ORIGINAL ARTICLE

Chronic obstructive pulmonary disease and longitudinal changes in pulmonary function due to occupational exposure to respirable quartz

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▸ Additional supplementary tables are published online only. To view these files please visit the journal online (http://dx.doi.org/10.1136/oemed-2012-100775).

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Received 13 March 2012
Revised 24 July 2012
Accepted 22 August 2012
Published Online First 20 September 2012

ABSTRACT

Objectives The present study sought to examine the long-term effects of exposure to respirable quartz on pulmonary function with particular focus on chronic obstructive pulmonary disease (COPD).

Methods The study is based on the Wismut cohort of former uranium miners. Spirometric data were ascertained together with quantitative estimates of cumulative exposure to respirable quartz for each of 1421 study subjects born between 1954 and 1956. The case definition for COPD is based on the criteria of the Global Initiative for Chronic Obstructive Lung Disease. Linear mixed regression models were fitted to identify significant determinants of longitudinal changes in lung function parameters.

Results An average of five spirometries were available for each miner. It was shown that cumulative exposure to 1 mg/m^3-year respirable quartz leads, on average, to a relative reduction in forced expiratory volume in 1 s/ orced vital capacity (FEV_1/FVC) of 2.75% ($p<0.001$). A nested case–control approach demonstrated that the risk for COPD stage I increases with increasing cumulative exposure to respirable quartz (OR 1.81 per 1 mg/m^3-year).

Conclusions This paper adds further evidence on the long-term effects of exposure to respirable quartz, which include a decline in pulmonary function parameters and an increase in the incidence of COPD.

What this paper adds

- ▸ Prolonged exposure to high levels of quartz dust has long been known to cause silicosis.
- ▸ The literature suggests that an elevated risk of developing chronic obstructive pulmonary disease is associated with occupations characterised by high exposures to quartz dust.
- ▸ Cumulative exposure to respirable quartz causes a significant reduction in the forced expiratory volume (FEV_1)/forced vital capacity (FVC) ratio and FEV_1, adjusting for smoking status.
- ▸ The incidence of chronic obstructive pulmonary disease shows a markedly and statistically significant relative risk increase following respirable quartz exposure.
- ▸ Our results suggest allowable air levels of respirable quartz should be lowered.

INTRODUCTION

Chronic obstructive pulmonary disease (COPD) is a major cause of chronic morbidity and mortality worldwide, especially in those over 40 years of age, and is projected to be the fourth most common cause of mortality by 2030, accounting for 7.8% of all deaths.[1] There is consensus that smoking is the most frequently encountered risk factor for COPD. An increasing body of epidemiological studies demonstrates that specific occupational exposures, including organic and inorganic dusts as well as some chemical agents and fumes, are also associated with the development of COPD.[2] Respirable quartz is one of those exposures believed to be related to COPD.[3 4] Prolonged exposure to high concentrations of respirable quartz has long been known to increase the risk of silicosis. There are, however, questions as to whether respirable quartz can cause other pathological changes in the lungs leading to the development of COPD, and whether these changes can occur during the first half of the working life and, moreover, at exposure levels within current occupational limits.

The present study sought to examine the long-term effects of exposure to respirable quartz on pulmonary function, in particular focusing on COPD as defined by the criteria of the Global Initiative for Chronic Obstructive Lung Disease (GOLD).[5]

METHODS

Study population

The study is based on the Wismut cohort, which is perhaps the world's largest cohort of former uranium miners. This cohort was primarily established to examine the long-term health effects of chronic exposure to radon, long-lived radionuclides, and external gamma radiation.[5] A stratified random sample of about 60 000 males, employed for at least 6 months between 1949 and 1989 at the former uranium mining company 'Wismut' in Saxony and Thuringia, was selected at the beginning of the 1990s. Further details of the cohort composition are described elsewhere.[6] During the first post-war years, uranium mining was characterised by appalling working conditions (dry drilling with only natural ventilation and no protection from radiation). Later on, the working conditions improved substantially. The concentration of

To cite: Möhner M, Kersten N, Gellissen J. *Occup Environ Med* 2013, **70**, 9–14.

respirable dust decreased sharply after 1955 because of the changeover to wet drilling and the stepwise introduction of several ventilation measures. By 1970 the working conditions had improved to a point where international standards of industrial hygiene and radiation protection were being met.

