

# Airborne Occupational Exposures and Lung Function in the Lifelines Cohort Study

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## Abstract

**Rationale:** The association between airborne occupational exposures and lung function level is inconsistent in the general population. Moreover, little is known about the association between occupational exposures and annual lung function decline.

**Objectives:** We investigated the association between occupational exposures and lung function level and annual lung function decline in the population-based Lifelines cohort study.

**Methods:** We included 55,631 adults with baseline spirometry and reliable job code—13,759 of these subjects were aged  $\geq 30$  years and underwent spirometry again after 4.5 years of follow-up. Occupational exposures in the current or last-held job at baseline were estimated with the ALOHA+ job-exposure matrix. Linear regression analyses adjusted for covariates were used to test the association between each occupational exposure—biological dust,

mineral dust, gases and fumes, pesticides, solvents, and metals—and lung function level and annual lung function decline. Interactions were used to test effect modification by sex or smoking.

**Results:** Exposures to biological dust, mineral dust, gases and fumes, insecticides, fungicides, and aromatic solvents were associated with a lower lung function level at baseline. The effects were larger in males and smokers compared with females and nonsmokers, respectively. However, no association between occupational exposures and the rate of annual lung function decline was found between baseline and follow-up.

**Conclusions:** In this study, airborne occupational exposures are associated with lower lung function level but not with a faster lung function decline. These negative effects are more pronounced among males and smokers.

**Keywords:** occupational exposure; lung function/forced expiratory volume; lung function decline

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Pulmonary function parameters are reliable traits to assess the physiological and pathological status of the airways. A lower lung function level is a risk factor for morbidity and mortality (1–3). A faster lung function decline is associated with a higher rate of hospitalization in the elderly population (4). Although tobacco smoking

is the primary preventable risk factor for lung function impairment (5), other factors such as airborne occupational exposures may also impair lung function.

Airborne occupational exposures may impair lung function by stimulating immune or inflammatory responses (6–8). It has been suggested that occupational

exposures account for 15–20% of the population-attributable risk of chronic obstructive pulmonary disease (9), with up to 31% in never-smokers (10). Therefore, it is important to find out which occupational exposures are associated with lung function level and enhanced lung function decline in the general population.

Earlier studies have investigated associations between specific occupational exposures in specific occupations (e.g., exposure to quartz dust, organic dust, and disinfectants in cement factories, cotton textile mills, and hospitals, respectively) and lung function (11–13). So far, relatively few studies have investigated the association between occupational exposures and lung function level in the general population using a job-exposure matrix (JEM), and the findings are inconsistent (14). In addition, the association between occupational exposures and annual lung function decline—which as such is a natural phenomenon after reaching the maximal lung function plateau level in young adulthood (15)—still remains poorly understood. Previously, we have found that occupational exposures to insecticides and herbicides were associated with a faster annual lung function decline (16). A recent population-based study found that occupational exposure to vapors, gases, dusts, fumes, and aromatic solvents was associated with accelerated lung function decline (17). The associations between occupational exposures and lung function decline were (also) inconsistent in ECRHS-I (European Community Respiratory Health Survey) and SAPALDIA (Swiss Cohort Study on Air Pollution and Lung and Heart Diseases in Adults) (18, 19).

So far, little is known about the modifying effect of sex and smoking on the association between airborne occupational exposures and lung function. In our previous study, the negative effect of several exposures on lung function level and decline did not differ between males and females but were larger in ever-smokers compared with never-smokers (16, 20). Other studies reported inconsistent findings of the modifying effect of sex and smoking (18, 19, 21).

In our previous studies, we used a subset of the general population-based Lifelines cohort study. Recently, a much larger data set became available, including follow-up lung function measurements after 4.5 years. Therefore, in this study, we investigated the association between occupational exposures and baseline lung function level ( $n = 55,631$ ) and annual lung function decline ( $n = 13,759$ ) in this large sample of the general population. We further investigated whether the association between occupational exposures and lung

function level and decline was modified by sex and smoking.

