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Exposure to thoracic dust, airway symptoms and lung function in cement production workers

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ABSTRACT: **Cement dust exposure has previously been associated with airway symptoms and ventilatory impairment. The aim of the present study was to examine lung function and airway symptoms among employees in different jobs and at different levels of exposure to thoracic dust in the cement production industry.**

At the start of a 4-yr prospective cohort study in 2007, exposure to cement dust, symptoms and lung function were recorded cross-sectionally in 4,265 employees in 24 European cement plants. Bronchial exposure was assessed by 2,670 full-shift dust samples with cyclones collecting the thoracic aerosol fraction. A job exposure matrix was constructed by grouping dust concentrations according to job type and plant.

Elevated odds ratios for symptoms and airflow limitation (range 1.2–2.6 in the highest quartile), but not for chronic bronchitis, were found in the higher quartiles of exposure compared with the lowest quartile. Forced expiratory volume in 1 s (FEV_1) showed an exposure–response relationship with a 270-mL deficit of FEV_1 (95% CI 190–300 mL) in the highest compared with the lowest exposure level.

The results support the hypothesis that exposure to dust in cement production may lead to respiratory symptoms and airway obstruction.

KEYWORDS: **Airflow limitation, airway obstruction, cross-sectional studies, epidemiology, occupational exposure**

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The cement industry provides building material for land-based and off-shore installations. Cement is typically produced by heating a homogenous blend of limestone and clay, which is then adjusted to a suitable content of calcium, silicon, aluminium and iron in a kiln. During its heating to 1,450°C, clinker is formed, which contains calcium silicates, calcium aluminates and calcium ferrites. Clinker is subsequently ground with gypsum and other additives, resulting in a fine particulate powder called cement. In contact with water, clinker partly dissolves and forms an aqueous slurry of high alkalinity, giving clinker and cement strong irritant properties [1]. Cement production workers are exposed to airborne particles of raw materials, clinker, additives and to the final cement product, and their work has been linked to changes in lung function and airway symptoms [2].

Early studies on adverse respiratory effects of cement dust exposure include both non-positive studies and studies connecting cement production work with chronic airway inflammation and reduction of dynamic lung volumes [3, 4]. Other studies indicate a reduced forced vital capacity (FVC) or forced expiratory volume in 1 s (FEV_1) [5–9] and a higher prevalence of chronic respiratory symptoms [7–10] and chronic obstructive pulmonary disease (COPD) [11] in cement production workers.

Several studies of lung function in cement production workers were non-positive [10, 12–14]. Thus, the literature is conflicting and conclusions about exposure–response relationships or safe levels of exposure cannot be drawn [2].

To further investigate exposure–response relationships between cement dust exposure and respiratory effects, The European Cement Association (CEMBUREAU) has initiated a large, multi-national, 4-yr prospective study monitoring exposure and lung function in cement workers in 24 plants in eight countries. The cohort was established in 2007, with scheduled follow-up in 2009 and 2011, including spirometry tests and full-shift personal exposure

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measurements of the thoracic aerosol fraction in selected workers. Inhaled particles can penetrate and deposit in different parts of the human respiratory system, from the nose and mouth, to the bronchi and alveoli of the lung. Particles with a mass median aerodynamic particle size of 10 μm and geometric standard deviation of 1.5 are defined as the thoracic aerosol fraction and may penetrate into the lung [15]. The thoracic fraction was chosen because it was considered to be the most relevant health-related aerosol fraction with regards to bronchial exposure. This fraction estimates the particles that deposit in the bronchi, the site of hypothesised obstructive lung changes, better than inhalable dust, total dust or respirable dust [16]. The aims of the present study were to describe the cohort and present the initial cross-sectional analysis of lung function and airway symptoms and associations with exposure to thoracic dust in the cement production industry.

METHODS

Study population

Initially, all cement plants who were members of CEMBUREAU were candidates for participation in the study. We intended to include plants representing different geographical regions and exposure levels. 25 plants agreed to participate in the study, but for practical reasons, one plant in Turkey was excluded. The inclusion criteria at the plant level were: 1) completeness of personal records; 2) the possibility to perform spirometry tests on all employees as well as quantitative exposure measurements; and 3) no previous production of asbestos cement. Workers employed in the quarries were excluded to reduce distortion of the results by possible exposure to lung-reactive gases and dust other than cement dust. Furthermore, employees in out-sourced services were excluded to prevent problems with the tracking of individuals. 24 plants in eight countries were included, contributing 4,265 employees to the cross-sectional examinations performed in 2007 (table 1). Permissions from ethical research committees (REK Sør-øst, Oslo, Norway and Swedish committee for ethics, Stockholm, Sweden) were obtained. All participants signed a written consent form after receiving oral and written information about the study.

The questionnaires used in the study were translated into all nine languages spoken in the participating plants and the translations were checked by independent translators using the English version as the standard.

