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Increased Decline in Pulmonary Function Among Employees in Norwegian Smelters Reporting Work-Related Asthma-Like Symptoms

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Abstract

Objective—To investigate associations between work-related asthma-like symptoms (WASTH) and annual pulmonary function decline among employees of 18 Norwegian smelters.

Methods—A 5-year longitudinal study in which WASTH was defined as a combination of dyspnea and wheezing that improved on rest days and vacation.

Results—A total of 12,966 spirometry examinations were performed in 3084 employees. Crude annual decline in forced expiratory volume in 1 second (FEV_1) ($dFEV_1$) was 32.9 mL/yr (95% confidence interval, 30.5 to 35.3), and crude annual decline in forced vital capacity (FVC) (dFVC) was 40.9 mL/yr (37.8 to 43.9). After adjustment for relevant covariates, employees reporting WASTH showed higher $dFEV_1$ by 16.0 m:/yr (3.4 to 28.6) and higher dFVC by 20.5 mL/yr (6.0 to 35.0) compared with employees not reporting WASTH.

Conclusion—Work-related asthma-like symptom was associated with greater annual declines in FEV_1 and FVC, indicating a restrictive pattern.

The Norwegian smelting industry produces ferrosilicon alloys (FeSi), silicon metal (Si-metal), ferromanganese (FeMn), silicon manganese (SiMn), ferrochrome (FeCr), silicon carbide (SiC), and titanium(II) oxide (TiO_2). These manufacturing processes emit several air pollutants into the workplace environment, including particulates and gases that are potentially harmful to airways.[1,2] Factory workers are exposed to particles of the raw materials that are characteristic of each production type (ie, substances containing silicon, iron, manganese, chrome, and titanium) as well as minerals composed of these elements, such as quartz. Other exposures include particles and gases originating from combustion in

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the furnaces, mainly carbon-containing dust that is contaminated by impurities of the anode, such as sulfur and other trace elements. Furthermore, several vehicles in the production halls produce air pollution, including diesel exhaust.

Apart from chrome,[3] which constitutes only a minor part of the production, none of the predominantly involved elements are known sensitizers. Thus, the air pollution in a smelting workplace is dominated by nonspecific airway irritants. A subgroup of occupational asthma is caused by irritants,[4,5] and such asthma may therefore occur in these work settings. Furthermore, subjects with occupational asthma reportedly exhibit an accelerated decline in forced expiratory volume in 1 second (FEV_1),[6] and it has been suggested that occupational asthma may cause chronic obstructive pulmonary disease.[7]

We previously found that dust exposure in smelters is associated with an accelerated annual decline in lung function[8,9] and with increased prevalence of airflow limitation,[10] indicating an elevated risk of chronic obstructive pulmonary disease.[11] Moreover, our prior findings indicate that increasing dust exposure is positively associated with the incidence of work-related asthma-like symptoms (WASTH) in the absence of doctor-diagnosed asthma.[12] These results suggest the possibility that WASTH represent a risk indicator of rapid decline in pulmonary function. Nevertheless, the association between WASTH and annual decline in pulmonary function has not been examined.

This study aimed to investigate whether WASTH was associated with accelerated annual decline in lung function.

METHODS

Study Population

All 20- to 55-year-old employees of 18 Norwegian smelters and related workplaces producing FeSi, Si-metal, FeMn, SiMn, FeCr, or SiC were invited to participate in this longitudinal respiratory study. A total of 3084 employees agreed to participate, representing approximately 90% of the workforce. The study started between 1996 and 1998 at different plants, and continued until 2003. New employees (n = 777) were included if they started to work in the industry during the study period. The employees were followed up annually, with a total of 12,996 observations. Examinations included spirometry measurements and a respiratory questionnaire, with a potential maximum of six data points for any one participant.[13] Spirometry was performed as recommended by the European Community for Coal and Steel,[14] and details have been previously published.[15] The respiratory questionnaire asked the subjects to report their symptoms during the last year. Table 1 shows the characteristics of the study participants. The study was approved by the Regional Ethics Committee, South East Norway (208–04085).

