Respirable quartz dust exposure and airway obstruction: a systematic review and meta-analysis

Irene Brüske,[1] Elisabeth Thiering,[1] Joachim Heinrich,[1] Katharina M Huster,[2] Dennis Nowak[2,3]

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[1]Helmholtz Zentrum München, German Research Center for Environmental Health, Institute of Epidemiology I, Neuherberg, Germany
[2]Ludwig-Maximilians-University, Institute and Outpatient Clinic for Occupational, Social and Environmental Medicine, Inner City Clinic, University Hospital of Munich, Munich, Germany
[3]DZL Munich, Member of the German Center for Lung Research (DZL), Munich, Germany

Correspondence to
Dr Irene Brüske, Institute of Epidemiology I, Helmholtz Zentrum München, German Research Center for Environmental Health, Ingolstädter Landstraße 1, Neuherberg 85764, Germany; brueske@helmholtz-muenchen.de

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ABSTRACT
Studies on exposure to respirable quartz dust at the workplace and the development of chronic obstructive pulmonary disease (COPD) were selected into a systematic review and meta-analysed to obtain an overall estimate of forced expiratory volume in 1 s (FEV_1) and FEV_1/forced vital capacity (FVC) reduction. PubMed and Embase were searched from 1970 to 2010. In total, 257 cross-sectional and longitudinal studies were identified that reported on inorganic dust exposure and had available lung function data. Of the 55 publications which met our inclusion criteria, 11 reported on associations with occupational exposure to respirable quartz dust. The combined average effect estimate of respirable quartz dust on spirometric parameters was obtained using a random effects model meta-analysis. Between-study heterogeneity was assessed via the I^2 statistic. Most studies found a significant negative association of FEV_1 and FEV_1/FVC related to increasing exposure to crystalline quartz at the workplace. One study found an effect only for smokers, and one did not observe such an effect at all. The meta-analysis of cross-sectional studies showed that the mean ratio FEV_1 to FVC was reduced and FEV_1 of workers exposed to respirable quartz dust was 4.6% less than predicted compared with workers with no/low exposure. Both results showed a statistically significant difference. Occupational exposure to respirable quartz dust was associated with a statistically significant decrease in FEV_1 and FEV_1/FVC, revealing airway obstruction consistent with COPD.

BACKGROUND
Chronic obstructive pulmonary disease (COPD) is a common disease. Although smoking is a known risk factor for COPD, several other risk factors are believed to substantially contribute to the burden of this disease. Community-based studies from China,[1] France,[2] Italy,[3 4] New Zealand,[5] Norway,[6] Spain[7 8] and the USA[9–13] have reported that occupational exposure to vapour, dusts, gases and fumes increases the risk of airway obstruction consistent with COPD. The population-attributable risk of COPD from occupational exposure is estimated to be between 15% and 20%.[14]

Recently, we conducted a systematic review and meta-analysis to quantitatively evaluate the association between occupational exposure to poorly soluble low-toxicity particles, also referred to as biopersistent granular (bg) dust,[15] and the development of COPD.[16] Based on data from cross-sectional studies, we found that the mean forced expiratory volume in 1 s (FEV_1) of workers exposed to bg dust was 160 mL lower or 5.7% less than predicted compared with that of workers with no/low exposure. The risk of airway obstruction, defined as FEV_1/forced vital capacity (FVC) <70%, increased by 7% per 1 mg/m^3 cumulative bg dust exposure. In the longitudinal analysis, there was a consistent decline of FEV_1 by 1.6 mL (95% CI 1.24 to 1.93 mL) per 1 mg/m^3 years bg dust.

The inhalation of respirable quartz dust may be even more detrimental to health than the inhalation of bg dust. Particles deposited in the alveolar space get phagocytosed and removed from the lung tissue to the lymph system. If the phagocytosed particles contain crystalline quartz, macrophage death will occur leading to the promotion of inflammatory cell egress and connective tissue growth finally resulting in silicosis. However, the correlation between signs of silicosis in chest X-rays and the impairment of lung function is only weak.[17] In a highly exposed study population of South African gold miners, most (68%) participants developed signs of chronic airway obstruction but only a few (1.4%) showed signs of silicosis.[18 19]

This study aimed at a quantitative approach to evaluate the extent of obstructive lung function impairment induced by respirable quartz dust at the workplace.

MATERIALS AND METHODS
Following the PICOS criteria, the *P*articipants, *I*ntervention, *C*omparison, *O*utcome, and *S*tudy Design were defined a priori.[20 21] As part of our initial search, all epidemiological studies (cohort, case-control and cross-sectional) written in English or German that examined respirable quartz dust at the workplace (and included exposure level measurements) in relation to spirometric measurements of lung function were identified.

