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Occup. Environ. Med. 2008;65;261-267; originally published online 10 Oct 2007; doi:10.1136/oem.2007.034298

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Effects of talc dust on respiratory health: results of a longitudinal survey of 378 French and Austrian talc workers

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Accepted 20 September 2007
Published Online First
10 October 2007

ABSTRACT

Objectives: The aim of this longitudinal study was to investigate the effects on respiratory health of talc dust, free of asbestiform fibres, at or below airborne concentrations of 2 mg/m³.

Methods: The respiratory health and dust exposure of all workers with at least 5 years of employment at two talc producing facilities in France and Austria were surveyed between 1988 and 2003. Standard forced expiratory volumes and standard chest x rays were obtained on repeated occasions and recorded using strict quality control procedures. Of a target population of 430 subjects, 378 (88%) were examined at least twice. A quantitative exposure matrix was set up based on 4602 personal exposure measurements of respirable dust and qualitative descriptions of the industrial processes and individual protection devices.

Results: The mean duration of follow-up was 14.5 years with a mean estimated talc dust concentration during follow-up of 1.46 mg/m³. The prevalence of small radiological opacities and lung function parameters were significantly related to cumulative exposure at inclusion but not to exposure during the study period. Overall, the forced expiratory volume in 1 s decreased by 66 ml per 100 years.mg/m³, which is less than that reported for other types of mineral dusts.

Conclusions: Although early exposure levels to talc as assessed at inclusion were associated with decreased lung function and an increased prevalence of small radiological opacities, there was no evidence of detrimental effects of talc exposure, as assessed within the study period, on lung function and small radiological opacities.

High levels of inhaled talc have been shown to induce so-called talcosis, a form of pneumoconiosis involving radiological opacities and loss of lung function. Moreover, increased mortality from non-malignant respiratory diseases has been observed in some talc-exposed populations^{1 2} but not in others.^{3 4} Furthermore, a deterioration in lung function and an increase in small radiological opacities have been shown in three small talc exposed populations.⁵⁻⁷ On the other hand, inhaled talc not containing asbestos or asbestiform fibres does not seem to be associated with any increased cancer risk⁸ as confirmed by the International Agency for Research on Cancer who, in February 2006, stated that inhaled talc is not classifiable as to its carcinogenicity to humans. Thus, the American Conference of Governmental Industrial Hygienists, which is currently reviewing its threshold limit value for talc, bases its assessment on its role in non-malignant respiratory diseases. The

present paper reports on a long-term longitudinal survey of the respiratory health of two populations of talc workers in France and Austria.

METHODS

The deposits and the mills

The deposits are quarried in open-air pits in the French Pyrenees (France) and the Styrian mountains (Austria) and the talc is milled and conditioned in nearby mills. In Austria the ore was previously extracted in underground mines, but open pit extraction gradually replaced the underground mining which was shut down in 1989. At both sites the mined ore consists of a talc chlorite mixture which does not contain asbestiform fibres. This fact has been substantiated by the absence of any asbestiform fibre in yearly measurements of the marketed products since the 1970, using the CFTA J 4-1 method entitled "Asbestiform amphibole minerals in cosmetic talc", and since 2001 using transmission electron microscopy (TEM) in compliance with ISO standard 13794 and scanning electron microscopy in compliance with ISO standard 14966 performed in several accredited laboratories. The quartz content of the French talc is below 1%, while the Austrian talc contains up to 3% quartz.

Study design and subjects

The target study population consisted of all workers who had worked for at least 5 continuous years between 1989 and 2001 in these two talc producing facilities. This time span was chosen to ensure that mostly subjects with at least two respiratory health assessments were available for analysis. Respiratory health and exposure were surveyed from the mid-1980s onwards.

In the French site, the target population comprised 300 subjects of whom 11 (eight men and three women) declined access to their medical data. Lung function testing was carried out in the context of the compulsory yearly medical check up between 1988 and 2004. Forced expiratory manoeuvres were performed using a Vitalograph single breath wedge bellow (Vitalograph, Ennis, Ireland) until 1994 and subsequently using a Fukuda ST-250 spirometer (Fukuda Sangyo, Antipolo City, Philippines) under the supervision of the same experienced technician. Standard chest x rays were obtained at the time of recruitment and in a series of cross-sectional surveys of the population between 1987 and 2003. The standard ECSC⁹ respiratory health questionnaire was administered to the population in 1990/91, 1992/93 and 1999.