Definitions

Doctor-diagnosed asthma was defined as asthma diagnosed by a physician during childhood or adulthood before the participant started their current job. Work-related asthma-like symptom was defined as dyspnea with wheeze that improved on days off of work and during holidays in a participant without doctor-diagnosed asthma. An employee was considered to

have an allergy if they had a history of either hay fever or atopic eczema. Familial asthma was defined as current or previous asthma in parents, grandparents, sisters, or brothers. Employees were defined as previously exposed if they answered "yes" to the question "Have you previously been exposed on a regular basis to fumes, dust, or irritating vapors (gases) during your work?"

Occupational Exposures

The questionnaire was used to collect information about job category and smoking habits during the previous year. Current occupational exposure was assessed using a quantitative job exposure matrix that was constructed as the geometric mean of total dust exposure in each job category in each smelter, and is explained in detail elsewhere.[1,2] Briefly, dust from the working atmosphere was collected using personal samplers during the study period. The geometric mean of the dust exposure for the corresponding job title of the previous year was allocated to each employee. If an employee changed job categories during the year, a time-weighted average of the relevant geometric means was used. At each yearly examination, we updated information on job category, thereby enabling qualitative as well as quantitative determination of dust exposure.

Statistical Analyses

The analyses were performed using the software PROC GLIMMIX (for generalized linear mixed model) and PROC MIXED (for linear mixed model) SAS version 9.4 (SAS Institute Inc, Cary, NC). First, we used a generalized linear mixed model with logit link to investigate the univariate associations between the prevalence of WASTH and categories of relevant covariates during follow-up. Next, we used linear mixed models to investigate the univariate associations between FEV_1 as well as forced vital capacity (FVC) and follow-up time within categories of relevant covariates,[16] with follow-up time measured as years elapsed after inclusion. Age was expressed as age at baseline.[15] The coefficients of the univariate linear mixed model analyses were estimates of annual decline of FEV_1 ($dFEV_1$) and FVC (dFVC) with regard to the corresponding covariates.

Model fit was assessed using the Akaike information criterion, which revealed the lowest Akaike information criterion values (indicating a better fit) for models with an autoregressive moving average (ARMA 1,1) covariance matrix.[15] Multivariate models for FEV_1 and FVC were developed as follows. The initial model included all the covariates that were associated with WASTH prevalence and with $dFEV_1$ or dFVC, with a corresponding *P* value of <0.2. The initial model also included interaction terms between the covariates and follow-up time. Then backward reduction of the models was performed—starting with the removal of nonsignificant product terms with follow-up time that did not change the product term between WASTH and follow-up time by more than 20%. Thereafter, nonsignificant main effects were removed if their corresponding product terms with follow-up time were removed from the model. Thus, the final model contained significant main effects and significant product terms between the covariates with their corresponding main effects and follow-up time.

RESULTS

At baseline, 139 participants (4.5%) reported WASTH. Another 91 participants (3.0%) developed WASTH during follow-up (Table 1). There were a total of 449 reports of WASTH during the 12,996 follow-up examinations (3.5%). Compared with employees who never reported WASTH, those who reported WASTH showed a higher prevalence of smoking and a lower FEV_1 at baseline. Figure 1 shows the mean FEV_1, FVC, and FEV_1/FVC ratio according to WASTH status at each follow-up. Among the employees who reported WASTH, all three variables were lower and the annual declines in FVC and FEV_1 were steeper. The FEV_1/FVC ratio did not decline among employees reporting WASTH (0.05%/yr; 95% confidence interval [CI], −0.25% to 0.36%) or those who did not report WASTH (−0.03%/yr; 95% CI, −0.07% to 0.02%). The difference in annual change in the FEV_1/FVC ratio between employees reporting WASTH and those who did not report WASTH was 0.09% (95% CI, −0.32% to 0.14%). The coefficient between FEV_1/FVC ratio and age at baseline (among males) was −0.18% (95% CI, −0.21% to −0.15%).