For the present study, we selected only miners born in the 3 years from 1954 to 1956 to ensure that none of the study subjects had worked underground in the mines before 1971. Underground work in mines was strictly prohibited by law for youths under the age of 16.

Lung function data

The Wismut health service was founded in 1946 to conduct occupational health and medical examinations and treat employees and their relatives. Because exposures to silica dust and ionising radiation are typical of ore mining, Wismut physicians were very familiar with occupational diseases such as silicosis and lung cancer. Spirometry was used to detect pulmonary diseases among miners from the early days of the Wismut health service and measured values were standardised in 1970. Guidelines on occupational health and medical examinations required miners to have a medical history, a physical examination, an x-ray of the chest and a spirometry every second year.[7]

The Stollberg spirometer (made by Wismut) was generally used for spirometry. This spirometer can record both FEV_1 (forced expiratory volume in 1 s) and FVC (forced vital capacity). For the spirometry the seated miner was asked to inhale as much air as possible and then to exhale as deeply and quickly as possible into the spirometer without stopping. This manoeuvre was repeated at least three times and the highest values were recorded as being representative. The measured values of FEV_1 and FVC were entered on a form together with the room temperature and air pressure to allow for later BTPS standardisation (body temperature and ambient barometric pressure saturated with vapour). Details of smoking habits were also included on the form. Forms were evaluated using computer assisted analysis, including BTPS standardisation and comparison with predicted values. All forms were kept with the medical records.

Following closure of the East German uranium mines by the end of 1990 and the subsequent closure of most occupational health services in mining regions, the medical records are now stored by the Federal Institute for Occupational Safety and Health (Bundesanstalt für Arbeitsschutz und Arbeitsmedizin, BAuA), as legally mandated. For the purpose of this study, the medical records were accessed by specially trained staff with a view to collecting all available spirometric data for our study base.

Exposure assessment

Detailed information for the entire Wismut cohort regarding their occupational histories was collected by the German Statutory Accident Insurance (DGUV) from payrolls and personnel files.[6] This information comprises data on the mining facility/mine shaft, job type, number of shifts, and periods of absence on a daily basis.

The Institute for Research on Hazardous Substances (IGF) retrospectively estimated exposure to respirable and inhalable dust, crystalline silica and arsenic. Extensive side-by-side measurements for the original mine equipment from the 1950s until the 1980s were carried out with the originally used konimeters and modern standard respirable dust samplers. (A konimeter is a portable instrument for measuring airborne dust concentration where samples are obtained by sucking a known volume of air through a hole and allowing it to pass over a glass disc coated with grease on which the particles collect. Subsequently, the particles are counted with the help of a light microscope and the results are given as number of particles per ml.) The results were used to develop a procedure for recalculating konimetric data obtained under historical conditions into respirable dust mass. A detailed description of the measurements and the estimation methods is given elsewhere.[8] Based on those exposure estimates, DGUV developed a comprehensive job-exposure matrix (JEM). In this JEM, exposures are given in dust-years, whereby 1 dust-year is defined as exposure to 1 mg/m^3 of inhalable respective respirable dust over a full year, which is equivalent to 220 shifts of 8 h each. The corresponding estimates for respirable quartz also take into account the mean quartz content in the corresponding mine shaft. The quartz concentration in the respirable dust varied according to the lithography of the mines, being between 10% and 29% in Saxony and between 7% and 33% in Thuringia.[9] The mean quartz concentration for the members of the cohort was 13.3%.

Combination of the data from the job histories with the JEM yields estimates of the cumulative dust exposure for each miner for each calendar year of exposure. Results presented below are based on exposure to respirable quartz dust, where the cumulative exposure to respirable quartz is given in mg/m^3-years.