Spirometry and symptoms

Vitalograph 2160 spirometers (Vitalograph, Buckingham, UK) were made available to each plant. Spirometry was carried out by the occupational health service staff at each plant or by

TABLE 1 Study population characteristics of cement production plant employees in a multi-national cross-sectional study

	Total	Estonia	Greece	Italy	Norway	Spain	Sweden	Switzerland	Turkey
Plants	24	1	1	5	2	2	3	1	9
Employees	4265	112	100	541	249	330	331	93	2509
Total employees per country %	100	2.6	2.3	12.7	5.8	7.7	7.8	2.2	58.8
Age yrs	39.9±10	44.0±10	37.2±8.9	43.3±9.9	44.7±12	46.2±11	46.9±11	46.3±9.6	36.7±7.9
Males#	4002 (94)	50 (45)	92 (92)	536 (99)	211 (85)	318 (96)	303 (92)	91 (98)	2401 (96)
Asthma¶	116 (2.7)	6 (5.4)	3 (3.0)	24 (4.4)	19 (7.6)	17 (5.2)	16 (4.8)	5 (5.4)	26 (1.0)
Allergy+	527 (12)	31 (28)	13 (13)	102 (19)	71 (29)	94 (29)	68 (21)	24 (26)	124 (4.9)
Smoking information									
Never-smoker§	2055 (48)	41 (37)	38 (38)	331 (61)	112 (45)	156 (47)	195 (59)	35 (38)	1147 (46)
Former smoker	353 (8.3)	8 (7.1)	8 (8.0)	32(5.9)	53(21)	56 (17)	74 (22)	21 (23)	101 (4.0)
Smoker, unspecified	113 (2.6)	4 (3.6)	3 (3.0)	4 (0.7)	5 (2.0)	10 (3.0)	6 (1.8)	3 (3.2)	78 (3.1)
Current smoker									
1–9 cigarettes·day^{-1}	300 (7.0)	15 (13)	5 (5.0)	31 (5.7)	24 (9.6)	33 (10)	12 (3.6)	2 (2.2)	178 (7.1)
10–19 cigarettes·day^{-1}	730 (17)	30 (27)	14 (14)	77 (14)	40 (16)	33 (10)	29 (8.8)	10 (11)	497 (20)
≥20 cigarettes·day^{-1}	714 (17)	14 (13)	32 (32)	66 (12)	15 (6.0)	42 (13)	15 (4.5)	22 (24)	508 (20)
Smoking exposure pack-yrs	9.7±13	8.9±11	14±19	11±14	8.7±12	16±20	8.0±12	16±20	8.6±12
Job type reported									
Administration	629 (15)	15 (13)	20 (20)	48 (8.9)	34 (14)	41 (12)	40 (12)	14 (15)	417 (17)
Production	1406 (33)	48 (43)	34 (34)	142 (26)	73 (29)	132 (40)	109 (33)	28 (30)	840 (34)
Cleaning	80 (1.9)	16 (14)	1 (1.0)	43 (7.9)	4 (1.6)	5 (1.5)	5 (1.5)	1 (1.1)	5 (0.2)
Maintenance	1132 (27)	1 (0.9)	27 (27)	147 (27)	62 (25)	79 (24)	93(28)	28 (30)	695 (28)
Foreman	66 (1.5)	5 (4.5)	1 (1.0)	7 (1.3)	3 (1.2)	11 (3.3)	6 (1.8)	0 (0.0)	33 (1.3)
Laboratory	235 (5.5)	3 (2.7)	6 (6.0)	47 (8.7)	16 (6.4)	10 (3.0)	9 (2.7)	4 (4.3)	140 (5.6)
Other	543 (13)	12 (11)	11 (11)	95 (18)	9 (3.6)	43 (13)	26 (7.9)	2 (2.2)	345 (14)
Several job types	174 (4.1)	12 (11)	0 (0.0)	12 (2.2)	48 (19)	9 (2.7)	43 (13)	16 (17)	34 (1.4)
Previous exposureƒ	1643 (39)	64 (57)	48 (48)	247 (46)	129 (52)	154 (47)	239 (72)	42 (45)	720 (29)

Data are presented as n, mean±SD or n (%), unless otherwise stated. #: percentages are calculated by country; ¶: self-report of doctor-diagnosed asthma; +: self-report of allergy; §: never-smoker category includes those having smoked for <1 yr; some of whom reported a life-time dose >0 pack-yrs; ƒ: previous occupational exposure to dust or gases.

research staff familiar with the local conditions. All technicians participated in training sessions and received written manuals and instruction videos to standardise procedures. Site visits were performed to secure compliance with the study protocol.

Spirometry was performed according to the American Thoracic Society (ATS)/European Respiratory Society (ERS) guidelines [17]. Reversibility testing was not considered feasible and thus not performed. For repeatability and end-of-test (EOT) criteria, a 150-mL difference between the best and second best test of FVC and FEV_1 and 100-mL increase of volume during the last 2 s of the FVC manoeuvre were chosen, respectively. A valid FVC measurement should meet both the repeatability and EOT criteria. We calculated the FEV_1/FVC and the percentage of the predicted values for FVC (FVC % predicted) and FEV_1 (FEV_1 % predicted) using published reference values for Europeans [18]. Airflow limitation was determined according to two alternative definitions, using $FEV_1/FVC < 0.7$ as a common definition of COPD or $FEV_1/FVC <$ lower limit of the normal (LLN) calculated for age and sex [18].