Studies had to be published in PubMed applying Medline (Medical Literature Analysis and Retrieval System Online) or in Embase (Excerpta Medica Database) between 1970 and 2010. A non-systematic search for grey literature, abstracts and so on yielded no additional studies with data that could be used in the meta-analysis. The following MeSH terms were used: 'occupational exposure' OR 'air pollutants, occupational' AND 'pulmonary disease, chronic obstructive' supplemented by the text fields 'respiratory function tests' OR 'respiratory function' OR 'lung function' OR 'pulmonary function'. The results of the search are available online (http://www.ncbi.nlm.nih.gov/sites/myncbi/collections/public/1ZWv6xXSbB7btnaSyJhbNPU5E/). Eligible articles were reviewed by two investigators (IB, KH), and both independently extracted the following information: first author and year of publication; study region and industry; study type; time and duration of the study or duration of the follow-up in cohort studies; number of exposed/unexposed subjects or cases and controls; sex and age distribution of the study population; response rate; exposure assessment (interview, job-exposure matrix (JEM), type of dust measurement and average exposure to inhalable or respirable dust); and outcome assessment (symptoms/physician diagnosis, spirometry and applied procedure for lung function measurements). Based on a common protocol, both reviewers (IB, KH) assessed the validity of the study; a third reviewer (DN) was used in cases of discrepancies between the opinions of the main two reviewers. The inclusion criteria for the systematic review and meta-analysis were the following: (1) transparent procedure for the selection of study participants, no indication of selection bias; (2) response rate >70% and <100%: studies which provided no response rate, or which had a response rate of 100% likely attributable to a post hoc definition of the study population, were excluded; (3) internal comparison with no/low exposed controls from the same company, or controls from a different company with no exposure; (4) individual present or cumulative exposure preferably based on dust measurements (JEM was considered acceptable; company or questionnaire information was accepted only if the duration of exposure was also provided); (5) COPD diagnosis according to the GOLD criteria (FEV_1 <70%) or physician-diagnosed COPD, or obstructive signs in spirometry (questionnaire-derived symptom reports were considered insufficient); and (6) standardised pulmonary function test according to the ATS/ERS criteria at the time of the study.[22–24]

STATISTICAL ANALYSIS

We conducted a random effects meta-analysis and obtained an estimate of the average exposure effect across studies, as we assumed that the true effect of respirable quartz dust on health may differ by study. Between-study heterogeneity was assessed using the I^2 statistic and results are presented as part of the forest plots. According to the Cochrane handbook for systematic reviews of interventions (available from: http://www.cochrane-handbook.org), I^2 values of up to 40% might be interpreted as unimportant, 30% –60% as moderate, 50%–90% as substantial and 75%–100% as considerable heterogeneity. Publication bias was investigated by visual inspection of funnel plots. The results of the meta-analysis on lung function parameters assessed from cross-sectional and longitudinal analyses are presented in forest plots. The influence of individual studies was assessed by examining the results after excluding apparently influential studies from the meta-analysis.

Our primary outcomes were a reduced FEV_1 and FEV_1/FVC, which are the most important signs of airway obstruction. These parameters were measured in most studies. We defined these outcomes as the difference between the mean of FEV_1 and FEV_1/FVC among exposed study participants versus not/low exposed participants. Most studies used an internal comparison group of low exposed workers; a few had an external not exposed group of referents. Across studies, FEV_1 was measured in either litres or % predicted. FEV_1% predicted is defined as the FEV_1 of the patient divided by the average FEV_1 in the population for any person of similar age, height, sex and ethnicity. To combine both units (litres) and (% predicted), we calculated the standardised mean difference (SMD), which is the difference of the mean FEV_1 of exposed and low/not exposed study participants divided by the common SD. This measure is dimensionless. The FEV_1 to FVC ratio was also calculated differently across studies; either as a ratio in litre or in % predicted, or as a ratio of two predicted values. In the meta-analysis, the SMD of the ratio was the only common estimate of FEV_1/FVC used. Studies either adjusted for or stratified by smoking status. In the latter case, the results for smokers and non-smokers were maintained separately upon inclusion into the meta-analysis.

A systematic exclusion of each study in turn to assess its influence was done by using the metafor package in R and the suggested cut-offs.[25]

RESULTS

In total, 2012 publications were identified in PubMed and 3604 publications in Embase. After excluding duplicates, 3792 publications were deemed eligible. The title and abstract of all eligible papers were screened by two investigators (IB, DN). For details of the selection process see figure 1.

In all, 257 publications were eligible and reviewed with data abstraction. A total of 246 publications did not fulfil the inclusion criteria for the systematic review and meta-analysis. Ten publications[17 26–34] investigated the effects of occupational exposure to dust containing crystalline quartz and presented quantitative data on dust and lung function measurements. These studies are described in the review below.

REVIEW OF THE 10 STUDIES CONSIDERED FOR META-ANALYSIS GROUPED ACCORDING TO INDUSTRY

Granite quarry workers were investigated in Vermont, USA,[31] Sweden[17] and Spain[32] with inconsistent results. A cohort study from Vermont, USA,[31] consisted of 1216 men actively employed in the granite sheds. Yearly spirometries were carried out. In 1974, 668 subjects of the original group[35] had been studied for 4 years. Compared with the age-related decline in pulmonary

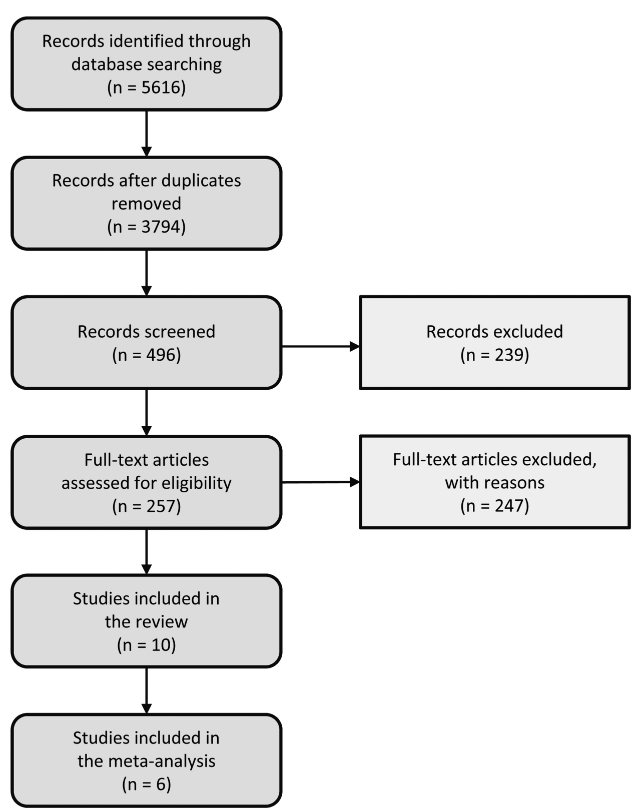

Figure 1 Flow diagram for inclusion and exclusion of studies (according to PRISMA).