## Methods

### Population

Participants of this study were recruited from the Lifelines cohort study. The Lifelines cohort study, a large observational population-based cohort study, started in 2006 and aimed to disentangle the role of genetic factors, lifestyle, and the environment in the development of chronic diseases and healthy aging. Inhabitants of the northern three provinces (Friesland, Groningen, and Drenthe) of the Netherlands were invited to participate in the study. The study population was recruited in three ways: participants aged 25–50 years through general practitioners (49%); family members (parents, partners, parents in law, and children) of the already registered participants (38%); and remaining study participants enrolled themselves via the Lifelines website (13%). Recruitment stopped in December 2013 after including 167,729 subjects (age range, 6 mo to 93 yr). The first follow-up visit was performed after a median of 4.5 years (range, 1.8–8.8 yr). Details on the Lifelines cohort study were published elsewhere (22).

### Lung Function

Four lung function parameters were measured: forced expiratory volume in 1 second ( $FEV_1$ ), forced vital capacity (FVC), forced expiratory flow, midexpiratory phase ( $FEF_{25-75}$ ), and  $FEV_1/FVC$ . Prebronchodilator spirometry was performed according to American Thoracic Society and European Respiratory Society guidelines (23) using the Welch Allyn SpiroPerfect device (Version 1.6.0.489, PC-based SpiroPerfect with CardioPerfect Workstation software; Welch Allyn).

### Occupational Exposures

We investigated exposure to biological dust, mineral dust, gases and fumes, insecticides, herbicides, fungicides, aromatic solvents, chlorinated solvents, other solvents, and metals. Occupational exposures were estimated using self-reported current or last-held job from the baseline questionnaire. The jobs were coded according to the International Standard Classification of Occupations 2008 (24) using a computer-assisted structured coding tool (CASCO

(25). During this procedure, a CASCO score was given to each coded occupation, which indicates the probability that the given code is correct (range, 0–100). We selected subjects with a CASCO score  $\geq 60$ , and all job titles were reviewed and, if necessary, recoded to achieve accurate job coding. The ALOHA+ JEM (26–28) was used to link occupational exposures (classified as no, low, and high) to the baseline jobs. For details, see the appendix.

### Covariates

The subjects' age, sex, and height were taken from the baseline and follow-up screening examinations. Smoking status, pack-years, education, and monthly income were extracted from the baseline and follow-up questionnaires (for details, see Table E1 in the online supplement).

### Statistical Methods

**Association between occupational exposures and lung function.** Linear regression models were used to investigate the association between baseline occupational exposure (no exposure as reference) and baseline lung function level and annual lung function decline adjusted for age, sex, height, pack-years, smoking, education, and monthly income. Two dummy variables for low and high occupational exposure were included in the regression model. The analysis on  $FEF_{25-75}$  was additionally adjusted for FVC. Annual lung function decline was calculated as the difference in lung function between follow-up and baseline divided by the duration of follow-up in years and only in subjects aged  $>30$  years at baseline. All exposures were tested separately and were not adjusted for the other exposures. A two-sided  $P$  value  $<0.05$  was considered statistically significant.

**Interaction analyses.** We performed interaction analyses (sex-by-occupational exposures and smoking-by-occupational exposures) to investigate if the associations differed between males and females and between current, ex-, and never-smokers.

**Sensitivity analyses.** To examine the independent effect of occupational exposures on small airways, we investigated the association between occupational exposures and  $FEF_{25-75}$  in subjects without large airways obstruction ( $FEV_1\%$  predicted  $\geq 80\%$  and  $FEV_1/FVC \geq 70\%$ ). To investigate if current exposure had a different effect on lung function than

previous exposure, the analyses were stratified by active workers (having a paid job at baseline) and nonactive workers (retired, unemployed or looking for a job, or unfit for work).

SPSS 22 (IBM Corp) was used for the data analysis.