Characteristics of the study population stratified by country are presented in table 1. Information on airway symptoms was collected on the day of the spirometry tests from all participants, using the International Union Against Tuberculosis and Lung Disease (IUATLD) questionnaire [19] with additional questions about respiratory and cardiovascular disease, allergy, asthma and smoking.

Exposure questionnaires and exposure assessment

In connection with spirometry, all participants filled out a questionnaire on personal historical occupational exposure developed by the National Institute of Occupational Health (NIOH, Oslo, Norway) and the National Coordinators of the study. Another questionnaire describing job types and work conditions on the day of exposure sampling was completed after each full-shift sampling by those employees selected to participate in exposure sampling. The same questions and categories were used as in the historical exposure questionnaire, with added information about the sampling (time, flow and equipment). Workers were selected for exposure measurements once or several times using a group-based strategy, but those who did not enter the cement production areas as part of their daily work were not selected for sampling. Personal full-shift samples of the thoracic aerosol fraction were collected using GK 2.69 thoracic cyclones (BGI Instruments, Waltham, MA, USA) in compliance with the thoracic sampling convention at a flow rate of 1.6 $L \cdot min^{-1}$ [16]. Dust was collected on 37 mm diameter PVC filters with pore size 5 μm (Millipore, Billerica, MA, USA; SKC Inc., Washington, PA, USA; and PALL Corp, Ann Arbor, MI, USA). Personal sampling pumps were adjusted to 1.6 $L \cdot min^{-1}$ before sampling. The airflow at the end of sampling was accepted if it was between 1.28 and 1.92 $L \cdot min^{-1}$, otherwise the measurement was considered not valid. The dust mass on the filters was determined by gravimetry according to a standard procedure using a Sartorius MC5 Micro Balance (Sartorius AG, Goettingen, Germany). The use of personal respiratory protection was reported in the questionnaire.

Statistical analysis

The exposure measurements were grouped by plant and job type in a job exposure matrix (JEM), where a group median exposure was calculated for each job type and plant combination. Job type categories used in the JEM were administration, production, cleaning, maintenance, foreman, laboratory and other, and an eighth category of workers reporting tasks in several job types. An exposure value was allocated to each employee based on the median value calculated in the JEM, which was independent of individual measurement values or non-participation in the exposure sampling. Associations between exposure and airway symptoms, airflow limitation and lung function were investigated using exposure estimated by two alternative strategies: 1) job types using the administration as reference and 2) exposure estimated using the JEM. As estimates obtained for administration personnel entering production areas were not representative of the majority of the administration employees not doing so, the administration was excluded from analyses that were based on the JEM. The JEM exposure value was either used in models assuming a linear relationship with outcomes, or categorised in quartiles and used as dummy variables in models not assuming linear relationships.

Lung function was analysed using the observed values of FEV_1, FVC and FEV_1/FVC in models adjusted for sex, age, standing height and smoking by multiple regression. Participants reporting doctor-diagnosed asthma were excluded from the main analysis.

Data input was performed in Access 2003 (Microsoft Corp., Redmond, WA, USA). SPSS 18.0 (SPSS Inc., Chicago, IL, USA) was used for descriptive statistics, logistic and linear regression analysis. Potential confounders were assessed and adjusted for if they altered the effect estimates of associations by $\geqslant$15%.

RESULTS

Spirometry and symptoms

A total of 4,265 participants completed questionnaires and performed spirometry tests. The prevalence of symptoms was higher in the production, maintenance, other and several job type groups compared with administration and in those reporting previous occupational exposure to dust or gases compared with no previous exposure (table 2). We obtained 3,332 (78%), 3,966 (93%) and 3,206 (75%) valid tests regarding FVC, FEV_1 and FEV_1/FVC, respectively. Reduced dynamic lung volumes were found in most exposed groups compared with administration (table 3).

FEV_1 was more affected than FVC. Lung function did not seem to be influenced by previous occupational exposure to dust and gases (table 3). Smoking was associated with increased symptom prevalence and reduced dynamic lung volumes (data not shown). FEV_1/FVC decreased with age and the prevalence of airflow limitation increased with age, using either $FEV_1/FVC < 0.7$ or $FEV_1/FVC <$ LLN (data not shown). Differences in asthma, allergy and smoking habits between countries were found (table 1).