function parameters of healthy subjects taken from the literature the mean yearly decrement of granite workers was judged as excessive: 50–70 mL loss of FEV_1 (70–80 mL loss of FVC, respectively). Decrements were higher for study participants in the high exposure (≥0.5 mg/m^3) respirable dust category compared with those in the low (<0.5 mg/m^3) category both with about 10% of crystalline quartz. An effect of smoking was apparent in the data, but the level of FVC found in the cohort of non-smoking workers was below the predicted level for non-smoking not exposed subjects. The authors concluded that the excessive overall decline in FEV_1 and FVC at two to three times the normal rate was due to occupation. These results were later put into question by a re-evaluation of the longitudinal pulmonary function data in the same industrial setting over an 8-year period from 1979 to 1987.[27] Estimates of longitudinal loss were based on 711 workers with a mean age of 43 years and a mean duration of employment of 19 years. Workers participated at least in three of the surveys. The mean respirable dust concentration at the workplace was 0.6 mg/m^3 with a content of about 10% quartz. The average annual loss was 18 mL for FVC and 30 mL for FEV_1. After adjusting for age, height and smoking status, the losses of both FVC and FEV_1 were not correlated with years employed in the granite industry. One explanation for this discrepancy could be that FVC in the original study by Musk *et al*[31] was not measured accurately because of short expiratory times[36] resulting in an underestimation of the true FVC. On the other hand Eisen *et al*[37] could show that the study by Graham *et al*[27] was hampered by selection bias due to subjects lost to follow-up (dropouts). Whereas the 353 survivors included in the study were losing FEV_1 at an average rate of 44 mL/year, the 265 'dropouts' were losing FEV_1 at an average rate of 69 mL/year and were closer to the original study results.[31] The dose–response parameter in this group was estimated to be 4 mL/year loss per mg/m^3-year and was statistically significant. Both studies were not part of the meta-analysis, as spirometric parameters FEV_1 and FVC were not adjusted for covariates (eg, height, age).

In all, 45 granite crushers from Sweden and the same number of age and smoking matched control subjects could be examined by lung function tests twice in 1976 and 1988.[17] In 1988, the granite crushers had on average worked for 22 years and inhaled a cumulated amount of 136 mg of dust with 7 mg of silica in the respirable fraction. Over the 12 years, the changes in lung function were moderate but consistent with an average reduction of FEV_1 3.2% greater among the exposed group compared with the referent group ($p<0.01$). Five granite crushers and none of the referents had an FEV_1 less than 80% of predicted and the granite crushers reported more often symptoms of dyspnoea and wheeze than the referents. The change in lung function did not correlate significantly with the inhaled dose of respirable quartz in the granite crushers or with age or different smoking habits.

A cross-sectional study from Spain in 2004/2005 also investigated dust exposure and its effect on lung function in granite workers.[32] Overall, 490 active workers employed at least 1 year in their job were invited to participate. A total of 440 men took part with a mean age of 37 and on average 13 years of exposure. The respirable quartz dust fraction was 0.32 mg/m^3, higher for drillers 0.41 mg/m^3 and lower manual labourers 0.27 mg/m^3. Cumulative exposure (mg/m^3·years) was estimated with a JEM. In all, 77 workers (17.5%) had silicosis. Acceptable spirometries were available for 438 workers. The results of the linear regression analysis show a significant negative relation of % predicted FEV_1 with age, cumulative respirable quartz dust exposure and silicosis, controlling for pack-years. The study could not be included in the meta-analysis as present silicosis was part of the linear regression model. Adjusting for silicosis implies taking in part away the effect of highly exposed workers.

Exposure to diatomaceous earth with low crystalline quartz dust content is rarely reported to cause pneumoconiotic disease, whereas an association with airflow decrements is well established.[38] A cross-sectional study from the Netherlands[29] investigated the respiratory health of 175 male potato sorters from five plants. Mean respirable dust exposure was 2.21 mg/m^3 and the mean respirable quartz dust exposure was 0.27 mg/m^3 exceeding the Dutch standard of 0.15 mg/m^3. The effect of exposure on lung function was analysed by multiple regression analysis after adjustment for age, height and smoking. Only FEV_1 differed significantly between currently exposed workers and controls. The decrease in FEV_1 was found to be 124 mL after 11.8 years of employment.

Another cross-sectional study from the Netherlands[30] examined the ventilatory effects of exposure to low levels of concrete dust containing respirable quartz dust. The study population consisted of 144 male concrete workers and a control group of 110 male workers of an office equipment-producing factory. In total, 96 personal respirable dust samples were taken. The overall respirable dust concentration was 0.77 mg/m^3 and the average respirable quartz dust concentration was 0.059 mg/m^3. Workers exposed to respirable quartz dust showed a statistically significant lower FEV_1 to FVC ratio below the 5% percentile of the reference population.