Statistical methods

All analyses were performed using the STATA package release 12.[10] Linear mixed-effects regression models were used to estimate the exposure effects considered. Age (in linear-quadratic form), height, body mass index and smoking status were abstracted from medical check-up records and considered as confounding factors in the model.

Linear mixed regression models were fitted to identify significant determinants of longitudinal changes in lung function parameters, especially the ratio FEV_1/FVC and FEV_1, taking into account additional terms for cumulative exposure to silica dust and smoking. Likelihood ratio tests were performed to select important confounding factors.

As a second approach, we investigated the determinants of longitudinal deviations from corresponding reference values. Following a recommendation of Baur *et al*, we used the reference values of Brändli *et al* for comparison purposes.[11–13]

The model has the following form for the ratio FEV_1/FVC:

$$\begin{aligned} y_{it} &= \ln(FEV1_{it}/FVC_{it}) \\ y_{it} &= \beta_0 + \beta_1 \cdot age_{it} + \beta_2 \cdot age_{it}^2 + \beta_3 \cdot \ln(height_i) + \beta_4 \cdot bmi_{it} \\ &\quad + \beta_5 \cdot qyr_{it} + u_{0i} + u_{1i} \cdot ssyr_{it} + u_{2i} \cdot usyr_{it} + \varepsilon_{it} \end{aligned}$$

where qyr_{it} is the cumulative exposure to respirable quartz of miner i until his t-th spirometry. The number of years a miner smoked between the first and t-th spirometry for a continuous smoker and a miner with uncertain smoking status are denoted by $ssyr_{it}$ and $usyr_{it}$, respectively. The term u_{0i} was introduced as a random intercept for miner i. Moreover, random slopes u_{1i} and u_{2i} were considered to account for differences between miners regarding intensity of tobacco consumption. In the corresponding model for FEV_1, the natural logarithm of FEV_1 was used as the dependent variable, that is, $y_{it}=\ln(FEV1_{it})$.

In addition to modelling longitudinal changes in lung function parameters, nested case–control studies were conducted to investigate the association between respirable silica and COPD. In these studies, a miner was counted as a case once the GOLD criterion for COPD stage I respectively (?) stage II was matched for the first time. Three controls for stage I and five controls for stage II were matched individually to each case by attained age. ORs and two-sided 95% CIs were calculated by conditional logistic regression. Cumulative respirable quartz exposure was considered in the model as a linear variable. To account for non-linearity, cumulative exposure data were divided into quintiles, based on the distribution among controls. Moreover, the highest quintile was halved to account for highest exposures. Smoking status was again considered as a confounding factor.

RESULTS

Ascertainment of all information on lung function tests in the given birth cohort yielded a total of 8918 data records for 1942 miners. No information on spirometries could be found in the archives for a further 408 miners (17.4%). We excluded all lung function measurements from miners less than 18 years of age. Miners with only one data record were also excluded from further analysis. The database thereby decreased to 8252 data records for 1571 miners. In the next step we ensured data quality and controlled for the time-lag between consecutive spirometries for each miner. If there were two or more spirometries during a period of less than 6 months, only the spirometry with the highest values was kept. This procedure resulted in another 150 records being excluded. The final database contained 7122 data records for 1421 miners. No miner showed signs of silicosis during the time under study. Table 1 summarises the characteristics of the study population. Only a crude classification of miners was possible as regards their smoking habits: 185 miners (13%) were classified as non-smokers and a further 647 (45.5%) as continuous smokers during the study period. The remaining 589 miners (41.5%) could not be allocated to either group because of missing and/or inconsistent information on their smoking habits.