Univariate analyses revealed that WASTH was positively associated ($P < 0.2$) with most covariates—including age at baseline, male sex, smoking habits, a history of familial asthma, previous exposure to dust or fumes, the type of production, and the level of current dust exposure—but was inversely associated with baseline FEV_1 and FVC (Table 2). Annual decline in FEV_1 was positively associated with each of these covariates, with the exception of a family history of asthma with which it showed an inverse relationship. Univariate estimates for dFVC revealed positive associations with all of the covariates, except the family history of asthma and baseline FEV_1.

To investigate annual decline in spirometry according to WASTH status, we fit linear mixed models for FEV_1 and FVC with the covariate follow-up time, WASTH, and the product of follow-up time and WASTH. This revealed steeper changes in $dFEV_1$ (15.0 mL/yr; $P = 0.02$) and dFVC (27.2 mL/yr; $P = 0.0009$) among employees reporting WASTH compared with those who did not report WASTH.

Table 3 summarizes the full results of multivariate linear mixed analyses for FVC and FEV_1. Controlling for potential confounders, we found that participants who reported WASTH showed steeper $dFEV_1$ by 16.0 mL/yr (95% CI, 2.1 to 27.1) and steeper dFVC by 20.5 mL/yr (95% CI, 6.0 to 35.0). Both $dFEV_1$ and dFVC increased with increasing age, with FVC at baseline, and with increasing dust exposure. In addition, dFEV1 was positively associated with increasing smoking status (from never to former to current) and with FVC at baseline.

DISCUSSION

Our present findings revealed that WASTH was significantly associated with increased $dFEV_1$ and dFVC. It is important to identify subjects with increased risk of occupational health disorders to prevent future disability. The detection of subjects with increased annual decline in pulmonary function requires repeated spirometry examinations over several years. This is a costly practice, and interpretation of the results can be difficult although it can be

facilitated by available software.[17] On the other hand, regular surveillance or at-risk employees via a self-administered questionnaire is much cheaper and should be considered as an alternative. Our present results confirmed that a combination of dyspnea and wheezing that improves on rest days and vacations seems to identify subjects with increased annual decline in pulmonary function. We found similar results in our previous small longitudinal study in the aluminum industry using the same questionnaire as in this study.[18] Nevertheless, such a method should not be routinely implemented without a validation study including estimations of the sensitivity, specificity, and costs—which was beyond the scope of this study.

Our present results also showed that smoking was associated with $dFEV_1$ but not dFVC, and dust exposure was associated with increased annual decline in FEV_1 as well as FVC. Nevertheless, subjects reporting WASTH did not show faster annual decline in the FEV_1/FVC ratio than individuals who did not report WASTH. Hence, dust exposure could possibly have a restrictive effect on pulmonary function in these settings, which is most pronounced among subjects reporting WASTH.

Our previous investigations of annual decline in lung function and dust exposure from this cohort showed only a borderline significant association between annual decline in FVC and dust exposure.[8,9] These prior publications expressed spirometric volumes per squared height, and treated dust exposure as a continuous covariate. The available data suggest that a restrictive component of the association between pulmonary function and dust exposure should be considered. It has also been previously reported that susceptible workers exposed to silica can develop obstructive, restrictive, or mixed patterns of reduced lung function.[19] Moreover, the presently found association between the FEV_1/FVC ratio and age among males was very close to the European reference values (0.18% in both).[14] This suggests that the total workforce had an annual decline of the FEV_1/FVC ratio within the normal range, whereas WASTH was associated with a decline showing a restrictive pattern. This could be a false result, as it is easier to get reproducible measures of FEV_1 than FVC. Nevertheless, it is unlikely that FVC measurements could be systematically reduced during follow-up; therefore, we believe that there was a steeper decline in FVC than FEV_1.

