Supplementary material.

Thoracic dust exposure in cement production is associated with decline of lung function

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Methods for exposure estimation

Exposure estimation from mixed effect models was performed in order to obtain estimated arithmetic values of exposure in groups of workers based on representative samples classified by combination of plant, job type, year, and season of sampling.

The data set for exposure assessment in this study was compiled from 7085 whole-shift samples and their respective filled-in questionnaire about work performance and sampling data in 24 cement production plants. Questionnaire data included measurement of airflow through the sampling filter and time at the start and end of the sampling. Twelve percent of the measurements were excluded before data analysis. The reasons for exclusion included obvious errors such as double-exposed filters, incorrect weight determination, particles with a larger size than expected, incorrect sampling procedure (in two plants), flow rate outside the accepted range, extreme observations (data points with standardized residuals above 3.29 or below -3.29 calculated from a linear regression model including job type, plant and year as indicator variables), and other technical problems as mentioned in Table A1 of Notø and coworkers (18). The modeling of exposure was performed using 6111 samples of thoracic aerosol mass obtained from the sampling campaign performed in 22 plants during three time periods, in 2007, 2009, and 2011-2012. Values below the detection limit (2.4%) were all positive and were used as observed in the statistical modeling.

The exposure data had a right-skewed distribution and were ln-transformed before parametric statistical analysis.

The exposure data have a multilevel dependency structure. Repeated measurements for workers are nested within job types and plants, while the workers are distributed over seasons and years. Mixed model regression analyses were performed with the predictors; plant, job type, year, and season as fixed effects and interaction between plant and job type and between plant and year, identity of the worker as random intercept, and plant specific residuals using restricted maximum likelihood estimation with a variance component covariance structure (18,19).

Models with different combinations of fixed effects were constructed by forward selection and subsequent likelihood ratio tests using maximum likelihood estimation. All models were finally estimated by restricted maximum likelihood.

The mixed models with fixed effects can be represented mathematically as described below:

$$y_i = \mu + \beta^{(1)}_{Plant_i} + \beta^{(2)}_{Job_i} + \beta^{(3)}_{Year_i} + \beta^{(4)}_{Season_i} + \beta^{(5)}_{Plant_i,Job_i} + \beta^{(6)}_{Plant_i,Year_i} + u_{Worker_i} + \varepsilon_i$$

Here, μ is intercept, $u_{Worker_i}$is a random intercept for worker, representing between-worker variation, with variance ${\sigma^2}_{bw}$, while ε_i is the residual term, representing within-worker variation. The residual variance ${\sigma^2}_{ww,Plant_i}$is allowed to differ between plants.

Estimated arithmetic means (AMs) of the thoracic aerosol level for all plant, job type, year, and season combinations were calculated from the regression coefficients of the mixed model and the variances of the random effect and the residuals using a method according to Seixas (20):

$$AM_{Plant_i,Job_i,Year_i,Season_i,} = e^{\left(\mu+\beta^{(1)}_{Plant_i}+\beta^{(2)}_{Job_i}+\beta^{(3)}_{Year_i}+\beta^{(4)}_{Season_i}+\beta^{(5)}_{Plant_i,Job_i}+\beta^{(6)}_{Plant_i,Year_i}+\frac{{\sigma^2}_{bw}}{2}+\frac{{\sigma^2}_{ww,Plant_i}}{2}\right)} \quad \text{(equation1)}$$

Model fit was evaluated by likelihood ratio tests and by inspection of standardized residuals. It is well acknowledged that this estimation of AM yields less biased estimates of cumulative exposure represented by the estimated AM times the follow-up time for each individual than using an alternative estimation based on the geometric mean exposure. In addition the estimated arithmetic means of the thoracic aerosol level in the job groups as described above (AM_{est}) were compared to their observed arithmetic means (AM_{obs}) by linear regression of the ln-transformed AMs. The regression equation $\ln AM_{est} = c + b*\ln AM_{obs}$ was back-transformed to $AM_{est} = e^c*AM_{obs}^b$. Linearity of the association between untransformed AM_{est} and AM_{obs} was evaluated by a Wald test of b=1.