## Results

### Descriptive Characteristics at Baseline

A flowchart of the selection of subjects is presented in Figure 1. Descriptive statistics of population characteristics are given in Table 1. At baseline, the mean age was 44 years, the mean height was 175 cm, and the median pack-years in ever-smokers was 8. The proportion of females ( $\approx 60\%$ ) was higher than males, more than half of the subjects were ever-smokers and had medium education, and approximately 43% of the subjects had a high monthly income. At baseline, the highest exposure prevalence was found for gases and fumes (low exposure = 39.8%, high exposure = 6.4%), followed by biological dust (low = 29.4%, high = 5.4%) and other solvents

(low = 24.5%, high = 2.6%) (Figure 1 and Table E2). The correlation between occupational exposures at baseline and follow-up is shown in correlograms (Figures E1 and E2). The population characteristics and occupational exposures stratified by sex and smoking are given in Tables E3–E6.

### Association between Occupational Exposures and Baseline Lung Function Level

Exposures to biological dust, mineral dust, insecticides, and fungicides were associated with a lower FEV<sub>1</sub> level (Tables 2 and E7). For example, subjects with high exposure to biological dust had 20-ml-lower FEV<sub>1</sub> compared with subjects without this exposure. Similarly, exposures to biological dust, mineral dust, gases and fumes, insecticides, fungicides, aromatic solvents, and other solvents were associated with a lower FEV<sub>1</sub>/FVC. Exposures to biological dust, mineral dust, gases and fumes, insecticides, fungicides, and aromatic solvents were associated with a lower FEF<sub>25–75</sub> level. Exposures to biological dust, aromatic solvents, and other solvents were

significantly associated with a higher FVC level.

### Sex-by-Occupational Exposures Interactions on Baseline Lung Function Level

Six occupational exposures (biological dust, mineral dust, gases and fumes, insecticides, fungicides, and other solvents) had a significant negative interaction with male sex on lung function level (Tables 2 and E9). This indicates that the negative effects of occupational exposure on lung function were larger in males than in females. For FEV<sub>1</sub> and FVC, the largest differences between males and females were seen for exposure to insecticides and fungicides, whereas for FEF<sub>25–75</sub>, exposure to biological dust, mineral dust, and gases and fumes showed the largest differences between males and females.

### Smoking-by-Occupational Exposures Interactions on Baseline Lung Function Level

Three occupational exposures (mineral dust, gases and fumes, and aromatic solvents) showed a significant negative interaction with current smoking on lung function level (Tables 2 and E11), indicating that the negative effects of occupational exposure on lung function level were larger in current smokers compared with never-smokers.

### Association between Occupational Exposures and Annual Lung Function Decline

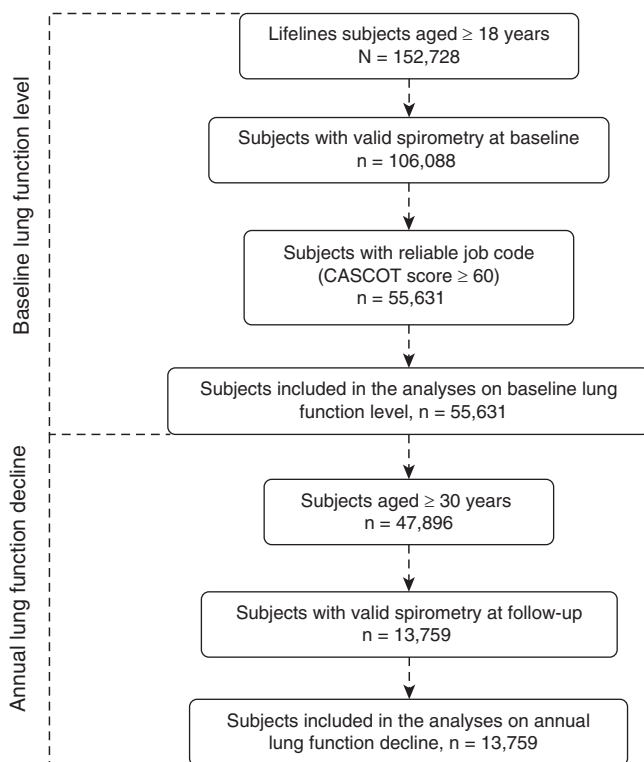
Only occupational exposure to biological dust was significantly associated with a faster annual FEV<sub>1</sub> decline (Tables 3 and E8). Exposures to mineral dust and to gases and fumes were significantly associated with a faster annual FVC decline and with a slower annual FEV<sub>1</sub>/FVC decline.