The underlying pathophysiologic mechanism that corresponds to WASTH is unclear. In this study, current smoking was associated with accelerated decline in FEV_1 but not in FVC, indicating different underlying mechanisms in subjects reporting WASTH compared with the effects of smoking. Moreover, the association between pulmonary function and other covariates, foremost smoking, differed in subjects reporting familial asthma compared with individuals who did not report familial asthma. This difference could be caused by clustering. Hence, it is possible that the effect modification of the association between decline in pulmonary function and WASTH could be spurious.

Compared with individuals having pulmonary function in the lowest range, subjects with high baseline FVC and FEV_1 showed faster annual decline in both FVC and FEV_1. Similar results have been reported in general populations.[20,21] This suggests that a low level of pulmonary function to some extent counteracts the effect of other covariates that are determinants of accelerated decline, such as age. Our present data include some evidence of

slower annual decline of lung function with increasing age among subjects reporting WASTH. Although the corresponding *P* value was nonsignificant, a selection effect of subjects with WASTH cannot be excluded.

In this study, we ignored exposure levels on the basis of our previous findings that dust exposure was associated with the outcome ($dFEV_1$) as well as the determinant (WASTH). Regarding the identification of subjects reporting WASTH for preventive purposes, the exposure level is of minor importance. Hence, annual surveillance of the workforce using a questionnaire could probably identify individuals with increased risk of decline in lung function and thereby prevent unnecessary spirometry of healthy individuals. Moreover, the health costs could be reduced. Nevertheless, the sensitivity and specificity of such strategy should be investigated. This was not done in this study. We believe that such subjects should be clinically examined with repeated spirometry examinations regardless of their exposure levels.

The main limitation of this study was the lack of clinical interpretation of the concept of WASTH. The symptoms are compatible with work-related asthma. Nevertheless, as occupational asthma has not been reported from these industries, it is unlikely that it is a major problem in this context. Rather, the spirometry results indicated a restrictive pattern among employees reporting WASTH. The clinical interpretation of these results is difficult, but it seems that WASTH identifies individuals at increased risk of loss of lung function. Thus, these findings should be of interest from a preventive point of view.

CONCLUSION

Work-related asthma-like symptom was associated with an increased annual decline in FEV_1 as well as FVC, indicating a restrictive pattern. Identification of subjects reporting WASTH could be a useful tool for occupational health monitoring among smelters.