Hertzberg *et al*[28] evaluated cross-sectionally and longitudinally pulmonary function tests in a cohort of employees of a Midwest automotive foundry in the USA. The cohort consisted of current as well as former 1072 workers employed before 1986. There were 1028 individuals without evidence of parenchymal changes from exposure to asbestos or respirable quartz dust. Spirometric data were available for 815 individuals who were either white or African-Americans. In all, 696 (523) individuals had one or more tests for which two or more efforts were adjudged to be acceptable and reproducible for FEV_1 (FVC) and who had smoking status and exposure level known. Analysis of spirometric data showed decreasing % predicted FVC and FEV_1 and decreasing FEV_1/FVC in relationship to increasing respirable quartz dust exposure only among smokers. Logistic regression analyses of abnormal FVC and abnormal FEV_1 values (where abnormal is defined as <95% confidence limit of predicted) showed ORs of 1.49 and 1.68, respectively, for occurrence of abnormal result with 40 years of exposure at a respirable quartz level of 0.1 mg/m^3. Longitudinal data analysis of FEV_1 results over time (among the 242 individuals with five or more acceptable FEV_1 results) showed a 1.1 mL/year decline in FEV_1 for each milligram per cubic metre of mean respirable quartz dust exposure ($p=0.001$), after adjusting for ethnicity and pack-years smoked. Similar analyses revealed a 1.6 mL decline/year in FVC for each milligram per cubic metre of mean silica exposure ($p=0.0108$).

Tunnelling as a part of construction work is associated with heavy exposure to gases and particles, quartz, oil mist and nitrogen dioxide (NO_2), notably as only tunnels longer than 200 m are usually mechanically ventilated during excavation. To assess the occurrence of respiratory symptoms and airflow limitation in tunnel workers due to these exposures was the aim of the National Institute of Occupational Health, Oslo, Norway, in three investigations by Ulvestad *et al*[33 34] and by Bakke *et al*.[26] In 1991, all tunnel and other heavy construction workers (n=417), employed at 15 work sites were invited to participate in a cross-sectional study.[33] The medical tests were carried out at the work sites and the health service team returned to the sites several times until the attendance rate was 100%. The study group consisted of 212 male tunnel workers (tunnel face workers, shotcreters and concrete workers). This group was compared with a reference group comprising 90 white-collar construction employees and 205 heavy construction workers (carpenters and iron fixers) without former experience in tunnelling. Factors such as age, height, working hours and smoking habits were very similar between the groups. The tunnel workers had a higher geometric mean exposure to total dust and respirable dust than the reference subjects. They were also exposed to significantly higher levels of quartz, oil mist and NO_2. Exposure to particles in the tunnels showed high variability. The highest 8 h weighted averages (8 h TWA) were: total dust 55.9 mg/m^3, respirable dust 9.3 mg/m^3, quartz 1.98 mg/m^3 and oil mist 4.4 mg/m^3. FVC (% predicted) and FEV_1 (% predicted) in the tunnel workers decreased significantly with years employed in the same job compared with other heavy construction workers. FEV_1 decreased by 17 mL for each year of exposure to tunnel work (p=0.001) compared with 0.5 mL for each year of exposure in outdoor construction workers, and by 9 mL for each pack-year of cigarette consumption in tunnel workers (p=0.001) compared with 7 mL in outdoor heavy construction workers (p=0.08). The prevalence of COPD was 14% in the tunnel workers and 8% in the reference subjects (p=0.03).

The original cohort was re-examined 8 years later, in 1999.[34] Overall, 345 subjects (83%) participated in the follow-up: 96 tunnel workers, a reference group of 178 heavy construction workers and 71 white-collar employees. As neither tunnelling technology nor outdoor concrete construction technology had changed substantially since 1980, the concentrations measured during the years 1996–1999 were considered to be representative for exposure during the study period 1991–1999. The mean exposure of each agent in each job group was assigned to each worker within that group to estimate cumulative exposure. The exposure for the white-collar employees was estimated to be 1/10 of the 8 h time weighted averages measured in the drillers. The cumulative exposure figures were individually adjusted for sick leave and other longer periods of absence. Mean exposures were multiplied by the actual numbers of years (months) that each subject had worked within the 8-year study period. During the 8-year follow-up period, after adjustment for age and current smoking, the decrease in FEV_1 was associated with cumulative exposure to respirable dust ($p<0.001$) and quartz (p=0.02). The regression model predicts that in a worker 40 years of age, the annual decline in FEV_1 in a non-exposed non-smoker would be 25 mL, in a non-exposed smoker 35 mL, in a non-smoking driller 50 mL and in a non-smoking shotcreter 63 mL, while reduction in FVC was not related to cumulative exposure. It was difficult to distinguish between the various tunnelling pollutants and the detrimental effects on the airways as cumulative exposure to total dust, respirable dust, quartz, NO_2 and oil mist were highly correlated.

In an extension of the above described cross-sectional and longitudinal study by Ulvestad *et al*, another study from these authors[26] was performed with the objective to confirm the findings of a relationship between cumulative exposure to respirable dust/quartz dust and lung function changes in other tunnel workers and also to investigate whether exposures other than respirable dust and a-quartz were associated with lung function changes. A total of 651 male construction workers (drill and blast workers, tunnel concrete workers, shotcreting operators, and tunnel boring machine workers) were followed up by spirometric measurements in 1989–2002 for an average of 6 years. Outdoor concrete workers, foremen and engineers served as a low exposed referent population. The total number of spirometric measurements was 1995, which were performed on 651 workers. Of these, 428 workers had more than two measurements (1549 observations). The mean follow-up time between the first and the last check-up was 6.0 years with on average three spirometries. Of the 651 workers, 191 were workers already investigated in the study by Ulvestad *et al*.[33] The annual decrease in FEV_1 in low exposed non-smoking workers was 21 and 24 mL in low exposed ever smokers. The annual decrease in FEV_1 in tunnel construction workers was 20–31 mL higher than in the low exposed workers depending on job group for both non-smokers and ever smokers. After adjustment for age and observation time, cumulative exposure to NO_2 showed the strongest association with a decrease in FEV_1 in both non-smokers and ever smokers. The authors concluded that despite this finding of the association between lung function decrease with NO_2 exposure, respirable dust and quartz may also contribute to the observed effects, as the exposure levels of these agents were moderately correlated to NO_2.