In the Austrian population, lung function as well as standard radiographs were obtained in an occupational health clinic. The health check ups were compulsory for all dust exposed subjects and were offered to all other employees and took place in 1988, 1990, 1994, 1998 and 2002. Of 130 subjects, 29 mostly administrative staff never received an occupational medical check up. From 1990 onwards, lung function tests were carried out using a Jaeger MasterLab spirometer (Jaeger, Hoechberg, Germany) which replaced the previous Jaeger Body-Test plethysmograph. A standard respiratory health questionnaire was administered to the exposed population in 1988 and repeated for all active employees in 2003.

Lung function measurements were selected according to the criteria of the American Thoracic Society¹⁰ and the European Respiratory Society¹¹ on the basis of the graphical trace left by the measuring devices; however, reproducibility was not recorded and could not be checked later. It is therefore likely that some results did not rely on three reproducible measurements of lung function.

The radiographs were obtained using conventional screen-film systems and were coded according to the International Labor Office coding scheme¹² for pneumoconiosis by a panel of three experienced readers. A total of 1153 study radiographs, 50 trigger films (20 asbestos workers, 4 coal miners and 26 talc workers not belonging to the study population) and a sample of 164 radiographs from non-exposed telecommunication workers¹³ were read in randomised order after an initial consensus reading of the trigger radiographs. In order to avoid a drift in the readings, the readers were reminded of the agreed coding by their clerical assistant each time a trigger radiograph had been reread. For each discordant reading of the study *x* rays, the radiograph was read in consensus. A discordant reading was defined as either a reading of three different profusions with more than two steps difference (ex: 0/0, 0/1, 1/1) or a reading for which only one reader had coded a pleural abnormality. The recorded profusion was the median profusion unless it had been reread in consensus, in which case the latter was retained. In addition to the chest radiograph, a helicoidal computed chest tomography (hCT scan) with standard acquisition parameters for parenchymal and mediastinal slices¹⁴ was obtained for all 24 Austrian study subjects still employed in 2006 and all three French study subjects still employed in 2004 for whom a pleural abnormality had been coded in the radiological reading assay. The tomograms were assessed blind to any exposure assessment by two independent readers. The result of the scanner was considered to be a gold standard in assessing pleural abnormalities. Therefore if no pleural abnormality was detected on the tomogram, the pleura was recoded as normal.

Occupational and non-occupational exposure assessment

The talc exposure of all jobs had been systematically measured since 1985 at the French site and since 1988 at the Austrian site using the CIP10 personal dust sampler¹⁵ (Arelco, Fontenay sous Bois, France) worn by the worker for at least half a shift. This dust sampler measures the gravimetric dust concentration at a flow rate of 10 l/min. The head of the sampler acts as a particle selector that enables the respirable (alveolar) fraction to be collected.

A standardised list of all past and present jobs was set up with the help of local personnel at the two sites. Individual job histories were obtained from the initial questionnaire for the French population and were updated using the medical files of the company. The Austrian job histories were coded using the personnel files and validated using the questionnaires.

A quantitative site-specific job exposure matrix (JEM) for job-time period combinations was set up. The assessed exposure levels were based on the arithmetic mean of the exposure measurements computed by 5-year periods for each job code since the beginning of the availability of the exposure measurements. These time periods were sometimes broken down into smaller periods as some discontinuities in the work conditions were mentioned in the interviews with long-term employees (eg, increases in production, temporary lack of control of new processes or the wetting of the dirt roads for truck drivers). Finally, these means were modulated by the type of individual protective equipment used and the frequency of their use. For example, in the French site, the plant electricians had worn dust masks with a nominal protection factor of 4 since the mid-1990s when in exposed workshops. The (arithmetic) mean of the 53 exposure measurements in the 2000–2004 period among electricians was 3.7 mg/m³. However, all measurements above 3 mg/m³ were associated with the tasks for which dust masks were worn. We assumed that when worn, the dust mask reduced the exposure to 30% of the measured exposure and the corresponding line in the JEM was set to 1.5 mg/m³. Prior to 1990 the mean of the 41 available measurements was 5.1 mg/m³ and the corresponding line in the JEM was set to 5 mg/m³. Earlier historical semi-quantitative exposure estimates had been obtained in the late 1980s for the French site for use in the initial cross-sectional study based on the qualitative descriptions of the workplaces, the processes and how they changed by former workers in the French site (see Wild *et al*⁷ for more details). For example, for the electricians, no evolution in their jobs was described so the earliest measured levels were assumed to be representative of the time before the exposure was measured. On the other hand, the milling machine operators were measured at 2.2 mg/m³ between 1985 and 1989 (83 measurements), and set to 2.5 mg/m³ between 1983 and 1989 in the JEM. But, based on descriptions of past working conditions, the JEM exposure was set to 8 mg/m³ between 1968 and 1982 and 20 mg/m³ before 1968. The lines in the JEM corresponding to the Austrian jobs were obtained in a similar way. However, historical exposure levels before exposure measurements were available, were obtained only in 2005 based on overall job descriptions by long-serving middle management and were validated by the occupational physician. The precise description of job codes, exposure measurements and corresponding JEM are available from the authors in an unpublished report.