### Sex-by-Occupational Interactions on Annual Lung Function Decline

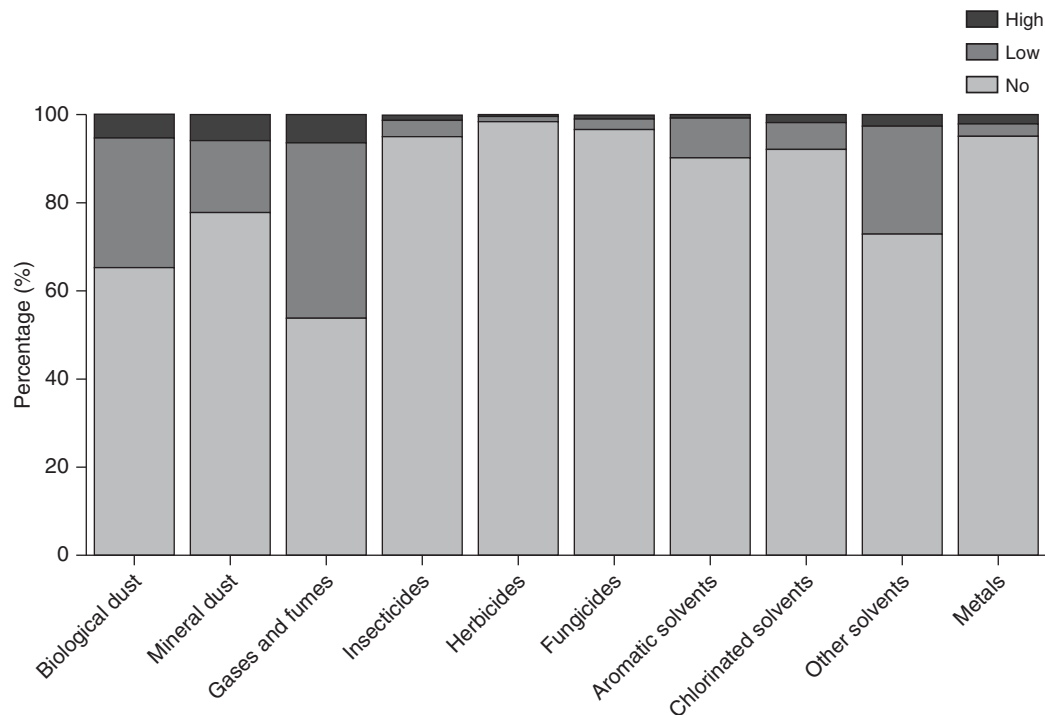
Only one significant occupational exposure-by-sex interaction on annual lung function decline was found: high exposure to aromatic solvents was associated with a slower annual FEF<sub>25–75</sub> decline in males compared with females (Tables 3 and E10).

### Smoking-by-Occupational Exposures Interactions on Annual Lung Function Decline

Three occupational exposures (biological dust, insecticides, and fungicides) showed a



**Figure 1.** Flowchart of the selection of study subjects. CASCOT = computer-assisted structured coding tool.



**Figure 2.** Distribution of 10 occupational exposures at baseline lung function analyses. Each occupational exposure was categorized into no, low, and high groups. The distribution of these occupational exposures was similar in annual lung function decline analyses.

significant negative interaction with current smoking on annual lung function decline (Tables 3 and E12). This means that smokers with these exposures had a faster lung function decline compared with nonsmokers with these occupational exposures.