Results

The full model is shown in Table S1. The estimated arithmetic means from equation 1 were plotted against the measured arithmetic means (Figure S1).The estimated arithmetic mean exposure is largely in agreement with the observed arithmetic mean exposure for each combination of plant and job type, but also shows substantial differences. However, low observed values were lower than the modeled data and high observed values were higher than the modeled data. This probably originated from the averaging effect of the regression model. The final mixed effect model explained 65 % of the between-worker variance and 4% (range 0-31) of the within-worker variance. A test of linearity of the association between untransformed AM_{est} and AM_{obs} was highly significant, t=13.4 (F=179), p=0.000, R^2_{adj}=0.74.

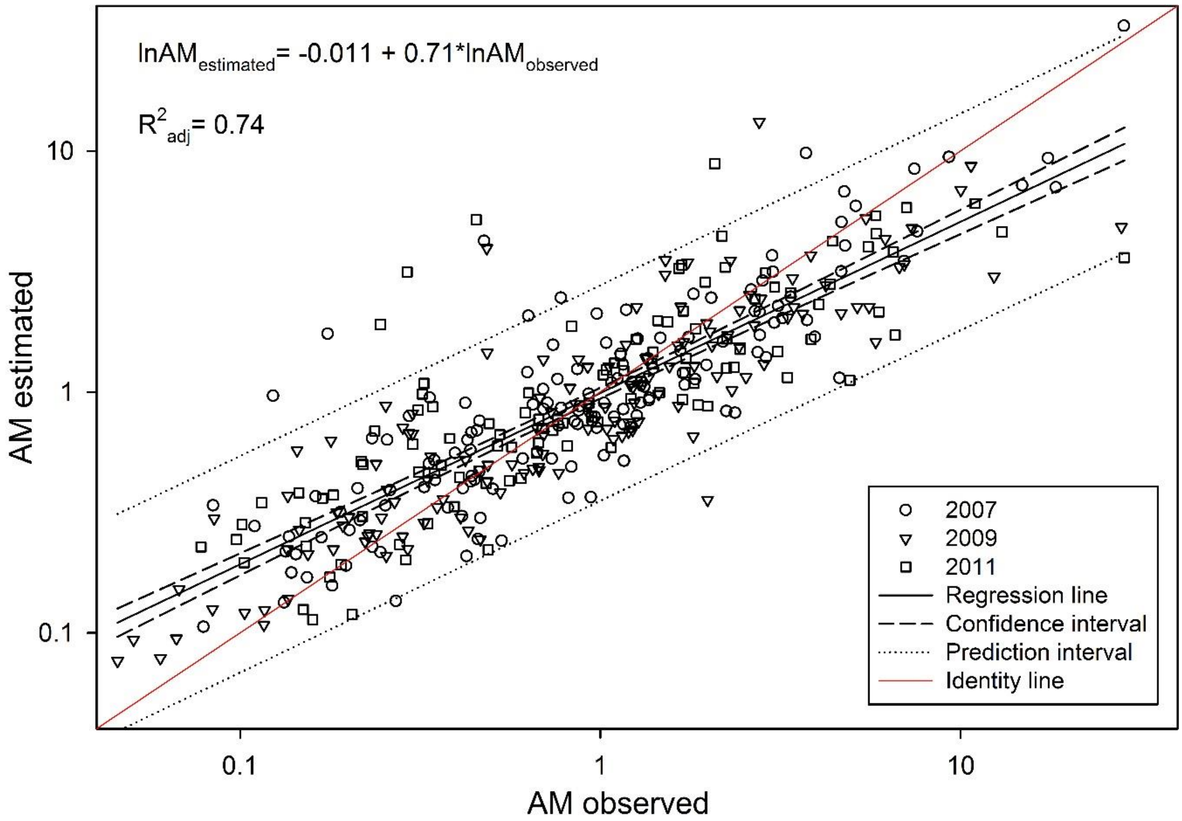

Figure S1: Observed arithmetic mean of personal thoracic measurements plotted against the estimated arithmetic mean values for each combination of plant, job type, and sampling year.

Prediction of individual exposures for participants in the lung function study.

The individual exposure estimates of workers participating in the lung function study were based on the estimated arithmetic means for plant, job type, year, and season (equation 1). As the sampling for exposure assessment was performed mostly in one or two out of four seasons in each plant during each measurement campaign, there was not enough data to model the seasonal variation in each plant. As shown in the models, common estimates of the seasonal variation for all 22 plants which were included in the modeling therefore ~~was included and~~ were used to predict exposure variation between seasons. We included a limited number of measurements on administration employees serving tasks within the production department areas, and the levels of these workers were generally low, amounting typically to about 20% of the levels among the production workers in the same plant or lower. We did not have measurement data suited for estimation of exposure in the administration job group as a whole.