Occupational, medical and smoking histories were obtained from the questionnaires and the occupational physicians. At the French site, smoking habits had been recorded yearly during the occupational health check ups from the beginning of the 1990s onwards. In Austria, smoking history could only be obtained for subjects who had filled in a health questionnaire.

Statistical methods

Statistical analysis consisted of modelling the different health outcomes at the different points in time at which they were measured (date of questionnaire, *x* ray or lung function test) as a function of the estimates of the different occupational and other independent variables at these time points. The cumulative talc exposure at each time point was obtained as the sum, over all jobs held from date of hire to this time point, of the duration of this job in years, multiplied by the concentrations coded in the JEM expressed in mg/m³. The resulting cumulative exposure indices were thus expressed in years.mg/m³.

Lung function parameters were modelled using linear mixed models, fitted by maximum likelihood, the random effect part being the subject, in order to account for the correlation induced by the longitudinal nature of the data. The binary data (self-declared symptoms and radiological anomalies) were analysed using marginal logistic regression, fitted using generalised estimation equation techniques¹⁶ using the Stata package (Stata, College Station, TX, USA)

Each health outcome was modelled as a function of age, occupational talc exposure, smoking (either as smoking status or in pack-years of cigarettes) and other potential confounders. For each outcome, two talc exposure models were fitted. The first model fitted the overall cumulative exposure evaluated at each time point, thus assuming a constant effect of exposure. The second model fitted both the cumulative exposure at inclusion (ie, for each health outcome, at the moment at which it was first measured) and the cumulative exposure since inclusion. In this second model, the coefficient of the exposure at inclusion can be interpreted as the coefficient in a cross-sectional study including only the first end-point measurement with respect to estimates of the past (cumulative) exposure based on a mostly semi-quantitative exposure estimate. The coefficient with the cumulative exposure since inclusion estimates the mean individual longitudinal evolution of the end-point within the study period based on an actually measured exposure.

The linearity of the effects of the main continuous independent variables (age, pack-years, cumulative exposure) was tested by fitting quadratic terms.

Ethics

Each French study participant who could be contacted, signed an informed consent form. The study was approved by the French data protection authority (Commission Nationale Informatique et Libertés) and its committee on biomedical research. The Austrian law does not require a formal approval as long as the data are treated anonymously.

RESULTS

In the French talc mill, overall exposure decreased from a geometric mean exposure of 1.95 mg/m³ with a 3.9 geometric standard deviation (GSD) in 1986 (502 measurements) to 0.80 mg/m³ (GSD 4.3) in 2003 (208 measurements). These high GSDs are mainly due to the very different exposures according to different job codes; for instance in the 1985–1989 period plant cleaners were measured at an arithmetic mean of 11.3 mg/m³ based on 97 measurements, and office workers were measured at 0.16 mg/m³ based on 156 measurements. Between 2000 and 2004, the highest exposure was measured in the granulation area (9.7 mg/m³, 26 measurements) where workers wore dust masks, so that the corresponding JEM exposure value was 3 mg/m³. The lowest exposure was measured in process automation (0.1 mg/m³ based on 11 measurements) and in other jobs not directly in contact with production.

At the extraction site exposure decreased steadily from a geometric mean exposure of 0.67 mg/m³ (GSD 4.4) in 1990 based on 233 measurements to 0.37 mg/m³ (GSD 3.1) in 2003 based on 162 measurements. The between-job variance was slightly lower than in the mill. The highest exposure was consistently measured in the laboratory where samples are milled and ranged from 18.8 mg/m³ (19 measurements) in the 1990–1994 period to 5.6 mg/m³ (44 measurements) in 2000–2004. The laboratory workers wore high performance dust

masks so that the corresponding JEM was coded 2 mg/m³ since 1992 and 20 mg/m³ previously. All other jobs had exposure means below 1 mg/m³ in 2000–2004.