### Sensitivity Analyses

After restricting our analyses to subjects without large airways obstruction, the significant negative association between occupational exposures to biological dust and gases and fumes and  $FEF_{25-75}$  level remained (Table E7). In nonactive workers, three occupational exposures (insecticides, herbicides, and fungicides) showed a statistically significant positive association with annual lung function decline (Table E15). For example, nonactive workers with high exposure to herbicides had 43-ml-slower annual  $FEV_1$  decline than nonactive workers with no exposure to herbicides. For details, see Table E13–E16.

### Discussion

The majority of the investigated occupational exposures at baseline were

associated with a lower  $FEV_1$ ,  $FEV_1/FVC$ , and  $FEF_{25-75}$  level but not with FVC level. These findings indicate that the detected changes were obstructive in nature. We also found that the negative effect of occupational exposures at baseline on lung function level was higher in males compared with females and in current smokers compared with nonsmokers. In addition, apart from a few significant associations, occupational exposures at baseline were not associated with annual lung function decline. No interaction between sex and occupational exposures and smoking and occupational exposures on annual lung function decline was found.

Exposures to biological dust, mineral dust, gases and fumes, insecticides, fungicides, aromatic solvents, and other solvents were associated with large airways obstruction—indicated by a lower level of  $FEV_1$  or  $FEV_1/FVC$ . In line with our current findings, earlier population-based studies, including our previous study, also found that these occupational exposures were associated with large airway obstruction (20, 27, 28). In addition, we found an association between exposure to biological dust, mineral dust, gases and fumes, insecticides, fungicides, and aromatic solvents and small airways

obstruction—indicated by a lower level of  $FEF_{25-75}$ . Most of these significant associations were found in the low-exposure group. However, the direction of the association is usually the same between “low” and “high” exposure, and possibly because of lower study power, the association is not significant in the high-exposure group. Workers may be exposed to different hazardous substances, and the main route of these exposures to enter the body is through inhalation. After entering the respiratory system, these exposures can stimulate an immune or inflammatory response, which results in narrowing of the airway passages (6–8). Therefore, we assume that occupational exposures may impair lung function as a result of an intense immune or inflammatory response triggered by these exposures.

After restricting our analyses to subjects without large airways obstruction, exposure to biological dust and gases and fumes was associated with a lower  $FEF_{25-75}$  level. This indicates that the effects of biological dust and gases and fumes on the small airways are a primary response and independent from effects on the large airways. We also observed a similar association in our previous study (29). In this study, we observed that biological dust

**Table 1.** Distribution of baseline characteristics of the study participants

Baseline Characteristics	Analyses on Baseline Lung Function Level	Analyses on Annual Lung Function Decline
Number of participants	55,631	13,759
Age, yr, mean (SD)	44 (12)	47 (10)
Females, %	60.7	61.4
Height, cm, mean (SD)	175 (9)	174 (9)
Pack-years in ever-smokers, median (IQR)	8 (13)	9 (13)
Smoking, <i>n</i> (%)		
Never-smoker	25,111 (45.1)	6,036 (43.9)
Ex-smoker	17,510 (31.5)	5,064 (36.8)
Current smoker	10,956 (19.7)	2,441 (17.7)
Education, <i>n</i> (%)		
Low	8,731 (15.7)	2,228 (16.2)
Medium	29,218 (52.5)	7,136 (51.8)
Highest	17,487 (31.4)	4,335 (31.5)
Unclassifiable	67 (0.1)	14 (0.1)
Monthly income, <i>n</i> (%)		
Low	8,164 (14.7)	1,521 (11.1)
Medium	14,871 (26.7)	4,071 (29.6)
Highest	23,891 (42.9)	6,205 (45.1)
Don't know/don't tell	7,659 (13.8)	1,788 (13.0)
FEV <sub>1</sub> , L/s, mean (SD)	3.5 (0.8)	—
FVC, L, mean (SD)	4.5 (1.0)	—
FEV <sub>1</sub> /FVC, % mean (SD)	77.0 (7.0)	—
FEF <sub>25–75</sub> , L, mean (SD)	3.1 (1.2)	—
Change of FEV <sub>1</sub> , ml/s, mean (SD)	—	–32 (48)
Change of FVC, ml, mean (SD)	—	–27 (64)
Change of FEV <sub>1</sub> /FVC, % mean (SD)	—	–0.27 (0.82)
Change of FEF <sub>25–75</sub> , ml, mean (SD)	—	–59 (116)
Active workers, <i>n</i> (%)	45,555 (81.9)	11,322 (82.3)