Table 2 shows the statistically significant determinants of the ratio FEV_1/FVC. Quartz dust was found to be a very important determinant. The corresponding estimate for cumulative respirable quartz is −0.0279. Therefore, cumulative exposure to 1 mg/m^3-year respirable quartz causes an average change in FEV_1/FVC by a factor of $e^{-0.0279}=0.9725$, which is equivalent to a relative reduction of 2.75%. The corresponding parameter estimate for age is −0.0076. Hence, the annual decline in FEV_1/FVC for a non-smoker is 0.76% (ignoring for simplicity the quadratic term). The random slope for smoking is characterised by two parameters, the mean and the SD. For a continuous smoker on average an additional annual decline of 0.18% was calculated, but the SD for this parameter is relatively large, that is there is a large variation in the slope parameter.

The mean annual exposure to respirable quartz in our study population was 0.072 mg/m^3. Therefore, the mean annual effect of quartz is of the same magnitude as that of smoking.

The quartz effect on FEV_1 was also significant (table 3). A cumulative exposure to 1 mg/m^3-year respirable quartz reduces FEV_1 by 2.07%, which is equivalent to 87 ml, taking the overall mean at study entry as the baseline.

To conduct the nested case–control study, we selected all study subjects for whom at least one spirometry with an FEV_1/FVC value of <0.7 was recorded. A total of 306 (21.5%) miners fulfilled this criterion. As 73 of them had already fulfilled the criterion during their first spirometry, their data were excluded. The remaining 233 miners were counted as COPD cases in the nested case–control approach once their FEV_1/FVC ratio fell below the threshold of 70%. The 1115 miners whose FEV_1/FVC ratio did not fall under the threshold, formed the group of potential controls. Three controls were individually matched to each case for age at spirometry and birthday. Altogether, 699 controls were matched to the 233 identified COPD cases in the study.

According to the GOLD criterion, 233 miners developed stage I+ COPD during the study period. Their mean age at diagnosis was 28.4 years. Table 4 shows the corresponding results of the conditional logistic regression models. Both models show a significant exposure–response relationship. Comparison of both models using Akaike's information criterion[14] shows that the categorical model was found to be only slightly superior, but using the Bayesian information criterion,[15] the linear model was found to be clearly superior to the categorical model.

Moreover, 132 miners matched the criterion for COPD stage II+. The corresponding results are given in online supplementary table S1. The linear model was found to describe the relationship better than the categorical model. This model yields OR 1.42 (95% CI 0.92 to 2.20) per mg/m^3-year respirable quartz.

Table 1 Characteristics of the study population

	Mean	Range	SD
Age at entry into the Wismut company (years)	20.4	14.6–33.6	3.6
Duration of employment* (years)	12.8	0.87–19.9	4.8
Age at first spirometry considered in the study (years)	23.4	18.0–33.5	3.9
Height (cm)	176	157–196	6
Body mass index (kg/m^2)	23.8	16.8–42.7	3.0
FVC at study entry (litres)	5.1	3.1–7.8	0.7
FEV_1 at study entry (litres)	4.2	2.0–6.2	0.6
FEV_1/FVC at study entry (%)	82.9	53.9–98.6	7.2
Number of spirometries	5	2–15	2.6
Time elapsed between first and last spirometry (years)	7.8	0.6–17.0	4.5
Mean annual exposure to respirable dust (mg/m^3)	0.55	0–2.07	0.33
Mean annual exposure to respirable quartz (mg/m^3)	0.074	0–0.370	0.048

*Truncated at 31 December 1990 and excluding period of apprenticeship at age <16.
FEV_1, forced expiratory volume in 1 s; FVC, forced vital capacity.

DISCUSSION

Only a few studies have investigated longitudinal changes in lung function parameters in workers exposed to quartz dust.[16–19] We conducted a longitudinal study in 1421 uranium miners covering the first half of their working lives and found evidence of a positive association between exposure to respirable quartz and a decline in the FEV_1/FVC ratio and in FEV_1.

Another commonly used criterion for lung function impairment is FEV_1 as a percentage of the corresponding reference value. Estimation of the effect of respirable quartz using a linear mixed-effects regression model yields an additional decline of 1.9% (95% CI 0.9 to 2.9) per mg/m^3-years. It should be noted, however, that the corresponding likelihood ratio test shows that age must not be removed from the model. This suggests that the reference function for FEV_1 does not correctly fit the age dependency in our young cohort. Hence, we focus on analysis of the absolute values of FEV_1/FVC and FEV_1.