Overall, 176 job-time periods were identified. An exposure greater than 5 mg/m³ was coded for 28 job periods all of which ended before 1992. The highest current JEM levels are in the granulation workshop and bag filling stations at 3 mg/m³. Before 1985 a number of highly exposed jobs were recorded, the highest of which was at a bag filling station at 20 mg/m³ until 1984 and one old milling workshop before 1967.

In the Austrian talc mill, the geometric mean exposure between 1988 and 1995 was 0.75 mg/m³ (GSD 3.67) based on 416 measurements. Since 1996 it has changed little, remaining at 0.30 mg/m³ (GSD 3.25) based on 237 measurements. A total of 386 measurements were obtained at the extraction site between 1992 and 2000. While in the first 2 years the geometric mean exposure was 0.65 mg/m³ (GSD 5.3), since 1994 the exposure has been stable at 0.32 mg/m³ (GSD 3.4). The JEM contained 47 job-time period combinations. An exposure higher than 5 mg/m³ was coded for 13 job periods in a talc company taken over in the late 1980s in which no measurements had been performed but in which the exposure was described as high. Currently no exposure exceeds 1 mg/m³.

Table 1 presents the population and study characteristics along with mean assessed exposure at inclusion and between inclusion and last examination (see supplementary online tables A and B for data by site).

In all, 1421 valid spirometries were selected from those available from the quality control process. Overall, ignoring the exposure, forced expiratory volume in 1 s (FEV₁) decreased by 25 ml per year (95% CI –21 to –29) and increased by 57 ml per centimetre height in non-smoking males (which is compatible with the prediction equations from the European Respiratory Society¹⁰ values of 29 ml/year and 43 ml/cm) and decreased by 40 ml/year among smokers. The standardised values (based on expected values according to age, sex and height) decreased with total cumulative exposure (see supplementary table C) but not with the cumulative exposure since inclusion (see supplementary table D). This is confirmed in the regression models adjusted for cumulative smoking (table 2). FEV₁ decreased by 6.58 ml per 10 years.mg/m³ of the overall cumulative exposure, which was non-significant but borderline. In the model of both cumulative exposure as assessed at time of first spirometry and cumulative exposure since inclusion, only the former decreased with borderline statistical significance by 7.26 ml per 10 years.mg/m³, while the increase by 7.75 ml per 10 years.mg/m³ exposure since inclusion had a very large confidence interval, including the estimated overall decrease. In the same model FEV₁ decreased by 6.16 ml per pack-year. It is notable that no such difference can be seen for smoking: when separating pack-years at inclusion and pack-years since inclusion as the estimated effect of cumulative smoking is virtually identical.

Similarly, forced vital capacity (FVC) decreased overall by 7.71 ml per 10 years.mg/m³, and when separating according to period of exposure it decreased significantly by 8.47 ml per 10 years.mg/m³ of exposure at inclusion and increased non-significantly by 10.24 ml per 10 years.mg/m³ exposure since inclusion. Finally, when considering the FEV₁/FVC ratio, the only significant effect was the effect of smoking, as no effect of the exposure could be detected in either of the two models.

Overall, 1153 standard radiographs from the study population were read. Of those radiographs, 40 (3.8%) were assessed as 1/0 or higher, all of which were from male subjects. This prevalence, as well as the prevalence of all 0/1+ opacities, was found to