Exposure

The geometric mean of 2,670 exposure samples was 0.85 $mg \cdot m^{-3}$ (geometric standard deviation 4.6). The group median values of thoracic dust levels in the JEM ranged from 0.07 to 36 $mg \cdot m^{-3}$. Using weighting by number of employees in each job type by plant group, exposure medians were divided into quartiles, resulting in delimiting values of 0.49, 1.08 and 1.73 $mg \cdot m^{-3}$

TABLE 2 Prevalence of self-reported symptoms during the last 12 months in categories of job type and previous occupational exposure in cement production plant employees

	Subjects n	Coughing	Wheezing and dyspnoea	Coughing, wheezing and dyspnoea	Chronic bronchitis
Job type					
Administration	629	100 (16)	23 (3.7)	11 (1.7)	9 (1.4)
Production	1406	286 (20)	87 (6.2)	64 (4.6)	57 (4.1)
Cleaning	80	15 (19)	2 (2.5)	1 (1.3)	3 (3.8)
Maintenance	1132	253 (22)	71 (6.3)	42 (3.7)	39 (3.4)
Foreman	66	16 (24)	3 (4.5)	3 (4.5)	2 (3.0)
Laboratory	235	51 (22)	15 (6.4)	11 (4.7)	8 (3.4)
Other/unknown	543	107 (20)	29 (5.3)	19 (3.5)	13 (2.4)
Several job types	174	45 (26)	22 (13)	15 (8.6)	8 (4.6)
Previous exposure#					
No	2622	493 (19)	135 (5.1)	85 (3.2)	71 (2.7)
Yes	1643	380 (23)	117 (7.1)	81 (4.9)	68 (4.1)

Data are presented as n (%), unless otherwise stated. #: previous occupational exposure to dust or gases.

between the quartiles. One JEM group of 37 employees with a level of 36 mg·m^{-3} was excluded as outliers from the JEM. The exposure levels by job type category are shown in figure 1. 95% gave information on their use of personal respiratory protection. No use, occasional use and use most of the time were reported by 18, 39 and 43% of employees, respectively. The use of personal respiratory protection was more prevalent most of the time in the highest quartile of median exposure, (65%), declining to 54% in the second highest quartile, 31% in the second lowest and finally, 35% in the lowest quartile.

TABLE 3 Lung function among cement production plant employees stratified on selected exposure variables and covariates

	FVC % pred	FEV1 % pred	FEV1/FVC %	FEV1/FVC <0.7	FEV1/FVC <LLN#
Valid data n	3332	3966	3206	3206	3206
Sex					
Female	107.7±16.2	100.8±14.7	80.3±6.7	13 (5.9)	13 (5.9)
Male	102.4±13.4	98.9±14.1	80.0±5.7	126 (4.2)	96 (3.2)
Allergy					
No	102.4±13.6	98.6±14.1	80.0±5.8	120 (4.3)	92 (3.3)
Yes	105.3±14.0	101.3±14.1	79.8±5.7	19 (4.8)	17 (4.3)
Doctor-diagnosed asthma					
No	102.7±13.7	99.1±14.0	80.1±5.7	124 (4.0)	95 (3.0)
Yes	105.0±15.3	94.7±18.3	76.1±7.9	15 (18)	14 (17)
Job type					
Administration	103.3±14.5	100.1±14.1	80.4±5.6	20 (4.0)	15 (3.0)
Production	103.5±14.1	99.0±14.1	79.8±5.9	46 (4.4)	37 (3.5)
Cleaning	104.6±12.1	101.0±11.5	79.5±5.3	3 (5.2)	3 (5.2)
Maintenance	102.1±12.4	99.4±13.5	80.2±5.8	29 (3.4)	23 (2.7)
Foreman	101.6±11.5	94.8±17.1	77.7±7.0	7 (14)	6 (12)
Laboratory	102.5±12.9	98.8±15.1	80.5±5.5	4 (2.3)	4 (2.3)
Other/unknown	100.8±14.1	97.2±14.3	80.2±5.5	15 (3.7)	12 (2.9)
>1 category	104.5±15.7	98.0±16.2	78.3±7.1	15 (13)	9 (7.8)
Previous exposure¶					
No	102.6±13.9	99.0±14.1	80.2±5.9	82 (4.1)	73 (3.7)
Yes	103.0±13.3	99.0±14.2	79.7±5.6	57 (4.6)	36 (2.9)

Data are presented as mean±SD or n (%), unless otherwise stated. FVC: forced vital capacity; % pred: % predicted; FEV1: forced expiratory volume in 1 s. #: lower limit of the normal (LLN) using the European Community for Coal and Steel/European Respiratory Society prediction equations for predicted values minus 1.64 mean squared deviation about the regression line (~5th percentile); ¶: previous occupational exposure to dust and gases.