*Definition of abbreviations:* FEF<sub>25–75</sub> = forced expiratory flow, midexpiratory phase; FEV<sub>1</sub> = forced expiratory volume in 1 second; FVC = forced vital capacity; IQR = interquartile range; SD = standard deviation.

affects both large and small airways and that gases and fumes particularly affect the small airways. The aerodynamic diameter of these airborne occupational exposures may explain this difference (30). Biological dust might affect both small and large airways owing to its wider range in aerodynamic diameter (from  $\leq 4 \mu\text{m}$  to  $30 \mu\text{m}$ ) (31). On the other hand, due to smaller particle size ( $\leq 2 \mu\text{m}$ ) (32, 33), gases and fumes might affect only the small airways.

The negative effect of occupational exposures on lung function level was stronger among males than females. In our previous study with a smaller sample size, we did not observe this difference (20). A recent meta-analysis showed that the negative effect of exposure to biological dust and mineral dust on lung function level was larger in males than females (34). Most likely, differences in exposure intensity and composition of these dusts may explain this phenomenon. Males may experience higher exposures in blue-collar jobs (e.g., welding and construction) (35). In our study, we indeed observed that the

prevalence of occupational exposure was higher among males compared with females. We further observed that in males, the large airways were most affected by high exposure to insecticides and fungicides (FEV<sub>1</sub>), whereas the small airways (FEF<sub>25–75</sub>) were most affected by gases and fumes exposure. The aerodynamic diameter may explain the respective effect of pesticides—ranges from  $4 \mu\text{m}$  to  $16 \mu\text{m}$  (36)—and gases and fumes ( $\leq 2 \mu\text{m}$ ) (32, 33) on lung function. Finally, it should be noted that the prevalence of exposure to insecticides and fungicides was very low in females (less than 2% were exposed). Therefore, our study findings may not be informative for these exposures among females.

In this study, we found that the negative effects of several occupational exposures on lung function level (FEV<sub>1</sub>, FEV<sub>1</sub>/FVC, and FEF<sub>25–75</sub>) were larger among current smokers compared with nonsmokers. In line, our previous studies showed that exposure to mineral dust, insecticides, and herbicides had a larger negative effect on FEV<sub>1</sub> level in smokers but not on FEV<sub>1</sub>/FVC

and FEF<sub>25–75</sub> level (20, 29). We further found that the negative effects of several occupational exposures on annual lung function decline (FEV<sub>1</sub>, FEV<sub>1</sub>/FVC, and FEF<sub>25–75</sub>) were larger among current smokers compared with nonsmokers, which are also in line with our previous study findings (16). Thus, our current study findings suggest that smokers are more susceptible to the negative effect of occupational exposures on lung function.

Studies have shown that smoking is associated with a lower lung function level and faster lung function decline (37, 38). Smoking components trigger the inflammatory response and thereby impair lung function (39–41). Occupational exposures are also proinflammatory agents (6–8). The biological mechanism predisposing pulmonary inflammation in response to smoking may also follow a similar pathway in response to occupational exposure. Therefore, occupational exposure may enhance the pulmonary inflammatory response in smokers, and thus, the total negative effect may be much larger owing to the synergistic effect of these environmental exposures.