Table 1 Basic descriptions of the study population

	All subjects	All subjects with at least 2 examinations
n (%)	398 (93%)	378 (88%)
Men, n (%)	349 (94%)	335 (90%)
Women, n (%)	49 (84%)	43 (74%)
At inclusion in the study population		
Age, mean (SD) min–max	33.3 (8.8) 18.2–59.6	32.6 (8.3) 18.2–51.8
Duration of past exposure in years, mean (SD) min–max	10.9 (8.4) 0–36.5	10.6 (8.1) 0–36.5
Past cumulative exposure in years.mg/m ³ , mean (SD) min–max	41.3 (69.6) 0–359	40.9 (70.1) 0–359
Mean past exposure level in mg/m ³ , mean (SD) min–max	3.4 (5.1) 0–30	3.5 (5.3) 0–30
Smoking status at inclusion		
Missing, n	16	7
Non-smoker, n (%)	147 (38%)	145 (39%)
Current smoker, n (%)	181 (47%)	178 (48%)
Pack-years of cigarettes, mean (SD)	12.5 (11.1)	12.1 (10.8)
Ex-smoker, n (%)	54 (14%)	48 (13%)
Since first examination (inclusion)		
Duration of follow-up in years, mean (SD) min–max	14.0 (5.7) 0–25.3	14.5 (4.8) 0.6–25.3
Cumulative exposure in years.mg/m ³ , mean (SD) min–max	21.6 (29.0) 0–209.6	22.6 (29.3) 0–209.6
Mean exposure level in mg/m ³	1.45 (1.64) 0.1–13.2	1.46 (1.65) 0.1–13.2
Number of lung function measurements per subject, mean (SD) min–max	4.1 (2.7) 1–14 (n = 344)	4.8 (2.5) 2–14 (n = 283)
Number of x ray measurements per subject, mean (SD) min–max (n)	3.0 (0.9) 1–5 (n = 388)	3.1 (0.8) 2–5 (n = 359)
Number of questionnaire measurements per subject, mean (SD) min–max (n)	1.8 (0.9) 1–3 (n = 376)	2.7 (0.4) 2–3 (n = 180)
Smoking status at last examination		
Missing, n	27	18
Non-smoker, n (%)	146 (39%)	144 (40%)
Current smoker, n (%)	86 (23%)	83 (22%)
Pack-years of cigarettes, mean (SD)	26.9 (15.8)	26.7 (17.1)
Ex-smoker, n (%)	139 (37%)	133 (37%)

increase with the exposure estimation at inclusion but not with the cumulative exposure since inclusion (see supplementary tables C and D). In a marginal logistic regression model adjusted for smoking status, restricted to the group of 1054 radiographs from males (table 3), the probability of observing a 1/0+ radiograph increased significantly with the cumulative exposure assessed at the time of the first available radiograph but decreased non-significantly with the cumulative exposure since inclusion. The readers recorded 24 pleural abnormalities: seven costophrenic angle obliterations, 16 pleural plaques (of which 13 were unilateral), and one calcification. In none of four subjects with pleural abnormalities diagnosed by x ray, or in 23 other workers, did the hCT scan detect any pleural abnormality. No statistically significant increase was observed with increasing talc exposure. This was also true when considering only pleural plaques (data not shown).

The number of standardised respiratory symptoms questionnaires was low with only 689 questionnaires. The prevalence of declared symptoms was low with 17 cases of chronic bronchitis and 21 cases of self-declared breathlessness (table 4). Except for the expected effect of quantitative smoking on the prevalence of both chronic bronchitis and the related but less specific symptom of usual cough or phlegm, no significant effect could be shown.

DISCUSSION

The present study presents the results of a 15-year survey of the exposure and respiratory health endpoints of two populations of talc workers with a nearly complete follow-up. To our knowledge, no subject left employment due to respiratory

Table 2 Random effect linear regression models of the lung function parameters as a function of confounders and cumulative exposure variables (n = 1368)*

	FEV ₁ (ml)†	FVC (ml)‡	FEV ₁ /FVC (%)
	Regression coefficient (95% CI)	Regression coefficient (95% CI)	Regression coefficient (95% CI)
Regression model including confounders§ and total estimated cumulative exposure			
Pack-years of cigarettes	−6.11 (−9.46 to −2.75)	−3.72 (−7.40 to −0.04)	−0.073 (−0.116 to −0.029)
Total cumulative exposure per 10 years.mg/m ³	−6.58 (−13.81 to 0.65)	−7.71 (−15.45 to 0.03)	−0.000 (−0.090 to 0.090)
Regression model including confounders, cumulative exposure at inclusion and cumulative exposure since inclusion			
Pack-years of cigarettes	−6.16 (−9.52 to −2.81)	−3.79 (−7.47 to −0.10)	−0.073 (−0.117 to −0.030)
Cumulative exposure at inclusion per 10 years.mg/m ³	−7.26 (−14.65 to 0.13)	−8.47 (−16.38 to −0.57)	−0.004 (−0.096 to 0.087)
Cumulative exposure since inclusion per 10 years.mg/m ³	7.75 (−25.49 to 40.99)	10.24 (−28.22 to 48.70)	0.105 (−0.364 to 0.574)

*n, number of valid measurements; †FEV₁, forced expiratory volume in 1 s; ‡FVC, forced vital capacity; §the confounders are, in addition to pack-years, the type of apparatus, sex, sex-specific age and height and medical histories.