Several strengths and weaknesses of the study must be considered when interpreting the results. The main strength of the

Table 2 Determinants of longitudinal changes in the FEV_1/FVC ratio

	Estimates		Deviation from the reference values according to Brändli *et al*[12]	
	Coefficient	95% CI	Coefficient	95% CI
Intercept	1.4759	0.9267 to 2.0252	−0.0187	−0.0231 to −0.0143
Age (years)	−0.0076	−0.0127 to −0.0025	–	–
Age, squared (years^2)	0.000134	0.000041 to 0.000227	–	–
Height (natural log, cm)	−0.3030	−0.4090 to −0.1969	–	–
Respirable quartz (mg/m^3-years)	−0.0279	−0.0362 to −0.0196	−0.0205	−0.0286 to −0.0124
Continuous smoking (years)	−0.0018	−0.0029 to −0.0007	−0.0017	−0.0030 to −0.0003
Uncertain smoking status (years)	−0.0015	−0.0025 to −0.0004	−0.0013	−0.0026 to 0.0001
Follow-up (years)	–	–	0.0021	0.0009 to 0.0034
Random-effects parameters				
SD (continuous smoking)	0.0047	0.0038 to 0.0058	0.0047	0.0039 to 0.0058
SD (uncertain smoking status)	0.0044	0.0034 to 0.0055	0.0043	0.0034 to 0.0054
SD (intercept)	0.0613	0.0582 to 0.0646	0.0621	0.0590 to 0.0654
SD (residual)	0.0687	0.0674 to 0.0701	0.0688	0.0675 to 0.0702

FEV, forced expiratory volume in 1 s; FVC, forced vital capacity.

study is the well-founded quantitative exposure estimation procedure. A further strength is that the study cohort members have been monitored from a young age, as 89% of the study base started their professional career with Wismut when aged under 25 years. Hence, other occupational risk factors can be largely discounted. However, the follow-up is limited to 31 December 1990 when uranium production ceased. Hence, our study only covers miners aged 18–36 years, at which age COPD is seldom diagnosed.

A weakness of the study is that the spirometric data were gathered through routinely performed medical check-ups in different medical facilities over a period of 20 years. Therefore, we cannot exclude that the basic conditions for the spirometries might have changed over time. By 1970, 10 000 cases of silicosis had already been recognised as occupational diseases and a further 8700 cases were recognised during our study period.[20] These data support the fact that during the follow-up of our study cohort the main focus of occupational physicians was on diseases of the respiratory system, indicating that the Wismut health service had staff well trained in all appropriate diagnostic procedures.

The study has other potential shortcomings. Our database did not allow a reliable estimate of the tobacco consumption of our study subjects to be generated. Therefore, we could only include smoking as a qualitative variable in our models and combine this information with the duration of the observation. To account for variability in smoking habits, we considered the period of continuous smoking during the time of observation with a random slope parameter.

Comparison of the duration of employment of the uranium mines with the period covered by spirometry reveals a large discrepancy, which can be attributed to different causes. The most important cause might be that the length of employment includes apprenticeship and additional forms of vocational training. Moreover, most young miners were drafted into military service for 18 months or 3 years. As some spirometries from the early years did not fit the quality criteria, they were excluded from further analysis. Table 1 shows that there is an average

Table 3 Determinants of longitudinal changes in forced expiratory volume in 1 s (FEV_1) given in litres