Meta-analysis of six studies

Not all studies that were selected for the systematic review could also be integrated into the meta-analysis. Studies not adjusting for covariates,[27,31] including silicotic workers[32] or with overlapping populations,[33] were not selected for the meta-analysis, which finally consisted of six studies[17,26,28–30,34] described in brief in table 1.

In the cross-sectional analysis, we combined studies with endpoints measured in the same units. Comparing the mean FEV_1 in % predicted from cross-sectional analyses, it was −4.62% (95% CI −2.06 to −7.18%) lower for workers exposed to silica containing dust (see figure 2) than for no/low exposed workers. Taking the SMD between exposed and no/low exposed workers we also observed a statistically significant reduction of FEV_1 (see figure 3). Different studies applied different methods to obtain the ratio FEV_1 to FVC. Only the SMD of the ratio could be used as a common estimate of FEV_1/FVC for meta-analysis. The mean difference of the ratio FEV_1 to FVC between study participants exposed to silica containing dust at the work place and low/no exposed participants was significantly decreased (−0.41 (95% CI −0.28 to −0.54); see figure 4).

Three publications reported on the mean longitudinal decline of FEV_1 per year, which was 50–70 mL in the Vermont granite workers,[31] 33 mL in the reanalysis by Graham *et al*,[27] and 66 mL in smokers and 16 mL in non-smokers tunnel workers.[26] The last two publications compared this decline with low/non-exposed workers and found a mean difference in FEV_1 of minus 12 mL in the exposed workers.

DISCUSSION

The meta-analysis revealed a moderate heterogeneity (I^2 19% and 41%) between the studies, which had to be expected considering the variant exposure conditions at the workplace in different countries from Europe and abroad over such a long time span. The visual inspection of funnel plots (see online supplementary figures S1–3) was not suggestive of publication bias. When calculating Egger's test statistics, the meta-analysis including most studies (figure 3: SMD FEV_1 (%predicted or l)) indicated no significant publication bias.

Only for the SMD of the ratio FEV_1 to FVC (see figure 4) we found a study[30] that was influential on the main result of the

Table 1 Studies selected for meta-analysis on silica containing dust and airway obstruction by first author

First author/year of publication	Country	Design	Mean duration of employment (years)	Exposed: Yes	Exposed: No/low exposed	Exposure level (mg/m^3)
Malmberg *et al* (1993)[17]	Sweden	Longitudinal; follow-up 12 years	21.7	45	45	Granite quarry; 1976–1988 AM concentration of respirable quartz 0.16
Jorna *et al* (1994)[29]	Netherlands	Cross-sectional and longitudinal	Not mentioned	72	55	Potato sorters; GM concentration of respirable quartz 0.13
Meijer *et al* (2001)[30]	Netherlands	Cross-sectional	11.3	144	110	Cement factory; AM concentration of respirable quartz 0.06
Ulvestad *et al* (2000)[34]	Norway	Cross-sectional	13	212	205	Tunnel workers; GM concentration of respirable quartz 0.034
Bakke *et al* (2004)[26]	Norway	Longitudinal extension of Ulvestad *et al* (2001)[33]	Not mentioned	69	220	Tunnel workers; AM concentration of cumulative respirable quartz 0.010–3.6 according to job
Hertzberg *et al* (2002)[28]	USA	Cross-sectional	18.3 (19.9 for retirees)	74	121	Foundry; Cumulative exposure (JEM) in five categories

AM, arithmetic mean; GM, geometric mean; JEM, job-exposure matrix.

meta-analysis. Excluding this study from the meta-analysis increased the loss of FEV_1/FVC (SMD −0.46 (−0.61; −0.31)).

Arithmetic or geometric means of exposure levels grouped by industry are presented in table 1. Eight[17 26 29–34] out of 10 studies reviewed found a significant negative association of FEV_1 and FEV_1/FVC related to increasing exposure to crystalline quartz at the workplace. One study found an effect only for smokers,[28] and one[27] did not observe such an effect at all. The meta-analysis of cross-sectional studies showed that the mean FEV_1 of workers exposed to silica containing dust was 4.6% less than predicted compared with workers with no/low exposure, which was a statistically significant difference.