Table 3 Population-averaged logistic regression models of the prevalence of small radiological opacities and pleural shadows as a function of confounders and cumulative exposure variables in the combined male study population

	Profusion $\geq 0/1$	Profusion $\geq 1/0$	Pleural abnormalities*
Number of positive radiographs (% of 1054†)	131 (12.4%)	40 (3.8%)	19 (1.8%)
Number of subjects with at least one positive finding (% of 343‡)	93 (27.1%)	31 (9.0%)	16 (4.9%)
	OR (95% CI)	OR (95% CI)	OR (95% CI)
Logistic regression model including confounders§ and total estimated cumulative exposure			
Smoker	1.61 (1.06 to 2.48)	1.75 (0.76 to 3.67)	– (–)
Obesity¶	– (–)	– (–)	3.78 (1.17 to 12.3)
Austrian site	1.75 (1.07 to 2.83)	1.42 (0.57 to 3.52)	3.03 (1.08 to 8.50)
Total cumulative exposure per 10 years.mg/m ³	1.044 (1.020 to 1.070)	1.048 (1.016 to 1.082)	1.048 (0.992 to 1.108)
Logistic regression model including confounders§, cumulative exposure at inclusion and since inclusion			
Smoker	1.52 (0.99 to 2.34)	1.62 (0.76 to 3.42)	
Obesity	– (–)	– (–)	3.63 (1.16 to 11.36)
Austrian site	1.54 (1.06 to 2.51)	1.20 (0.487 to 2.945)	3.63 (1.23 to 10.80)
Initial cumulative exposure per 10 years.mg/m ³	1.056 (1.031 to 1.085)	1.060 (1.028 to 1.095)	1.036 (0.960 to 1.119)
Cumulative exposure since inclusion per 10 years.mg/m ³	0.917 (0.838 to 1.004)	0.858 (0.708 to 1.041)	1.145 (0.980 to 1.336)

*Defined as any pleural abnormality on x ray not rejected by later high-resolution computed tomography; †number of radiographs obtained in the male study population; ‡number of male subjects with at least one radiograph; §the confounders are smoking and site (for small opacities) or obesity and site (for pleural shadows); ¶obesity is defined as a body mass index greater than 30 kg/m².

problems, and as the health check ups were compulsory we are confident that no informative drop-out occurred.

Exposure assessment during the study period can be considered reasonably precise, given the large number of exposure measurements which were all personal samples and obtained using the same measuring device. However, because of the number of jobs coded and the inherent variability of exposure measurement data, evaluation of individual exposure could not rely solely on measurements. Thus exposure evaluations were grouped by job and 5-year time periods (periods were sometimes shorter when information concerning changes in industrial processes was available from the company). Another important factor influencing individual exposure was the use of personal protective equipment which was taken into account at a per job-period level. However, some misspecification of

quantitative exposure levels is unavoidable even within the study period. On the other hand, this exposure misclassification is likely to be more important in the assessment of the initial cumulative exposure which was not based on actual measurements. At the French site, previous (pre-1985) exposure varied substantially between job codes and between time periods. Moreover, a job period exposure matrix had been set up by the end of the 1980s, so the relative accuracy of the exposure estimation is probably good. At the Austrian site, on the other hand, estimation of past exposure was certainly less precise as these estimates were obtained much later.

With respect to the measurement of health endpoints, the weakest evidence comes from the symptoms questionnaire which was only used a mean of about twice at the French site and less at the Austrian site. Moreover, the mean duration of

Table 4 Population-averaged logistic regression models of the prevalence of self-declared respiratory symptoms as a function of confounders and cumulative exposure variables in the combined study

	Chronic bronchitis*	Usual cough or phlegm†	Dyspnoea‡
Number of symptoms (% of 689)	17 (2.5%)	114 (16.6%)	21 (3.1%)
Number of subjects with at least one reported symptom (% of 376)	13 (3.5%)	85 (22.6%)	18 (4.8%)
	OR (95% CI)	OR (95% CI)	OR (95% CI)
Regression model including confounders§ and total estimated cumulative exposure			
Age in years	1.043 (0.988 to 1.103)		
Pack-years of cigarettes	1.027 (1.003 to 1.053)	1.029 (1.014 to 1.045)	
Total cumulative exposure per 10 years.mg/m ³	1.014 (0.963 to 1.068)	1.021 (0.993 to 1.050)	1.040 (0.997 to 1.087)
Regression model including confounders§, cumulative exposure at inclusion and since inclusion			
Age in years	1.039 (0.982 to 1.099)		
Pack-years of cigarettes	1.040 (1.014 to 1.067)	1.028 (1.013 to 1.044)	
Cumulative exposure at inclusion per 10 years.mg/m ³	1.032 (0.985 to 1.081)	1.014 (0.983 to 1.046)	1.031 (0.985 to 1.080)
Cumulative exposure since inclusion per 10 years.mg/m ³	0.473 (0.193 to 1.158)	1.250 (0.986 to 1.584)	1.402 (0.870 to 2.257)