	Estimates		Deviation from the reference values according to Brändli *et al*[12]	
	Coefficient	95% CI	Coefficient	95% CI
Intercept	−7.0211	−7.8808 to −6.1614	−0.0915	−0.0982 to −0.0849
Age (years)	0.0127	0.0067 to 0.0186	–	–
Age, squared (years^2)	−0.000285	−0.000392 to −0.000178	–	–
Height (natural log, cm)	1.6169	1.4508 to 1.7830	–	–
Body mass index (kg/m^2)	−0.0024	−0.0038 to −0.0009	–	–
Respirable quartz (mg/m^3-years)	−0.0209	−0.0323 to −0.0096	−0.0211	−0.0309 to −0.0112
Continuous smoking (years)	−0.0032	−0.0045 to −0.0018	−0.0032	−0.0044 to −0.0020
Uncertain smoking status (years)	−0.0028	−0.0042 to −0.0013	−0.0028	−0.0040 to −0.0015
Random-effects parameters				
SD (continuous smoking)	0.0053	0.0043 to 0.0066	0.0054	0.0043 to 0.0066
SD (uncertain smoking status)	0.0070	0.0059 to 0.0083	0.0071	0.0060 to 0.0083
SD (intercept)	0.1094	0.1048 to 0.1143	0.1089	0.1043 to 0.1137
SD (residual)	0.0760	0.0746 to 0.0775	0.0767	0.0752 to 0.0782

Table 4 Nested case–control approach for incidence of COPD stage I in terms of GOLD criteria according to exposure to respirable quartz (exposure in categories and as a continuous variable)

Cumulative exposure (mg/m^3-years)	Mean exposure (mg/m^3-years)	Cases	Controls	OR*	OR†	95% CI (OR†)	AIC (BIC)
<0.1412	0.0648	25	140	1.00	1.00	–	
0.1412–0.2950	0.2156	43	140	1.88	1.83	1.05–3.19	
0.2950–0.5560	0.4191	59	140	2.64	2.65	1.54–4.58	629.446 (663.194)
0.5560–0.9386	0.7351	53	139	2.51	2.47	1.39–4.38	
0.9386–1.2847	1.0765	18	70	1.81	1.78	0.86–3.69	
>1.2847	1.6184	35	70	3.73	3.83	1.93–7.57	
Per mg/m^3-year	0.5787	233	699	1.78	1.81	1.27–2.56	631.067 (645.530)

*Crude OR.
†OR adjusted for smoking.
AIC, Akaike information criterion; BIC, Bayesian information criterion; COPD, chronic obstructive pulmonary disease; GOLD, Global Initiative for Chronic Obstructive Lung Disease.

difference of 3 years between entry into the Wismut company and the first spirometry of a miner above 18 years of age. A further reason could be that the regulations concerning the frequency of spirometry were followed less strictly for surface employees. Thus, the difference in time between the last spirometry and withdrawal from the Wismut company may be much greater for surface workers. It must be noted, however, that exposure to respirable quartz was substantially lower for these workers than for underground miners.

After the political changes in East Germany in 1989, it was apparent that uranium production would soon cease. By 1989 only 484 (34%) of the miners had left their job in the mines. However, 19% of the workforce terminated their employment with the Wismut company in 1990. After 1990, the remaining miners were engaged in protecting mine shafts and rehabilitating land. To check whether health reasons could have played a role in early withdrawal from the uranium mines, we performed separate analyses for subgroups of the dataset, defined by occupational status at the end of 1989. It has been shown that the corresponding parameter estimates deviate only marginally from one another (see online supplementary table S2). No difference could be observed between the two subgroups with regard to their mean exposure concentration, although of course they differ markedly in terms of cumulative exposure.