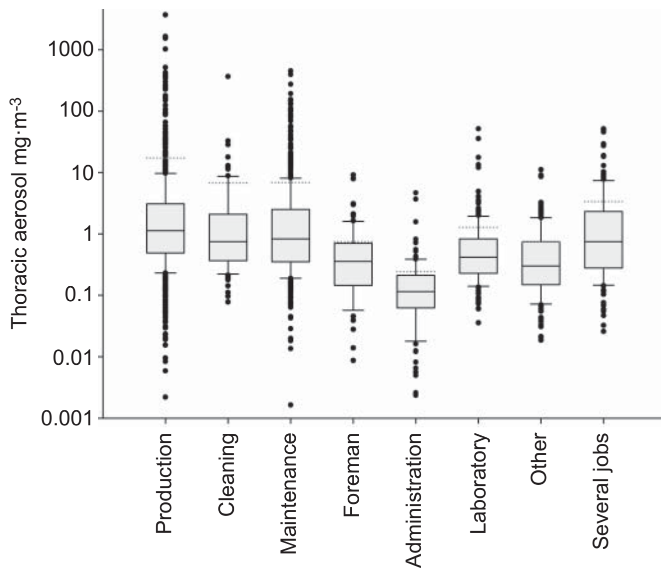

FIGURE 1. Thoracic fraction of dust measured by personal sampling according to job type. The median (central line in boxes), 25th–75th percentiles (boxes), 10th and 90th percentiles (whiskers) and extreme values (dots beyond the whiskers) by job type are shown. All plants were included (n=2,670 samples). Dotted lines represent the arithmetic means of exposure. The employees belonging to the administration job type and also participating in the sampling programme consist of employees working in administration, but serving tasks such as supervision in the production areas.

Associations between exposure and outcomes

The adjusted odds ratios (ORs) of symptom prevalence were higher in the production, maintenance, foreman, laboratory and several job type categories compared with administration, while airflow limitation was not associated with job type except among the foremen (table 4). Exposure from the JEM was associated with symptom prevalence (table 5) using the quartiles and the linear value of group median exposure. Reduced dynamic lung volumes were found in the production-related departments compared with administration (table 6). Exposure from the JEM was associated with reduced dynamic lung volumes using the quartiles and the nominal value from the JEM, showing a definite exposure–response relationship for FEV_1 (table 7).

Previous occupational exposure to dust and gases was associated with symptoms (table 4), but not with lung function (table 6). Among those with doctor-diagnosed asthma who were excluded from the primary analysis, both symptoms and reduced dynamic lung volumes were likewise associated with job type, but the associations were weaker (results not shown).

The set of dummy variables for plant confounded the effect estimates of cleaning on symptoms, of foreman on chronic bronchitis and of several job types on airflow limitation. For the lung volume analyses, adjustment for plant was necessary for all strata and job types. The coefficients for the set of dummy variables were highly significant both in models of symptoms and lung function, indicating that there are differences in the effect of job type according to plant (data not shown). In table 7 the associations are presented allowing for the use of personal respiratory protection, as the associations of FVC were confounded, but those of FEV_1 and FEV_1/FVC were not.

We analysed the influence of separate countries and age strata on the associations. Associations between exposure and lung function and symptoms were stronger among the non-Turkish participants, however, chronic bronchitis showed stronger associations among the Turkish participants. Associations with

TABLE 4 Odds ratios (ORs) of airway symptoms and airflow limitation by job type in cement production plant employees[#]

	Coughing	Wheezing and dyspnoea	Coughing, wheezing and dyspnoea	Chronic bronchitis	FEV_1/FVC <0.7[¶]	FEV_1/FVC < LLN[¶]
Valid data n	4149	4149	4149	4149	3124	3124
Job type						
Administration	1 (ref.)	1 (ref.)	1 (ref.)	1 (ref.)	1 (ref.)	1 (ref.)
Production	1.2 (0.9–1.6)	1.6 (0.9–2.7)	**2.7 (1.2–5.8)**	2.0 (0.9–4.4)	1.1 (0.6–1.9)	1.3 (0.6–2.6)
Cleaning	1.2 (0.6–2.5)	1.5 (0.3–7.4)	1.5 (0.2–13)	1.5 (0.4–6.3)	1.6 (0.4–6.5)	2.6 (0.6–11.6)
Maintenance	**1.6 (1.2–2.2)**	1.7 (1.0–2.9)	**2.2 (1.0–5.0)**	2.0 (0.9–4.4)	0.9 (0.5–1.7)	1.0 (0.5–2.2)
Foreman	**1.9 (1.0–3.7)**	1.1 (0.2–4.9)	3.0 (0.6–15)	3.2 (0.6–16)	2.9 (1.0–8.3)	**4.3 (1.3–14)**
Laboratory	**1.6 (1.0–2.4)**	1.5 (0.7–3.3)	**3.2 (1.2–8.6)**	2.1 (0.8–5.7)	0.7 (0.2–2.3)	0.8 (0.2–3.0)
Other/unknown	1.3 (0.9–1.8)	1.7 (0.9–3.1)	**2.6 (1.1–6.3)**	1.3 (0.5–3.2)	1.1 (0.5–2.2)	1.1 (0.5–2.5)
>1 category	1.5 (0.9–2.5)	**3.0 (1.4–6.5)**	**5.5 (2.0–16)**	1.5 (0.4–5.0)	1.7 (0.7–4.0)	1.3 (0.4–4.2)
Previous exposure[+]						
No	1 (ref.)	1 (ref.)	1 (ref.)	1 (ref.)	1 (ref.)	1 (ref.)
Yes	**1.2 (1.0–1.5)**	**1.6 (1.1–2.1)**	**1.8 (1.2–2.7)**	1.3 (0.8–2.0)	1.0 (0.7–1.6)	0.6 (0.4–1.1)