*Defined as chronic cough and phlegm for more than 3 months per year for at least the last 2 years; †defined as any usual cough or chronic phlegm fulfilling or not the criteria for chronic bronchitis; ‡defined as breathlessness while walking up a slight hill; §the confounders are pack-years of cigarettes for chronic bronchitis and usual cough and/or phlegm and age for dyspnoea.

follow-up was less than 5 years. Consequently, the statistical power showing any exposure effect is quite weak. Nevertheless, the prevalence of self-reported symptoms is low.

On the other hand, approximately three standardised chest *x* rays were available for each subject in both populations and the mean duration of radiological follow-up (the period between the first and last *x* ray) was much higher. The reading protocol was targeted towards increased sensitivity of detecting pleural anomalies as each radiograph was reread in consensus if one of the readers detected a pleural abnormality. This was probably at the price of poor specificity, as no pleural abnormalities were confirmed by hCT scan. Moreover, the statistically significant relationship with obesity suggests that the presence of sub-pleural fat (mentioned in three hCT scans of subjects diagnosed with a pleural plaque) might have been mistaken for pleural plaques.

With respect to small opacities, external validation was obtained by noting that the prevalence of the recorded profusions in the unexposed control population (22% 0/1+, 13% 1/0+) as assessed by the study reader panel, was intermediate between the readings from two earlier panels who had read these same *x* rays (one from the Institute of Occupational Medicine, Edinburgh (Dr Miller, Institute of Occupational Medicine, 2004, personal communication) and one within an earlier study).¹¹

The high number of validated spirometries at the French site and the long survey time compensate, at least partially, for the less than optimal quality of some of the forced expiratory manoeuvres. Although the within-measurement repeatability of the individual spirometries could not be assessed post hoc as only the best spirometry trace was kept in the archives, this is highly unlikely to influence assessment of the long-term evolution of individual respiratory health. One way of assessing the overall validity of the spirometries is by comparing the study estimates with the known effect of factors such as age, height and smoking. The effect of ageing both among non-smokers (25 ml/year) and smokers (40 ml/year) is on the low side of that expected, especially in comparison with cross-sectional studies. This may be due to a healthy worker effect and possibly to the rural environment in which the sites are located. Still, this decline is slightly greater than in the population considered by Burchfiel *et al*¹⁷ who report a 22 ml/year decline among non-smokers and 33 ml/year among smokers. The present paper presents statistical analyses using up-to-date statistical methodology specifically developed for longitudinal data. These analyses take into account two kinds of variables, some of which are intrinsic to each subject, such as sex, height and exposure burden as regards both smoking and occupational dust when entering the study, and some of which vary for each subject within the study, such as age, occupational exposure and quantitative smoking. In a longitudinal study, the parameter of primary interest is the effect of exposure on the mean decline in the respiratory parameter (or increase in prevalence of symptoms) of each person within the study and not differences between individuals. Thus the models which separate the cross-sectional (between-subject) and longitudinal (within-subjects) effects are more informative than the models incorporating the overall cumulative exposure in which both effects are confounded. In the present study the model separating exposure at inclusion and since inclusion have another justification, as the latter variable is based on actual exposure measurements, whereas the former is to a large extent dependent on expert quantification whose quality cannot be checked. Unfortunately, the precision of the longitudinal effects

is lower than that of the cross-sectional effects, as the within-subject exposure variance is much lower than the between-subject exposure variance.

The present study shows that talc exposure can lead to an increase in the prevalence of small radiological opacities and diminished expiratory volumes. However, only the cumulative exposure as assessed at the beginning of the survey in the late 1980s was associated with the health endpoints and their longitudinal evolution was only related to smoking and not to occupational exposure. In fact, after adjustment on the (cross-sectional) between-subject exposure at inclusion, the cumulative exposure within the study period (ie, since inclusion) was even negatively associated with the prevalence of small opacities (although this was not statistically significant). Similarly, expiratory volumes were positively associated with cumulative exposure within the study period. However, the confidence intervals were quite large so the estimated decrease in the expiratory volumes with the cumulative exposure at inclusion is still statistically compatible with their estimated increase with the study period exposure.

These results are surprising as exposure cannot improve health. We propose three alternative or complementary interpretations for these findings.