If the inhalation of respirable quartz dust causes COPD, the exposure should be associated with an accelerated decline in lung function, which will be detected in a longitudinal study design with repeated spirometries in study participants during a period of several years.[39] A study among foundry workers from USA[28] presented the decrease of FEV_1 per milligram per cubic metre respirable quartz dust at the workplace and found a loss of 1.1 mL per mg/m^3, which is very similar to the decrease of 1.6 mL (95% CI 1.24 to 1.93 mL) per 1 mg/m^3 years we found in a meta-analysis of occupational exposure to bg dust.[16] Other studies did not estimate the effect according to the cumulative measure (milligram per cubic metre-year) or per milligram per cubic metre respirable quartz dust concentration at the workplace, but presented their results as annual loss in FEV_1. As exposure levels varied between studies, a direct comparison of the annual decline in FEV_1 is somewhat arbitrary. Even so, the annual decline of FEV_1 among Vermont granite workers amounted to 30 mL[27] and 50–70 mL,[31] and 50–63 mL among Norwegian tunnel workers.[33]

There are occupational risk factors other than silica, such as vapours, gas and fumes, which can cause airway obstruction. In the meta-analysis, the studies from Norway[26 33 34] observed that exposure to gases from diesel exhaust, NO_2 and blasting contributed to an accelerated decline of FEV_1. Nevertheless, the authors concluded that it was the cumulative exposure to respirable dust and α quartz which was the most important risk factor for airflow limitation in underground heavy construction workers.[33] None of the other studies, which were performed in quarry mines, a foundry and a cement production plant, as well as among potato sorters, considered exposure to gases and fumes as potential confounders.

Whereas the development of silicosis takes some time before it becomes symptomatic, this seems not to be the case for signs of airway obstruction. At least, none of the studies included in the meta-analysis considered a latency period before performing spirometric measurements. Some studies were ethnically not homogeneous. But as FEV_1% predicted is defined as the FEV_1 of the patient divided by the average FEV_1 in the population for any person of similar age, height, sex and ethnicity, this potential effect modifier was implicitly adjusted for.

The observed limitation of pulmonary function in workers exposed to respirable quartz dust might be an underestimation of the true effect, since both cross-sectional and longitudinal studies in the workforce are often limited to a 'survivor' population because of the inability to monitor workers who leave their jobs. Only one study[28] was able to also include retirees in their

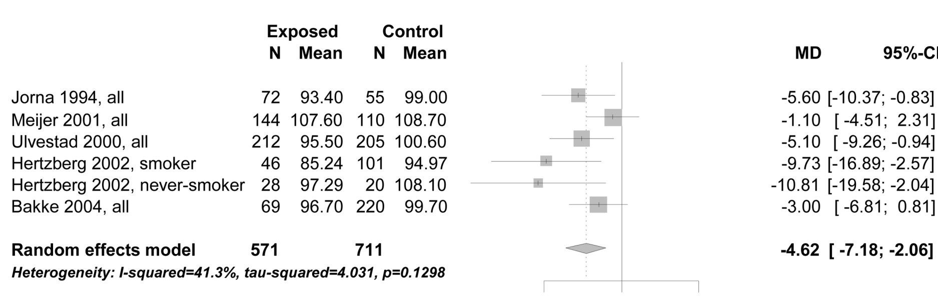

Figure 2 Mean difference (MD) of FEV_1 (% predicted) between study participants exposed to silica containing dust at the workplace and no/low exposed participants.

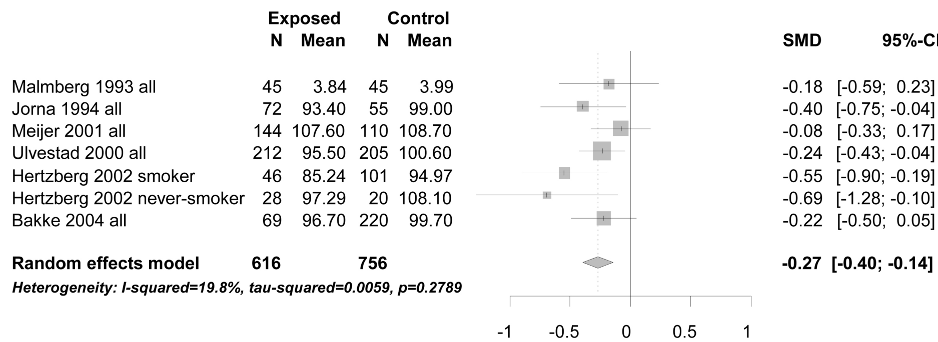

Figure 3 Standardised mean difference (SMD) of FEV_1 between study participants exposed to silica containing dust at the workplace and no/low exposed participants.

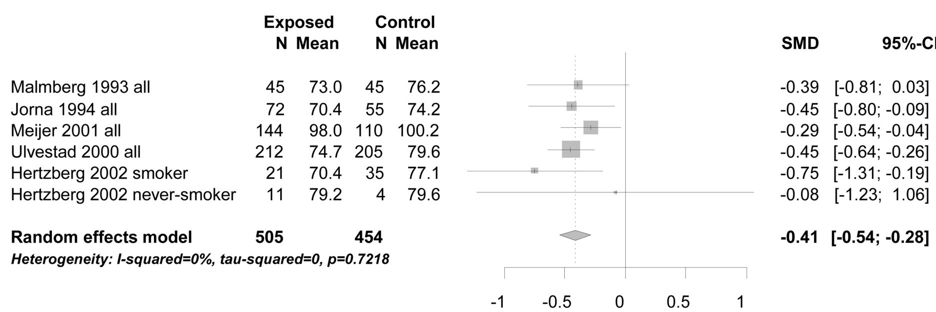

Figure 4 Standardised mean difference (SMD) of the ratio FEV_1 to FVC between study participants exposed to silica containing dust at the work place and low/no exposed participants.

study population. As the loss of FEV_1 per year is typically small, it tends to be hidden by measurement variability and will become obvious only in longer follow-up periods. Whereas Wang and Petsonk[40] consider a decrease of FEV_1 >8% or 330 mL per year at the workplace as probably pathological, other authors (Hnizdo *et al*,[41] Hnizdo *et al*[42]) have suggested a method with higher sensitivity to estimate the 'longitudinal limits of normal decline'. According to the authors, a decrease of more than 60 mL per year should be suggestive of an increasing airway obstruction.