Since the exposure measurements were obtained in 2007, 2009, and 2011-2012, while follow-up time of dynamic lung volumes included all years between baseline and follow-up investigations, we assumed that the exposures of of 2006 and 2008 were equal to 2007, while 2010 equals 2009, and 2012 equals 2011, season by season.

At baseline (time of inclusion), the individual exposures were taken as the average of exposure one year prior to baseline, to adjust for seasonal effects. For follow-up observations, the exposure was computed as the average between estimated exposure at baseline and exposure at the time of follow-up. If the time interval only comprises a part of a season, the exposure of that season is given weight equal to the part of the season covered (weight between 0 and 1). A change in job type during follow-up of a participant, if encountered, is assumed to occur exactly in the middle of the time interval between the observations before and after the job change.

The estimated AM exposures were classified into 5 exposure quintile groups. The quintiles were based upon the average individual exposures during the entire follow-up, from inclusion to the last follow-up. The ranges of predicted thoracic aerosol exposure in each of these quintile levels were 0.09-0.88, 0.89-1.55, 1.56-2.24, 2.25-3.35, and 3.36-14.6 mg m^{-3}, respectively. The participants belonging to administration at all observation times constituted a 6^{th} comparison group.

Table S1. Results from mixed model regression of ln-transformed values of thoracic dust in cement production workers including plant, job type, year and season, all as indicator variables

Factor	B[a]	SE[b]	p[c]	Factor	B[a]	SE[b]	p[c]
Intercept	0.35	0.27	0.18	**Plant x Job type**			
				1 x production	REF		
Job type				2 x cleaning	-0.84	1.27	0.51
Production	REF[d]			2 x maintenance	-0.54	0.58	0.35
Cleaning	1.18	0.27	< 0.001	2 x foreman	-0.18	1.31	0.89
Maintenance	0.78	0.52	0.14	2 x laboratory	-0.84	0.99	0.40
Foreman	-1.17	0.48	0.01	2 x other	0.03	0.77	0.97
Laboratory	-0.34	0.90	0.71	2 x multiple jobs	-2.05	0.45	< 0.001
Other	0.00	0.48	1.00				
Multiple jobs	0.33	0.25	0.18	3 x cleaning	-1.34	0.49	0.01
				3 x maintenance	-0.42	0.58	0.48
				3 x foreman	-0.22	0.55	0.70
Plant				3 x laboratory	-0.32	0.96	0.74
1	REF			3 x other	-1.13	0.69	0.10
2	-0.57	0.35	0.10	3 x multiple jobs	-0.35	0.73	0.63
3	-1.03	0.32	0.001				
4	-1.01	0.30	0.001	4 x cleaning	-1.15	0.33	0.001
5	-1.48	0.30	< 0.001	4 x maintenance	-0.81	0.54	0.14
6	-1.18	0.32	< 0.001	4 x foreman	-0.16	0.56	0.78
7	-1.26	0.28	< 0.001	4 x laboratory	-0.27	0.92	0.77
8	-0.33	0.31	0.29	4 x other	-0.75	0.51	0.14
9	-0.96	0.33	0.003	4 x multiple jobs	-0.74	0.51	0.15
10	-0.43	0.29	0.14				
11	-1.29	0.29	< 0.001	5 x cleaning	-0.80	0.33	0.02
12	-1.18	0.32	< 0.001	5 x maintenance	-0.75	0.54	0.17
13	-0.89	0.33	0.008	5 x foreman	0.35	0.60	0.55
14	-1.18	0.30	< 0.001	5 x laboratory	-0.34	0.93	0.72