- ▶ The first is that at the measured exposure levels (in general lower than 2 mg/m³), no discernible effects of exposure exist.
- ▶ A second explanation would be that the effect of talc exposure is not immediate, but lags in time. Thus, recent exposure (ie, since inclusion) would have no relevance and its effects would not yet be apparent. This was explored by fitting an exposure lagged by 5 years (see supplementary tables E and F). Qualitatively the results are similar, with slightly larger regression coefficients for the lagged exposure. However, the regression coefficients for the lagged cumulative exposure since inclusion are close to zero (spirometry) or negative (radiology).
- ▶ A third interpretation is simply that the results of the present study are too weak to be interpreted and that the difference in slopes between the two cumulative exposure variables is a statistical fluke. This might be an explanation for the results of the lung function tests, as this difference in slopes is not statistically significant. However, it appears clear from our data that the exposure levels which existed during the study period (ie, since the late 1980s) were not associated with an increase in the prevalence of small radiological opacities.

We are aware of three respiratory health studies of talc-exposed workers, including some exposure quantification. In a study of talc-exposed rubber workers,⁶ the authors estimated a statistically significant 26 ml decrease in FEV₁ per year in employment adjusted for age and smoking in a cross-sectional study of 69 workers, while no significant decrease was found for FVC. The measured dust concentration was lower than 1 mg/m³ for most of the jobs and the authors considered it unlikely that exposure had been much higher in the past. None of the workers had a chest *x* ray showing definite talc pneumoconiosis. In a cross-sectional study⁷ of 116 Vermont talc miners and millers and 1-year follow-up evaluation of 103 subjects, cumulative exposure was found to be significantly correlated with FEV₁/FVC but not with FVC or FEV₁. Moreover, exposure to talc was associated with small opacities. In this study, a 1.5 mg/m³ exposure was considered typical. The last study with a quantitative exposure estimation is the cross-sectional study of 166 French talc millers which is partially included in the

Main message

Talc not containing asbestiform fibres does not appear to have a specific effect on respiratory health.

present longitudinal study.⁸ In this earlier study, exposure was higher and both FEV₁ and FVC decreased significantly with cumulative exposure and the prevalence of small lung opacities increased.

Finally, a recent study¹⁸ among craft workers of soapstone (talc) contaminated with tremolite asbestos showed a high prevalence of small lung opacities and abnormal spirometries.

The main results of the present study are similar to the cross-section results among French talc millers. However, all dose-response relationships were shallower than in the earlier paper. The decrease in FEV₁ (respectively FVC) was estimated at 132 ml (resp 146 ml) for 100 years.mg.m⁻³ in this earlier study. This can be compared with the 66 ml (78 ml) in the present study. Soutar and Hurley¹⁹ have estimated the average loss of FEV₁ attributable to coal dust exposure to be 122 ml (still per 100 years.mg.m⁻³). A recent cross-sectional study of carbon black-exposed workers²⁰ estimated the loss at 120 ml, but found no effect whatsoever for FVC. Therefore, it seems unlikely that talc exposure is associated with any specific loss of FEV₁.

In conclusion, although early exposure levels to talc as assessed at inclusion were associated with decreased lung function and an increased prevalence of small radiological opacities, there was no evidence of detrimental effects of talc exposure, as assessed within the study period, on lung function and small radiological opacities.

Acknowledgements: We thank the Rio Tinto Minerals Company for its continued support of this study; Dr Brian Miller for providing the control x rays and their ratings by the IOM; Dr Abraham Bohadana for his critical assessment of the spirometries and for his involvement in the steering committee of this study; Dr Anna Jandl, Dr Irmgard Schiller and Dr Marc Zitter, the three x ray readers; Dr Christophe Paris for his reading of the scanners and comments on the draft paper; Dr Nicole Massin for her assessment of the medical antecedents; Bruno Roux for sharing his accurate knowledge of present and past working conditions at the French site and for answering numerous emails with respect to data quality problems; and Jocelyne Ferret, Paul Fragnier, Gertrud Gruber, Thomas Pänitsch, Richard Reder, Karl Rossegger, Christian Weber and Michaela Wiedner for their various contributions to this study.

Funding: The study was funded by INRS and AUVA. The Rio Tinto Minerals Company (formerly the Luzenac Group) provided funding for travel expenses, quality checking of the lung function measurements and quality checking of some of the x ray

measurements and data input. Most of the data were generated as part of the occupational health assessment of employees. The company did not influence the design of the study, its analysis or discussion. Publication was guaranteed, whatever the results, as part of the study protocol officially approved by the company.

Competing interests: None

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