Aiming at a quantitative assessment of the association between occupational exposures to crystalline quartz containing dust at the workplace and the development of obstructive findings in spirometry, the requirements for a study to be included in the meta-analysis were very specific and led to a remarkable drop between studies identified in the literature search (eligible n=256) and those finally included in the review (n=10) and meta-analysis (n=6). Therefore, the studies included in the meta-analysis cannot claim to be representative of all studies on the subject, but only for those with quantitative data on crystalline quartz containing dust exposure at the workplace and lung function measurements. More general reviews have already been published.[43–47]

At present, COPD as a compensable occupational disease is included in two international lists of occupational diseases, one proposed by the International Labour Organization[48] and the other established by the European Commission.[49] Both are only recommendatory in character; most EU-member states have their own lists, which are comparable just in some parts.[50]

In summary, this meta-analysis showed consistently a decline of FEV_1 and FEV_1/FVC related to cumulative respirable quartz dust exposure at the workplace.

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Provenance and peer review Not commissioned; externally peer reviewed.

REFERENCES

1 Xu X, Christiani DC, Dockery DW, *et al*. Exposure-response relationships between occupational exposures and chronic respiratory illness: a community-based study. *Am Rev Respir Dis* 1992;146:413–18.
2 Krzyzanowski M, Kauffmann F. The relation of respiratory symptoms and ventilatory function to moderate occupational exposure in a general population. Results from the French PAARC study of 16,000 adults. *Int J Epidemiol* 1988;17:397–406.
3 Viegi G, Prediletto R, Paoletti P, *et al*. Respiratory effects of occupational exposure in a general population sample in north Italy. *Am Rev Respir Dis* 1991;143:510–15.
4 Boggia B, Farinaro E, Grieco L, *et al*. Burden of smoking and occupational exposure on etiology of chronic obstructive pulmonary disease in workers of Southern Italy. *J Occup Environ Med* 2008;50:366–70.
5 Fishwick D, Bradshaw LM, D'Souza W, *et al*. Chronic bronchitis, shortness of breath, and airway obstruction by occupation in New Zealand. *Am J Respir Crit Care Med* 1997;156:1440–6.
6 Bakke PS, Baste V, Hanoa R, *et al*. Prevalence of obstructive lung disease in a general population: relation to occupational title and exposure to some airborne agents. *Thorax* 1991;46:863–70.
7 Sunyer J, Kogevinas M, Kromhout H, *et al*. Pulmonary ventilatory defects and occupational exposures in a population-based study in Spain. Spanish Group of the European Community Respiratory Health Survey. *Am J Respir Crit Care Med* 1998;157:512–17.
8 Jaen A, Zock JP, Kogevinas M, *et al*. Occupation, smoking, and chronic obstructive respiratory disorders: a cross sectional study in an industrial area of Catalonia, Spain. *Environ Health* 2006;5:2.
9 Weinmann S, Vollmer WM, Breen V, *et al*. COPD and occupational exposures: a case-control study. *J Occup Environ Med* 2008;50:561–9.
10 Blanc PD, Iribarren C, Trupin L, *et al*. Occupational exposures and the risk of COPD: dusty trades revisited. *Thorax* 2009;64:6–12.
11 Hnizdo E, Sullivan PA, Bang KM, *et al*. Association between chronic obstructive pulmonary disease and employment by industry and occupation in the US population: a study of data from the Third National Health and Nutrition Examination Survey. *Am J Epidemiol* 2002;156:738–46.
12 Mannino DM. Lung function decline and outcomes in an adult population. *Am J Respir Crit Care Med* 2006;173:985–90.
13 Mannino DM, Gagnon RC, Petty TL, *et al*. Obstructive lung disease and low lung function in adults in the United States: data from the National Health and Nutrition Examination Survey, 1988–1994. *Arch Intern Med* 2000;160:1683–9.
14 Balmes J, Becklake M, Blanc P, *et al*. American Thoracic Society Statement: Occupational contribution to the burden of airway disease. *Am J Respir Crit Care Med* 2003;167:787–97.
15 Greim H, Ziegler-Skylakakis K. Risk assessment for biopersistent granular particles. *Inhal Toxicol* 2007;19:199–204.