15	-1.09	0.38	0.004	5 x other	-1.13	0.52	0.03
16	-0.03	0.29	0.92	5 x multiple jobs	-1.29	0.50	0.01
17	0.55	0.32	0.09				
18	-0.78	0.30	0.009	6 x cleaning	-1.17	0.35	0.001
19	0.09	0.29	0.75	6 x maintenance	-1.01	0.56	0.07
20	1.17	0.31	< 0.001	6 x foreman	0.88	0.56	0.12
21	-0.22	0.30	0.46	6 x laboratory	-0.14	0.94	0.88
22	0.07	0.32	0.84	6 x other	-0.96	0.55	0.08
				6 x multiple jobs	0.04	0.56	0.94
Year							
2007	REF			7 x cleaning	-0.59	0.54	0.28
2009	-0.59	0.27	0.03	7 x maintenance	-1.15	0.54	0.04
2011	-0.56	0.27	0.04	7 x foreman	0.70	0.57	0.22
				7 x laboratory	0.05	0.92	0.96
Season				7 x other	-0.77	0.52	0.14
Winter	REF			7 x multiple jobs	-0.62	0.85	0.47
Spring	0.09	0.09	0.32				
Summer	0.14	0.10	0.17	8 x cleaning	-0.82	0.40	0.04
Autumn	0.31	0.07	< 0.001	8 x maintenance	-0.81	0.56	0.15
				8 x foreman	NM		
Plant x Year				8 x laboratory	-0.86	0.96	0.37
Plant x 2007	REF			8 x other	0.19	0.55	0.73
2 x 2009	0.84	0.35	0.02	8 x multiple jobs	-0.17	0.37	0.64
2 x 2011	0.12	0.35	0.74				
3 x 2009	0.65	0.30	0.03	9 x cleaning	-2.99	1.37	0.03
3 x 2011	NM[e]			9 x maintenance	-1.12	0.57	0.05
4 x 2009	-0.01	0.30	0.98	9 x foreman	0.34	0.67	0.61
4 x 2011	-0.13	0.30	0.66	9 x laboratory	-0.86	1.02	0.40
5 x 2009	-0.11	0.30	0.72	9 x other	-1.34	0.62	0.03
5 x 2011	0.76	0.30	0.01	9 x multiple jobs	-1.18	0.39	0.003

6 x 2009	0.55	0.30	0.07
6 x 2011	0.59	0.31	0.06
7 x 2009	0.49	0.29	0.10
7 x 2011	NM		
8 x 2009	-0.07	0.32	0.82
8 x 2011	1.05	0.33	0.002
9 x 2009	0.47	0.33	0.15
9 x 2011	0.44	0.34	0.20
10 x 2009	0.44	0.29	0.13
10 x 2011	0.31	0.31	0.32
11 x 2009	0.01	0.30	0.96
11 x 2011	0.43	0.32	0.17
12 x 2009	0.43	0.33	0.19
12 x 2011	0.44	0.33	0.18
13 x 2009	0.76	0.32	0.02
13 x 2011	0.88	0.34	0.01
14 x 2009	0.47	0.30	0.11
14 x 2011	0.42	0.32	0.19
15 x 2009	0.51	0.35	0.15
15 x 2011	1.39	0.37	< 0.001
16 x 2009	0.34	0.29	0.24
16 x 2011	-0.03	0.30	0.93
17 x 2009	0.05	0.33	0.89
17 x 2011	0.45	0.35	0.20
18 x 2009	1.13	0.32	< 0.001
18 x 2011	1.07	0.32	0.001
19 x 2009	0.25	0.33	0.45
19 x 2011	-0.21	0.33	0.53
20 x 2009	-0.08	0.31	0.79
20 x 2011	-0.23	0.33	0.48

10 x cleaning	-0.75	0.55	0.17
10 x maintenance	-1.13	0.55	0.04
10 x foreman	1.21	0.52	0.02
10 x laboratory	0.05	0.93	0.96
10 x other	-0.76	0.51	0.14
10 x multiple jobs	-0.72	0.53	0.18
11 x cleaning	NM		
11 x maintenance	-0.38	0.56	0.50
11 x foreman	0.81	0.65	0.21
11 x laboratory	-0.24	0.93	0.80
11 x other	-0.10	0.52	0.84
11 x multiple jobs	-0.42	1.15	0.72
12 x cleaning	-0.84	1.12	0.45
12 x maintenance	-0.50	0.57	0.38
12 x foreman	1.38	0.92	0.13
12 x laboratory	-0.27	0.98	0.78
12 x other	-0.23	0.57	0.68
12 x multiple jobs	-0.24	0.36	0.50
13 x cleaning	-0.88	0.42	0.04
13 x maintenance	-0.96	0.57	0.10
13 x foreman	-0.05	1.26	0.97
13 x laboratory	-1.46	1.02	0.15
13 x other	NM		
13 x multiple jobs	-0.44	0.53	0.41
14 x cleaning	-1.17	0.84	0.16