Data are presented as OR (95% CI), unless otherwise stated. Adjusted ORs and their 95% confidence intervals from logistic regression analysis are shown, adjusted for sex, age (yrs), smoking and plant. ORs statistically significant at the 5% level (two-sided) are shown in bold. FEV_1: forced expiratory volume in 1 s; FVC: forced vital capacity; LLN: lower limit of normal; ref.: reference category. [#]: employees reporting doctor-diagnosed asthma (n=116) were excluded from analysis; [¶]: airflow limitation was analysed using two alternative definitions: FEV_1/FVC <0.7 or FEV_1/FVC <LLN (using the European Community for Coal and Steel values for LLN as 5th percentile of predicted normal values); [+]: previous occupational exposure to dust and gases adjusted for sex, age (yrs), smoking, plant and job type.

TABLE 5 Odds ratios (ORs) of airway symptoms and airflow limitation by dust exposure level in cement production plant employees#

	Coughing	Wheezing and dyspnoea	Wheezing, dyspnoea and coughing	Chronic bronchitis	$FEV_1/FVC < 0.7$¶	$FEV_1/FVC <$ LLN¶
Valid data n	3495	3495	3495	3495	2599	2599
Exposure from JEM (quartiles) mg·m^{-3}						
< 0.49	1 (ref.)	1 (ref.)	1 (ref.)	1 (ref.)	1 (ref.)	1 (ref.)
0.49–1.08	1.2 (0.9–1.6)	**2.8 (1.7–4.5)**	**2.4 (1.3–4.4)**	1.0 (0.6–1.6)	1.5 (0.8–2.8)	1.4 (0.7–3.0))
1.09–1.73	1.0 (0.8–1.3)	**2.6 (1.6–4.2)**	**2.2 (1.2–4.0)**	0.6 (0.3–1.0)	1.7 (1.0–3.2)	**2.2 (1.1–4.4)**
>1.74	1.2 (0.9–1.6)	**2.6 (1.6–4.4)**	**2.3 (1.3–4.4)**	**0.5 (0.2–0.8)**	1.9 (1.0–3.5)	1.8 (0.9–3.8)
Exposure from JEM (linear) mg·m^{-3}						
Exposure effect+	1.03 (0.99–1.08)	**1.10 (1.02–1.18)**	**1.09 (1.00–1.19)**	0.88 (0.77–1.00)	1.06 (0.95–1.17)	1.05 (0.94–1.18)

Data are presented as OR (95% CI), unless otherwise stated. Adjusted ORs and their 95% confidence intervals from logistic regression analysis are shown adjusted for sex, age (yrs) and smoking. The data are a comparison between strata of exposure from the job exposure matrix (JEM) based on the median exposure allocated to each individual. ORs statistically significant at the 5% level (two-sided) are shown in bold. FEV_1: forced expiratory volume in 1 s; FVC: forced vital capacity; LLN: lower limit of normal; ref.: reference category. #: employees reporting doctor-diagnosed asthma (n=116) and employees in the administration (n=629) were excluded from analysis; 52 employees with a median exposure >26 mg·m^{-3} were excluded as outliers, as these were likely to be unrepresentative samples; ¶: airflow limitation was analysed using two alternative definitions: $FEV_1/FVC < 0.7$ or $FEV_1/FVC <$ LLN (using the European Community for Coal and Steel values for LLN as 5th percentile of normal values); +: exposure effect in mg·m^{-3} assuming linear associations between exposure taken from the exposure matrix and outcome, adjustments were made for sex, age (yrs) and smoking.

dynamic lung volumes did not change substantially on exclusion of participants country by country. When restricted to age <45 yrs, associations of job types with symptoms, chronic bronchitis, and airflow limitation were stronger except for the other and several job type groups. Using JEM values for exposure among those <45 yrs of age, associations with symptoms were stronger, except for chronic bronchitis, which was unchanged, and airflow limitation, which showed reduced estimates of effect.

DISCUSSION

In this multi-national study, we have demonstrated that exposure to dust in cement production plants is associated with airway symptoms as well as reduced dynamic lung

TABLE 6 Lung function differences according to job type and previous occupational exposure to dust and gases in cement production plant employees#

