numbers of workers exposed to silica according to Carex in 1990-1993

Industry	Carex Data 1990-1993	
	Number Exposed	Number in Industry
Crude petroleum and natural gas production	1670	53300
Metal ore mining	1161	1225
Other mining	16240	28150
Food manufacturing	360	414150
Beverage industries	24	88100
Tobacco manufacture	1	9950
Manufacture of textiles	338	182000
Manufacture of wearing apparel, except footwear	494	189500
Manufacture of leather and products of leather or of its substitutes	158	16825
Manufacture of footwear	100	38500
Manufacture of furniture and fixture, except primary of metal	398	144325
Printing, publishing and allied industries	756	354750
Manufacture of industrial chemicals	618	130000
Manufacture of other chemical products	5662	175175
Petroleum refineries	114	18075
Manufacture of miscellaneous products of petroleum and coal	290	1125
Manufacture of rubber products	703	53025
Manufacture of plastic products nec	1750	136900
Manufacture of pottery, china and earthenware	21769	54450
Manufacture of glass and glass products	6932	43275
Manufacture of other non-metallic mineral products	24406	70875
Iron and steel basic industries	3853	48425
Non-ferrous metal basic industries	2406	79325
Manufacture of fabricated metal products, except machinery and equipment	8002	292200
Manufacture of machinery except electrical	16253	692275
Manufacture of transport equipment	6420	456900
Manufacture of instruments, photographic and optical goods	1567	86225
Other manufacturing industries	1316	59375
Electricity, gas and steam	3382	140975
Construction	449930	1753450
Land transport	5123	671050
Water transport	1193	68175
Air transport	702	95700
Services allied to transport	588	180725
Sanitary and similar services	3760	274225
Education services	610	1455875
Research and scientific institutes	880	91100
Total	589929	

In the studies reviewed, a consistent finding is that, although smoking tends to decrease average values of lung function measurements, many studies do not show a significant different between smokers and non-smokers in the decline in, say FEV_1, with exposure to silica. A welcome aspect of the majority of the studies reviewed is the adjustment of smoking in the analyses.

Malmberg et al (1993) draw attention to the poor correlation between changes in lung function and chest radiographic changes indicating silicosis. In highly exposed populations, such as the South African gold miners where there is a relatively high occurrence of silicosis, those without silicosis appear to have a high risk of obstructive airway changes. Malmberg et al (1993) and Hnizdo and Vallyathan (2003) suggest that emphysema and airway obstruction in subjects exposed to silica seem to be independent of silicosis, and that silica exposure may cause obstructive lung function changes at lower concentrations and possible shorter latency time than is required for the induction of silicosis. However, once silicosis has developed lung function decreases more rapidly.

The results from the studies reviewed in this report tend to support this. In the Tanzanian cement workers study (Mwaiselage 2004) a decline of 1.7 ml/mg/m3 per year was estimated after adjusting for age, height and pack years; exposure for 30 years at 10 mg/m^3 (a very high exposure) was estimated to lead to a 500ml decline. Silicosis was not mentioned in this study. Two studies of Norwegian tunnel workers gave different estimates: 17ml for each year of tunnel work (Ulverstad 2000); 4.3ml/year (Humerfelt 1998). Silicosis prevalence was again not mentioned. However, in smaller follow-up study by Ulverstad (2001) where none of the tunnel workers had radiographic signs of pneumoconiosis it was estimated that an annual decline of FEV_1 corresponding to that predicted for a non smoking worker aged 40 years would be 50ml for tunnel drilling and 63ml for shotcreting, both jobs that incur high dust exposure. It should be noted that tunnel workers may be exposed simultaneously to dust, gases and fumes. In South African gold miners where silicosis prevalence is high an annual decline in FEV_1 of 9ml was estimated. In the Vermont granite workers in which silicosis cases occur, the estimates of lung function have varied as follow-up of the cohort has progressed from 50-70ml loss in FEV_1 (Musk 1997) to 0.03ml (Graham 1994). In the iron and steel industry FEV_1 decline was 43ml/year overall and 52, 43 and 36 ml/year for current, ex-smokers and non-smokers respectively (Wang 1997). In Taiwanese foundry where the overall prevalence of silicosis was 9% there was a decline in FEV_1 of 9.3ml/year for moulding work and 9.7 ml/year for furnace work, adjusting for age, height and smoking (Kuo 1999). In a US foundry study where silicosis cases were excluded a decline of 1.1 ml/year was estimated, adjusting for ethnicity and smoking (Hertzberg 2002). In the gold mining industry Hnizdo 1992 estimated that a 50 year old gold miner exposed for 24 years to $0.30mg/m^3$ would lose on average 236 ml i.e. about 10ml per year. Cowie (1998) in a 5 year follow-up of gold miners found losses of 57 ml for those with category 1 silicosis at the start of follow up, 100 ml for category 2, 128 for category 3 and 37ml for those with no initial silicosis (controlling for age, original lung function and smoking). The latter implies an annual loss of about 7.5ml.

These results suggest that the annual loss of FEV_1 associated with exposure to silica varies between under 1ml to over 100ml depending on smoking status and presence of silicosis. In the absence of silicosis loss due to silica exposure appears to be about <10 ml per year. This indicates that a disabling loss of lung function of 1 litre would take at least 10 years if the same rate of lung

function decline persisted and some of the studies indicate loss that would take over 20 years. There are unfortunately no very long term follow-up studies to address the latter issue.

Conclusions

A large number of workers are currently potentially exposed to silica within the UK although levels of exposure are known to have declined over recent decades in many industries. Epidemiological studies show a consistent significantly increased mortality risk and prevalence of respiratory symptoms in relation to silica exposure across many industries including construction, firebrick manufacture, pottery, granite quarrying and processing and foundry work. The evidence from studies where radiological silicosis was absent suggest that loss of lung function occurs with exposure to silica dust and that the effect of cumulative silica dust exposure on airflow obstruction is independent of silicosis. Silica dust concentrations of between 0.1 and 0.2 mg/m^3 can cause this loss of lung function. Excess loss of lung function appears to be less than 10 ml/year in the absence of silicosis. Assuming a consistent rate of lung function loss, disabling loss of 1 litre or more would take at least 10 years to occur, although estimates from some of the studies would imply a longer period of 20 years or more.

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Appendix 1

Current terms of prescription for Prescribed Disease D12

Disease number	Name of Disease or Injury	Type of Job Any job involving
D12	Chronic bronchitis and emphysema; or both where, with maximum effort, where there is accompanying evidence of a forced expiratory volume in one second which is: (i) at least one litre below the appropriate mean value predicted, obtained from the following prediction formulae which give the mean values predicted in litres: • For a man, where the measuremen is made without back-extrapolation, (3.62 x Height in metres) minus (0.031 x Age in years) minus 1.41; or, where the measurement is made with back-extrapolation, (3.71 x Height in metres) minus (0.032 x Age in years) minus 1.44 • For a woman, where the measurement is made without back-extrapolation, (3.29 x Height in metres) minus (0.029 x Age in years) minus 1.42; or, where the measurement is made with back-extrapolation, (3.37 x Height in metres) minus (0.030 x Age in years) minus 1.46 (b) **or** less than one litre.	Exposure to coal dust by reason of working underground in a coal mine for a period or periods amounting in the aggregate to at least 20 years (whether before or after 5 July 1948) and any such period or periods shall include a period or periods of incapacity while engaged in such an occupation.