21 x 2009	1.01	0.30	0.001
21 x 2011	0.74	0.32	0.02
22 x 2009	1.21	0.33	< 0.001
22 x 2011	0.79	0.38	0.04

14 x maintenance	-0.71	0.56	0.21
14 x foreman	0.96	0.82	0.24
14 x laboratory	NM		
14 x other	-0.07	0.53	0.90
14 x multiple jobs	-0.20	0.30	0.50
15 x cleaning	-0.61	0.56	0.27
15 x maintenance	-0.50	0.60	0.41
15 x foreman	NM		
15 x laboratory	NM		
15 x other	-1.14	0.65	0.08
15 x multiple jobs	-0.55	0.41	0.18
16 x cleaning	NM		
16 x maintenance	-0.92	0.55	0.09
16 x foreman	0.57	0.65	0.39
16 x laboratory	-0.16	0.93	0.86
16 x other	-0.98	0.58	0.09
16 x multiple jobs	-0.26	0.55	0.64
17 x cleaning	NM		
17 x maintenance	-1.16	0.55	0.04
17 x foreman	1.30	1.00	0.19
17 x laboratory	-0.50	0.94	0.60
17 x other	0.29	0.99	0.77
17 x multiple jobs	-0.18	0.67	0.79
18 x cleaning	-0.56	1.11	0.61
18 x maintenance	-0.49	0.55	0.37
18 x foreman	-1.20	1.14	0.29
18 x laboratory	0.01	0.94	0.99
18 x other	0.17	0.57	0.76

18 x multiple jobs	-0.53	0.52	0.31
19 x cleaning	-1.58	0.90	0.08
19 x maintenance	-1.27	0.55	0.02
19 x foreman	1.46	0.98	0.14
19 x laboratory	-0.87	0.96	0.37
19 x other	-1.02	0.67	0.13
19 x multiple jobs	0.43	0.67	0.52
20 x cleaning	0.19	1.14	0.87
20 x maintenance	-0.68	0.56	0.23
20 x foreman	NM		
20 x laboratory	0.18	0.96	0.85
20 x other	-1.15	0.53	0.03
20 x multiple jobs	-1.53	0.60	0.01
21 x cleaning	NM		
21 x maintenance	-1.22	0.55	0.03
21 x foreman	0.85	0.95	0.37
21 x laboratory	-0.40	0.93	0.67
21 x other	-0.30	0.53	0.57
21 x multiple jobs	-0.71	0.44	0.10
22 x cleaning	NM		
22 x maintenance	-0.55	0.57	0.33
22 x foreman	NM		
22 x laboratory	-0.84	0.99	0.40
22 x other	-0.15	1.41	0.91
22 x multiple jobs	0.32	0.72	0.66

Random effects	full modell		model without fixed effects	
	Estimate	**SE**	**Estimate**	**SE**
${}_{BW}S^{2\,f}$	0.38	0.03	1.10	0.05
${}_{WW}S^{2\,g}$, by plant nr				
1	1.15	0.16	1.17	0.19
2	1.21	0.16	1.23	0.16
3	0.72	0.09	0.70	0.09
4	0.73	0.06	0.90	0.08
5	0.55	0.05	0.79	0.08
6	0.74	0.08	0.76	0.08
7	0.27	0.03	0.33	0.04
8	0.78	0.10	0.75	0.10
9	1.45	0.15	1.51	0.16
10	0.84	0.07	0.83	0.07
11	1.03	0.09	1.08	0.11
12	0.94	0.11	0.88	0.10
13	0.94	0.11	0.87	0.10
14	0.90	0.07	0.83	0.07
15	1.08	0.13	1.11	0.13
16	0.73	0.06	0.82	0.07
17	1.18	0.14	1.19	0.15
18	0.76	0.08	0.70	0.08
19	1.14	0.13	1.14	0.14
20	0.95	0.10	1.33	0.16
21	1.01	0.09	0.97	0.09

22	1.50	0.15	1.69	0.19

B=regression coefficient

SE=standard error

p=p-value

$_{BW}S^2$=between worker variance

$_{WW}S^2$=plant specific within worker variance

REF=reference

NM=no measurements

Person identity and plant were used as random intercept, with person identity nested in plant.

Other covariates were used as fixed effects.