	FVC mL	FEV_1 mL	FEV_1/FVC %
Valid data n	3248	3857	3124
Job type			
Administration	0 (ref.)	0 (ref.)	0 (ref.)
Production	-70 (-140–6)	**-100 (-160– -40)**	-0.4 (-1.0–0.2)
Cleaning	**-200 (-390- -13)**	-150 (-300–1)	-1.1 (-2.7–0.3)
Maintenance	**-80 (-160– -4)**	**-77 (-140– -16)**	-0.2 (-0.8–0.5)
Foreman	+73 (-130–270)	-140 (-290–11)	-1.1 (-2.7–0.5)
Laboratory	**-120 (-240– -7)**	**-120 (-210– -25)**	-0.4 (-1,3–0.6)
Other/unknown	**-160 (-250– -71)**	**-130 (-210– -63)**	-0.1 (-0.8–0.7)
>1 category	**-190 (-340– -45)**	**-190 (-300– -85)**	0.2 (-0.9–1.4)
Previous exposure¶			
No	0 (ref.)	0 (ref.)	0 (ref.)
Yes	+23 (-30–75)	-18 (-59–23)	-0.2 (-0.6–0.2)

Data are presented as coefficient (95% CI), unless otherwise stated. Linear regression coefficients are interpreted as mL difference compared with administration (forced vital capacity (FVC) and forced expiratory volume in 1 s (FEV_1)) and % points of change compared to administration (FEV_1/FVC) with 95% confidence intervals. Adjustments were made for sex, age (yrs), standing height (cm), smoking and plant. Coefficients that were statistically significant at the 5% level (two-sided) are shown in bold. ref.: reference category. #: employees reporting doctor-diagnosed asthma (n=116) were excluded from analysis; ¶: previous occupational exposure to dust and gases were adjusted for sex, age (yrs), standing height (cm), smoking, plant and job type.

TABLE 7 Lung function differences by dust exposure level in cement production plant employees[#]

	FVC mL	FEV_1 mL	FEV_1/FVC %
Valid data n	2696	3244	2599
Exposure from JEM (quartiles) mg·m^{-3}			
<0.49	0 (ref.)	0 (ref.)	0 (ref.)
0.49–1.08	**-180 (-270– -99)**	**-140 (-200– -79)**	-0.4 (-1.0–0.3)
1.09–1.73	**-210 (-290– -120)**	**-210 (-280- -150)**	**-0.8 (-1.5– -0.2)**
Exposure >1.74 mg·m^{-3}	**-300 (-390- -220)**	**-270 (-330– -200)**	**-0.8 (-1.4– -0.2)**
Exposure from JEM (linear)[¶] mg·m^{-3}			
Exposure effect	**-32 (-48– -16)**	**-33 (-46– -21)**	**-0.15 (-0.27– -0.04)**

Data are presented as coefficient (95% CI), unless otherwise stated. Linear regression coefficients are interpreted as mL difference compared with the reference category (ref.) (forced vital capacity (FVC) and forced expiratory volume in 1 s (FEV_1)) and % points of change compared to the reference category (FEV_1/FVC) with 95% confidence intervals. Adjustments were made for sex, age (yrs), standing height (cm), smoking and the use of personal respiratory protection. Coefficients that were statistically significant at the 5% level (two-sided) are shown in bold. JEM: job exposure matrix. [#]: employees reporting doctor-diagnosed asthma (n=116) and employees in the administration (n=629) were excluded from analysis; 37 employees with a median exposure of >36 mg·m^{-3}, which was considered unrepresentative, and seven, nine and seven employees with uncertain height or age were excluded as outliers in the analysis of FVC, FEV_1, and FEV_1/FVC, respectively; [¶]: exposure effect per mg·m^{-3}, adjusted for sex, age (yrs), standing height (cm), smoking and the use of personal respiratory protection assuming linear associations between exposure taken from the JEM and outcome.

volumes (FEV_1 and FVC). This is in accordance with the study hypothesis. We utilised job types and exposure to the thoracic dust fraction, estimated by a within-study generated JEM as a measure of exposure.

Exposure–outcome associations

Exposure and airway symptoms were associated with ORs ranging between 1.2 and 2.6 in the highest quartile of exposure, comparable to a Danish study of cement production workers with a suggested median exposure level of 3 mg·m^{-3} of total dust and 0.5 mg·m^{-3} of respirable dust [11, 20]. Other studies including workers exposed to >10 mg·m^{-3} of total dust demonstrated excess symptoms among the highest exposed workers [8, 21–23]. The association of exposure with chronic bronchitis in the present study was weaker than with cough and wheezing. In a study from Taiwan with a mean exposure 3.6 mg·m^{-3} of respirable dust, ORs for symptoms ranged from 1.2 to 1.5, but were close to unity for chronic bronchitis [7], while in an earlier study, symptom prevalence was similar in workers exposed to 0.22, 0.55 and 1.2 mg·m^{-3} of respirable dust [24]. The median exposure level of 1.08 mg·m^{-3} of thoracic dust in the present study indicates lower respirable dust levels [15], probably similar to the latter Taiwan study [24].

Associations between FEV_1 and exposure were stronger than with FVC, both using job types and JEM values. These results support the hypothesis that inhalation of cement dust may lead to obstructive lung changes, which is in agreement with some studies where exposure was measured [6–8, 22, 23] but not with all [10, 12, 13, 24, 25]. The 270 mL lower FEV_1 estimated for the highest exposure category of the present study compares to the reduction found by YANG *et al.* [7], although their mean exposure of 3.6 mg·m^{-3} of respirable dust was probably higher than in our study. Also, using job titles for exposure, other studies found reduced lung function related to cement production [9, 26, 27].