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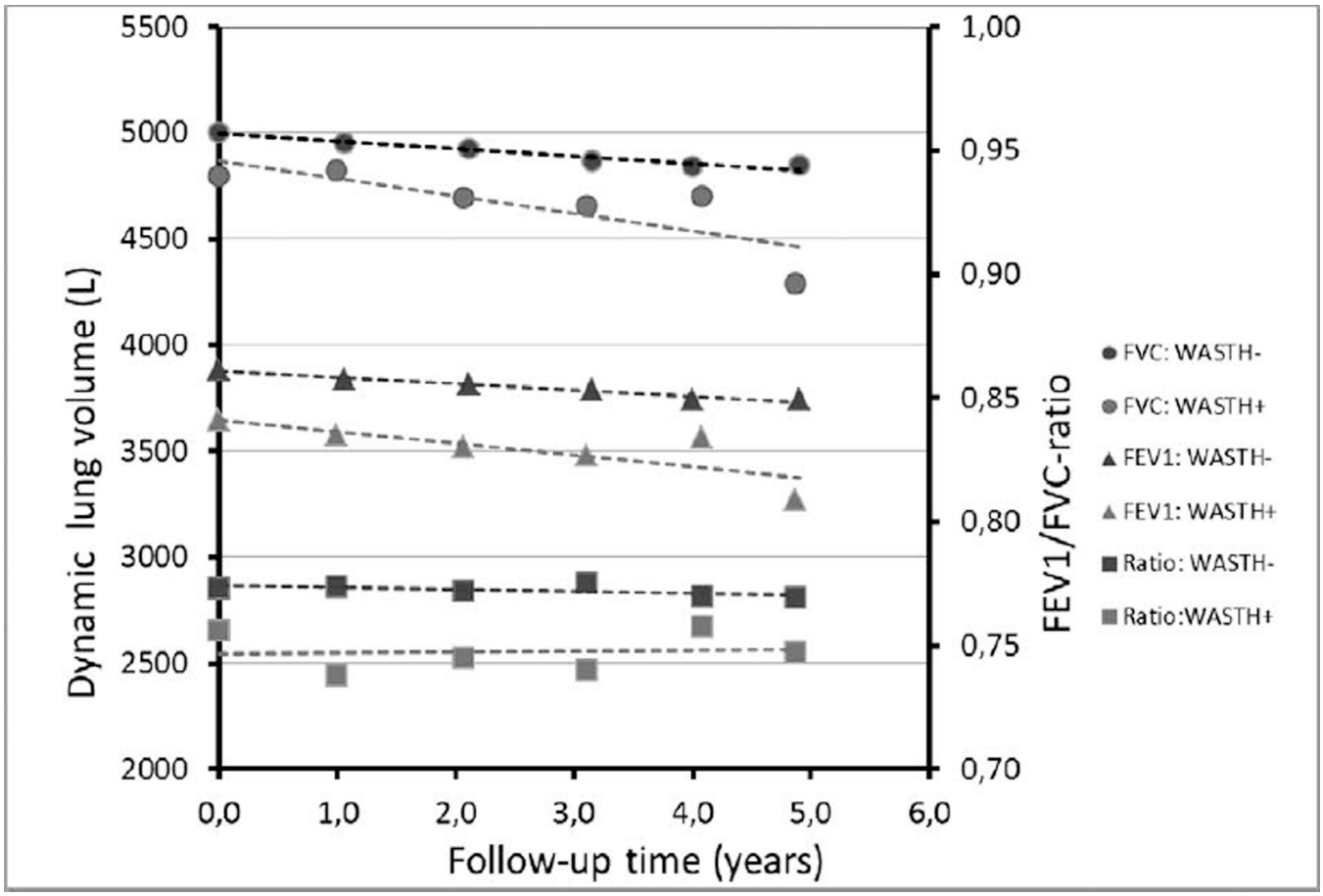

FIGURE 1.

The mean FVC, FEV_1, and FEV_1/FVC ratio with regression lines (dashed lines) during the follow-up. FEV_1, forced expiratory volume in 1 second; FVC, forced vital capacity.

TABLE 1

Descriptive Data at Baseline of Employees Who Did/Did Not Report Work-Related Asthma-Like Symptoms During the Follow-Up

	WASTH		
Characteristic	**At Baseline**	**Incident Cases**	**Never WASTH**
n (%)	139 (4.5)	91 (3.0)	2854 (92.5)
Age, yrs, mean (SD)	40.5 (8.4)	41.2 (9.0)	38.9 (9.2)
Male, *n* (%)	130 (93.5)	85 (93.4)	2,531 (88.9)
Smoking habits, *n* (%)			
Never	21 (15)	16 (18)	925 (32)
Former	22 (16)	19 (21)	566 (20)
Current	96 (69)	56 (62)	1363 (48)
Spirometry, mean (SD)			
FEV_1, L	3.65 (0.82)	3.75 (0.74)	3.89 (0.73)
FEV_1, % predicted	83 (15)	86 (12)	89 (12)
FVC, L	4.80 (0.97)	4.98 (0.98)	5.01 (0.92)
FVC, % predicted	90 (14)	94 (13)	95 (12)

FEV_1, forced expiratory volume in 1 second; FVC, forced vital capacity; SD, standard deviation; WASTH, work-related asthma-like symptoms.