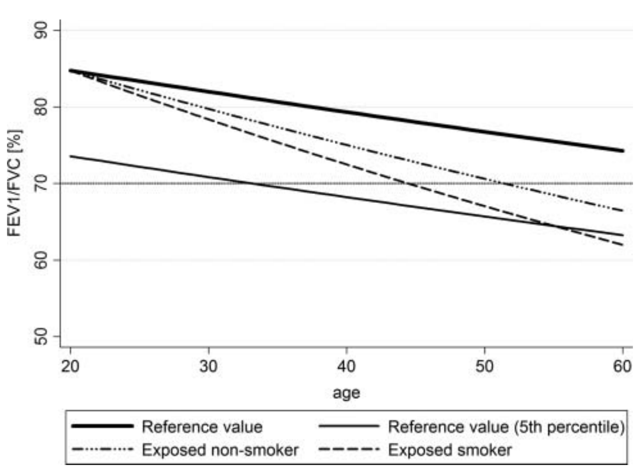

Figure 1 Predicted decline in forced expiratory volume (FEV_1)/forced vital capacity (FVC) ratio, assuming occupational exposure to 0.1 mg/m^3 respirable quartz over a period of 40 years (age 20–60) for a smokers and a non-smoker relative to appropriate reference values and their 5th percentile (male, 176 cm in height).

We also examined other factors which could have influenced the relationship between cumulative exposure to respirable quartz and decline in lung function parameters. Segmentation of groups by median age and by smoking status did not result in significantly different estimates for the model parameter associated with quartz dust (see online supplementary table S2). Moreover, we divided the dataset into two groups according to subjects' median exposure concentration. The corresponding estimates were −0.0321 and −0.0268, so exposure concentration does not seem to influence the examined relationship.

The results of the nested case–control study underline the strong relationship between respirable quartz and COPD. In this analysis smoking habits were not a significant confounding factor, but this might be explained by the fact that we did not have quantitative information on smoking habits. About 75% of the miners seem to have been smokers. It should be noted that the prevalence of COPD in the entire study cohort was very high at 22.5%, while the prevalence of COPD stage II or higher was 12.3%. Given that our cohort was still young at the end of follow-up (mean age at last spirometry 31.1 years), these values greatly exceed corresponding recent values for the general population, which for men aged 40–49 years are approximately 4.5% in European cities[21 22] and 2.2% in Germany.[23] Hence, we can expect that prevalence in younger age groups is less than 2%. Under this condition the ORs can be used as an estimate for the relative risk and we can calculate a rough estimate for the risk doubling dose. Therefore, the cumulative exposure for COPD stage I+ and COPD stage II+ risk doubling is estimated to be about 1.2 mg/m^3-years and 2.0 mg/m^3-years, respectively.

Predicted values were calculated to demonstrate how the estimated exposure–response relationship would change lung function parameters during an entire working life. We assumed an occupational exposure to respirable quartz over a period of 40 years of 0.1 mg/m^3, which is equivalent to the occupational exposure limit in several European countries. We assumed the worker was male with a height of 176 cm, the mean value of our study cohort. Our calculation is based on the reference function and the 5th percentile derived by Brändli *et al*.[12 13] We calculated the corresponding predictions for smokers and for non-smokers, applying the smoking related coefficient calculated from our data. As shown in figure 1, there is a substantial extra decline due to exposure to respirable quartz. A smoker will exceed the threshold value of 70% after 25 years of exposure, at the age of 45 years, and 10 years later he will exceed the 5th percentile of the corresponding reference function.

The analysis showed a consistent association between measures of cumulative exposure to respirable quartz and increased pulmonary function abnormalities. Our results suggest allowable air levels of respirable quartz should be lowered.

Acknowledgements The authors wish to acknowledge: the Department of Radiation Protection and Health, Federal Office for Radiation Protection, for the provision of the exposure data; Barbara Bartl, Ramona Ehlicke, Steffanie Lutz, Annett Müller, Roswitha Müller and Astrid Soja for data acquisition from the medical records; Roland Scheibner and Dr Manfred Lindtner for programming and managing the database of spirometric test results; and two unknown reviewers for helpful comments.

Contributors MM was responsible for study design, analyses and drafting the report. JG supervised the acquisition of data from the medical records in the Wismut health data archive. NK validated spirometric data and statistical analyses. JG and NK oversaw the study design, contributed to interpretation of the findings and helped write the report. All authors have seen and approved the final version of the paper.

Competing interests None.

Ethics approval The data protection officer of the Federal Institute for Occupational Safety and Health approved the study design.

Provenance and peer review Not commissioned; externally peer reviewed.

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