In contrast, the prevalence of airflow limitation was not significantly increased in the exposed workers, except among foremen. A possible interpretation is that serious airflow limitation is rare at the exposure levels in the present study. In a Danish study with a median exposure of 3.3 mg·m^{-3} of total dust, airflow limitation was associated with cement production work only after 30 yrs of employment [11].

The findings of reduced dynamic lung volumes and increased prevalence of airway symptoms in cement dust-exposed workers are further supported by an *in vitro* study with rat alveolar macrophages challenged with cement dusts; pro-inflammatory changes and tumour necrosis factor-α activation were significantly associated with the calcium oxide content of the dust [28].

Design aspects

The prevalence of COPD may be overestimated using the FEV_1/FVC <0.7 criterion, particularly at older ages [29]. Using the LLN to define COPD allows for the age-dependent decline of the dynamic lung volumes. In a sensitivity analysis, we excluded participants with an age of $\geqslant$45 yrs and found that the OR of airflow limitation in the two highest exposure quartiles was reduced by half, but still statistically significant. Otherwise, sensitivity analysis in restricted age intervals and countries demonstrated stable associations across strata of age and countries. We also excluded participants reporting doctor-diagnosed asthma to improve comparability to COPD studies that included reversibility testing [30], although some of the excluded participants would not obtain normal lung function after bronchodilator use and still meet the COPD criteria. Misclassification of airflow limitation in the present study would probably dilute the effect estimate if independent of exposure status [31].

Using a cross-sectional design, we cannot control the selection into or out of the population, which may result in biased estimates [31]. However, selection effects will be reduced in the future longitudinal analysis. The validity of spirograms was ensured, but since a non-valid spirometry is possibly related to outcomes [32], we chose not to require the most stringent of published criteria. The chemical composition of the dust could not be evaluated in this study. This may lead to a misclassification of exposure regarding the inflammatory components of the dust, thus leading to a dilution of exposure–outcome associations assuming non-differential misclassification [31].

Unmeasured confounders, as well as information bias on, for instance, smoking habits, may result in either attenuated or positively biased associations [31].

Exposure

As the main health outcome in this study is the decline of FEV_1 conditioned on dust exposure, particles that deposit in the bronchial tree represent the exposure of interest. Therefore, the thoracic fraction of the workplace aerosol was considered the more relevant. To our knowledge, the present study is the first epidemiological study to estimate exposure to the thoracic fraction of workplace aerosol. It is surprising that this has not been done before because the thoracic fraction estimates the dust entering the lung more accurately than either the total or respirable dust fractions, and the criteria for health relevant particle size fractions were agreed upon in 1993 [16], after the initial suggestion of its criteria by the ACGIH (American Conference of Governmental Industrial Hygienists) in 1968 [15]. A further strength of this study is that we used administrative personnel as well as blue-collar workers with low exposure levels as references, and both strategies resulted in similar associations.

In order to minimise confounding from exposure to crystalline silica, quarry workers were excluded. Crystalline silica may also be found in the raw materials and in trace amounts in the final product. However, measurements indicate that exposure levels to crystalline silica in the jobs types included in this study could occur, but the levels are typically below the current occupational exposure limit (S. Gardi, Italcementi Group, Bergamo, Italy; personal communication).

We used the median exposure levels of job groups as exposure estimates to minimise the influence of outliers. However, the arithmetic mean exposure levels are probably higher. The levels of exposure varied substantially between plants, although all plants used a similar dry production process except the Estonian plant, which used a wet process. Different dust control measures, such as ventilation and filter technology, may partly explain such exposure differences (S. Gardi; personal communication).

The differential use of personal respiratory protection with more prevalent use in the higher exposure groups is considered to potentially dilute the associations between exposure and outcomes in this study; however, confounding was only found regarding FVC. In the analyses using job types for exposure, no confounding by use of personal respiratory protection was demonstrated, probably due to collinearity of variables.

Conclusions and interpretations

This cross-sectional study demonstrates increased prevalence of airway symptoms and reduction of dynamic lung volumes in production-related jobs compared with administrative jobs, as well as in cement production workers exposed to a median of $\geqslant 0.5 \text{ mg}\cdot\text{m}^{-3}$ of thoracic dust compared with workers exposed to levels below this. We demonstrated an exposure–response relationship between exposure and reduced FEV_1. The results support the hypothesis that dust exposure in the cement production industry may lead to obstructive lung function changes and airway symptoms.

Interpretation of the study should be performed with caution, since we have no control with selection of employees into and out of the population. This study continues as a prospective study measuring the individual changes in lung function and symptom occurrence.

SUPPORT STATEMENT

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STATEMENT OF INTEREST

A statement of interest for the present study can be found at www.erj.ersjournals.com/site/misc/statements.xhtml

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