TABLE 2

Cumulative Number and Mean Prevalence (in Parentheses) of Work-Related Asthma-Like Symptoms During the Follow-Up, and Annual Decline in FEV_1 and FVC in mL/yr by Selected Covariates

Characteristics	WASTH *n* (%)	$dFEV_1$ Coefficient (95% CI)	dFVC Coefficient (95% CI)
Age at baseline, yrs			
<35	89 (2.6)	22.9 (18.5 to 27.4)	25.9 (20.5 to 31.3)
35–44	201 (3.7)	33.9 (30.0 to 37.8)	40.8 (35.9 to 45.6)
≥45	159 (3.9)	40.4 (36.3 to 44.5)	52.0 (46.9 to 57.1)
P value for trend	0.014	<0.0001	<0.0001
Sex			
Female	25 (1.8)	18.9 (36.3 to 44.5)	30.0 (24.0 to 36.0)
Male	424 (3.7)	34.1 (31.6 to 36.6)	41.3 (38.1 to 44.6)
P value between groups	0.0007	<0.0001	0.023
Smoking habits			
Never	65 (1.7)	25.7 (21.0 to 30.4)	33.3 (27.7 to 38.9)
Former	88 (3.0)	31.0 (25.8 to 36.2)	44.5 (38.1 to 50.8)
Current	296 (4.8)	37.3 (34.0 to 40.6)	40.4 (36.1 to 44.8)
P value for trend	<0.0001	<0.0001	0.061
Familial asthma			
No	332 (3.3)	33.7 (31.1 to 36.3)	40.5 (37.1 to 43.9)
Yes	117 (4.0)	28.0 (23.0 to 33.0)	38.6 (32.3 to 44.8)
P value between groups	0.062	0.056	0.594
Previous exposure			
No	71 (1.9)	27.5 (23.0 to 32.1)	36.4 (30.7 to 42.0)
Yes	378 (4.1)	34.1 (31.7 to 37.1)	41.6 (38.1 to 45.1)
P value between groups	<0.0001	0.009	0.118
Production			
SiC	46 (2.8)	15.9 (8.7 to 23.1)	37.0 (27.1 to 46.9)
FeSi Si-metal	244 (3.4)	32.0 (28.8 to 35.3)	43.1 (39.0 to 47.3)
FeMn/SiMn/FeCr	159 (3.8)	40.1 (36.1 to 44.0)	37.6 (32.9 to 42.4)
P value for trend	0.070	<0.0001	0.582
Dust exposure, mg/m3			
<1.0	109 (2.3)	27.7 (23.9 to 31.4)	34.5 (29.9 to 39.1)
1.9–2.9	200 (3.8)	31.8 (28.4 to 35.2)	37.1 (32.6 to 41.6)
≥3.0	140 (4.6)	41.8 (36.2 to 47.3)	53.5 (46.3 to 60.7)
P value for trend	<0.0001	0.0002	<0.0001
FEV_1 at baseline, mL			
<3500	205 (4.7)	25.5 (20.8 to 30.2)	36.3 (30.6 to 42.0)
3500–4490	196 (3.1)	34.4 (31.3 to 37.5)	41.4 (37.5 to 45.3)
>4490	48 (2.2)	37.0 (31.5 to 42.5)	42.8 (35.5 to 50.0)
P value for trend	<0.0001	0.0002	0.906
FVC at baseline, mL			

Characteristics	WASTH *n* (%)	$dFEV_1$ Coefficient (95% CI)	dFVC Coefficient (95% CI)
<4500	43 (4.5)	14.9 (4.5 to 23.7)	16.0 (3.0 to 29.1)
4500–5490	148 (4.5)	25.7 (21.0 to 30.3)	30.2 (24.4 to 36.0)
>5490	258 (3.0)	36.4 (33.5 to 39.4)	45.1 (41.5 to 48.7)
P value for trend	<0.0001	<0.024	<0.0001
All	449 (3.5)	32.9 (30.5 to 35.2)	40.9 (37.8 to 43.9)