16 Brüske I, Thiering E, Heinrich J, *et al*. Biopersistent granular dust and chronic obstructive pulmonary disease: a systematic review and meta-analysis. *PLoS ONE* 2013;8:e80977.
17 Malmberg P, Hedenstrom H, Sundblad BM. Changes in lung function of granite crushers exposed to moderately high silica concentrations: a 12 year follow up. *Br J Ind Med* 1993;50:726–31.
18 Cowie RL, Mabena SK. Silicosis, chronic airflow limitation, and chronic bronchitis in South African gold miners. *Am Rev Respir Dis* 1991;143:80–4.
19 Cowie RL, van Schalkwyk MG. The prevalence of silicosis in Orange Free State gold miners. *J Occup Med* 1987;29:44–6.
20 Liberati A, Altman DG, Tetzlaff J, *et al*. The PRISMA statement for reporting systematic reviews and meta-analyses of studies that evaluate health care interventions: explanation and elaboration. *Ann Intern Med* 2009;151:W65–94.
21 Stroup DF, Berlin JA, Morton SC, *et al*. Meta-analysis of observational studies in epidemiology: a proposal for reporting. Meta-analysis Of Observational Studies in Epidemiology (MOOSE) group. *JAMA* 2000;283:2008–12.
22 ATS. Standardization of spirometry—1987 update. Statement of the American Thoracic Society. *Am Rev Respir Dis* 1987;136:1285–98.
23 Brusasco V, Crapo R, Viegi G. Coming together: the ATS/ERS consensus on clinical pulmonary function testing. *Eur Respir J* 2005;26:1–2.
24 Quanjer PH, Tammeling GJ, Cotes JE, *et al*. Lung volumes and forced ventilatory flows. Report Working Party Standardization of Lung Function Tests, European Community for Steel and Coal. Official Statement of the European Respiratory Society. *Eur Respir J Suppl* 1993;16:5–40.
25 Viechtbauer W, Cheung MWL. Outlier and influence diagnostics for meta-analysis. *Res Synth Methods* 2010;1:112–25.
26 Bakke B, Ulvestad B, Stewart P, *et al*. Cumulative exposure to dust and gases as determinants of lung function decline in tunnel construction workers. *Occup Environ Med* 2004;61:262–9.
27 Graham WG, Weaver S, Ashikaga T, *et al*. Longitudinal pulmonary function losses in Vermont granite workers. A reevaluation. *Chest* 1994;106:125–30.
28 Hertzberg VS, Rosenman KD, Reilly MJ, *et al*. Effect of occupational silica exposure on pulmonary function. *Chest* 2002;122:721–8.
29 Jorna TH, Borm PJ, Koiter KD, *et al*. Respiratory effects and serum type III procollagen in potato sorters exposed to diatomaceous earth. *Int Arch Occup Environ Health* 1994;66:217–22.
30 Meijer E, Kromhout H, Heederik D. Respiratory effects of exposure to low levels of concrete dust containing crystalline silica. *Am J Ind Med* 2001; 40:133–40.
31 Musk AW, Peters JM, Wegman DH, *et al*. Pulmonary function in granite dust exposure: a four-year follow-up. *Am Rev Respir Dis* 1977;115:769–76.
32 Rego G, Pichel A, Quero A, *et al*. High prevalence and advanced silicosis in active granite workers: a dose-response analysis including FEV1. *J Occup Environ Med* 2008;50:827–33.
33 Ulvestad B, Bakke B, Eduard W, *et al*. Cumulative exposure to dust causes accelerated decline in lung function in tunnel workers. *Occup Environ Med* 2001;58:663–9.
34 Ulvestad B, Bakke B, Melbostad E, *et al*. Increased risk of obstructive pulmonary disease in tunnel workers. *Thorax* 2000;55:277–82.
35 Graham WG, O'Grady RV, Dubuc B. Pulmonary function loss in Vermont granite workers. A long-term follow-up and critical reappraisal. *Am Rev Respir Dis* 1981;123:25–8.
36 Wegman DH, Eisen E, Peters JM. Pulmonary function loss in Vermont granite workers. *Am Rev Respir Dis* 1983;128:776–7.
37 Eisen EA, Wegman DH, Louis TA, *et al*. Healthy worker effect in a longitudinal study of one-second forced expiratory volume (FEV1) and chronic exposure to granite dust. *Int J Epidemiol* 1995;24:1154–61.
38 Becklake MR. Chronic airflow limitation: its relationship to work in dusty occupations. *Chest* 1985;88:608–17.
39 Schouten JP, Tager IB. Interpretation of longitudinal studies. An overview. *Am J Respir Crit Care Med* 1996;154:S278–84.
40 Wang ML, Petsonk EL. Repeated measures of FEV1 over six to twelve months: what change is abnormal? *J Occup Environ Med* 2004;46:591–5.
41 Hnizdo E, Sircar K, Glindmeyer HW, *et al*. Longitudinal limits of normal decline in lung function in an individual. *J Occup Environ Med* 2006;48:625–34.
42 Hnizdo E, Sircar K, Yan T, *et al*. Limits of longitudinal decline for the interpretation of annual changes in FEV1 in individuals. *Occup Environ Med* 2007;64:701–7.
43 Trupin L, Earnest G, San Pedro M, *et al*. The occupational burden of chronic obstructive pulmonary disease. *Eur Respir J* 2003;22:462–9.
44 Balmes JR. Occupational contribution to the burden of chronic obstructive pulmonary disease. *J Occup Environ Med* 2005;47:154–60.
45 Blanc PD, Toren K. Occupation in chronic obstructive pulmonary disease and chronic bronchitis: an update. *Int J Tuberc Lung Dis* 2007;11:251–7.
46 Rushton L. Occupational causes of chronic obstructive pulmonary disease. *Rev Environ Health* 2007;22:195–212.
47 Fishwick D, Barber CM, Darby AC. Chronic Obstructive Pulmonary Disease and the workplace. *Chron Respir Dis* 2010;7:113–22.
48 International Labor Organization ILO. List of occupational diseases (revised 2010). In: ILO, ed. Identification and recognition of occupational diseases: criteria for incorporating diseases in the ILO list of occupational diseases. Geneva, 2010.
49 European Commission. Report on the current situation in relation to occupational diseases' systems in EU Member States and EFTA/EEA countries, in particular relative to Commission Recommendation 2003/670/EC concerning the European Schedule of Occupational Diseases and gathering of data on relevant related aspects. 2013. http://www.ilo.org/safework/info/publications/WCMS_125137/lang–en/index.htm
50 Krajewski-Siuda K. Different lists of occupational diseases in European Union Member States: is it a problem for the law harmonization? *Int J Occup Med Environ Health* 2004;17:487–90.