CI, confidence interval; $dFEV_1$, decline in $dFEV_1$; dFVC, decline in dFVC; FeCr, ferrochrome; FeMn, ferromanganese; FeSi, ferrosilicon alloys; FEV_1, forced expiratory volume in 1 second; FVC, forced vital capacity; SD, standard deviation; SiC, silicon carbide; Si-metal, silicon metal; SiMn, silicon manganese; WASTH, work-related asthma-like symptoms.

TABLE 3

Results of the Multivariate Analyses With 95% Confidence Intervals in Parentheses

Covariate	FVC, mL	FEV_1, mL
Intercept	−3724 (−4192 to −3256)	−1370 (−1807 to −932)
Follow-up time, yrs	2.8 (−10.6 to 16.0)	15.4 (3.0 to 27.7)
Height, cm	45.3 (42.7 to 47.9)	25.9 (23.4 to 30.6)
Male vs female	286 (218 to 354)	84.4 (18.2 to 151)
Age at baseline, yrs		
35–44	−25.1 (−50.0 to −0.31)	−34.7 (−56.5 to −12.8)
≥45	−358 (−401 to −314)	−377 (−418 to −336)
P value for trend	<0.0001	<0.0001
Smoking habits		
Former vs never	−30.0 (−64.3 to 4.3)	−55.0 (−85.3 to −24.6)
Current vs never	−29.9 (−57.7 to −2.1)	−49.7 (−74.4 to −25.0)
P value for trend	0.997	0.112
FVC at baseline, mL		
4500–5490	468 (424 to 512)	356 (272 to 440)
≥5500	979 (932 to 1025)	1013 (926 to 1101)
P value for trend	<0.0001	<0.0001
Dust exposure, mg/m^3		
1.0–2.9	−5.4 (−28.5 to 17.6)	0.48 (−19.8 to 20.7)
≥3.0	12.5 (−15.1 to 40.0)	11.3 (−13.0 to 35.5)
P value for trend	0.123	0.911
WASTH: yes vs no	6.6 (−27.5 to 40.7)	7.4 (−22.4 to 37.1)
Annual Decline	dFVC, mL/yr	$dFEV_1$, mL/yr
Age at base line, years		
35–44 vs <35	12.6 (5.5 to 19.7)	11.0 (4.8 to 17.2)
≥45 vs <35	24.8 (16.9 to 32.7)	25.7 (18.9 to 32.6)
P value for trend	<0.0001	<0.0001
Smoking habits		
Former vs never	5.9 (−1.7 to 13.4)	1.7 (−4.8 to 8.3)
Current vs never	4.8 (−1.6 to 11.1)	9.7 (4.2 to 15.2)
P value for trend	0.416	<0.0001
FVC at baseline, mL		
4500–5490 vs <4500	4.8 (−7.1 to 16.8)	15.2 (3.7 to 26.7)
≥5500 vs <4500	14.3 (2.8 to 25.7)	28.3 (17.4 to 39.3)
P value for trend	<0.0001	<0.0001
Dust exposure, mg/m3		
1.0–2.9 vs <1.0	0.50 (−5.6 to 6.6)	2.2 (−3.1 to 7.5)
≥3.0 vs <1.0	13.3 (6.2 to 20.3)	11.9 (5.7 to 18.1)
P value for trend	<0.0001	0.0009

Covariate	FVC, mL	FEV_1, mL
WASTH: yes vs no	20.5 (6.0 to 35.0)	16.0 (3.4 to 28.6)

$dFEV_1$, decline in $dFEV_1$; dFVC, decline in dFVC; FEV_1, forced expiratory volume in 1 second; FVC, forced vital capacity; WASTH, work-related asthma-like symptoms.