In this study, we found inconsistent and noninformative associations between occupational exposures and annual lung function decline. A recent Danish study observed a slightly larger decline in FEV<sub>1</sub> and FVC during 6 years of follow-up in association with baseline and follow-up exposure to wood dust (42). A recent meta-analysis found a small negative effect of organic dust exposure on lung function decline; however, the finding was not significant (12). In accordance, the ECRHS-I (European Community Respiratory Health Survey) study found no association between occupational exposures and lung function decline where relatively young subjects were followed from 1991–1993 to 1998–2002 (18). In our previous Vlagtwedde and Vlaardingen general population-based study, we found that occupational exposure to insecticides and herbicides was associated with a faster annual FEV<sub>1</sub> and FEV<sub>1</sub>/FVC decline compared with no exposure when the subjects were followed for a much longer period between 1965 and 1990 (16). This could be due to the fact that the study population and follow-up time were totally different compared with the current study population and follow-up time. In addition, the duration of follow-up was much longer (25 yr) in the Vlagtwedde and Vlaardingen



**Table 2.** Association between occupational exposures and baseline lung function level

Occupational Exposure	Exposure Level	Main Analyses*				Interaction with Male Sex†				Interaction with Current Smoking‡			
		FEV <sub>1</sub>	FVC	FEV <sub>1</sub> /FVC	FEF <sub>25-75</sub>	FEV <sub>1</sub>	FVC	FEV <sub>1</sub> /FVC	FEF <sub>25-75</sub>	FEV <sub>1</sub>	FVC	FEV <sub>1</sub> /FVC	FEF <sub>25-75</sub>
Biological dust	Low		↑	↓	↓	↓	↓		↓				
	High	↓			↓						(↓)	(↓)	(↓)
Mineral dust	Low	↓		↓	↓	↓			↓	↓	(↓)	(↓)	↓
	High			(↓)	(↓)								
Gases and fumes	Low			↓	↓	↓		↓	↓	↓			↓
	High	(↓)		↓	↓	↓							
Insecticides	Low	↓		↓	↓								
	High					↓	↓			(↓)			
Herbicides	Low												
	High							(↓)		(↓)		↓	(↓)
Fungicides	Low	↓		↓	↓			↓	(↓)				
	High					↓	(↓)		(↓)				
Aromatic solvents	Low	(↓)	↑	↓	(↓)					↓			↓
	High			↓	↓	(↓)							
Chlorinated solvents	Low												
	High												
Other solvents	Low	↑	↑	↓									
	High					↓		(↑)					
Metals	Low												
	High												

Definition of abbreviations: FEF<sub>25-75</sub> = forced expiratory flow, midexpiratory phase; FEV<sub>1</sub> = forced expiratory volume in 1 second; FVC = forced vital capacity. The linear regression was adjusted for age, sex, height, pack-years, smoking, education, and monthly income. The FEF<sub>25-75</sub> model was additionally adjusted for FVC.

\*No exposure as reference group.

†Females as reference group.

‡Never-smokers as reference group.

↑Positive associations or interactions.

↓Negative associations or interactions.

↑/↓ =  $P < 0.05$ .

(↑/↓) =  $0.05 \leq P < 0.10$ .

study than our current study (4.5 yr). A longer occupational exposure could have a larger effect on lung function decline. Therefore, complete occupational histories are required to understand this association in the Lifelines cohort study.

Another explanation of the inconsistent associations between occupational exposures and lung function decline in this study may be due to the “healthy worker effect” (43). This means that subjects who experienced negative health effects upon occupational exposures may have switched to other jobs with less exposure before the start of our study. Therefore, complete job histories are required to understand this phenomenon more explicitly.

Finally, we observed several positive associations between occupational exposures and annual lung function decline in nonactive workers. For instance, nonactive workers with high exposure to fungicides in their last-held job had a slower annual FEV<sub>1</sub> decline compared with

nonactive workers without fungicides exposure. This finding suggests that when the exposure to fungicides stopped (because of retirement), lung function decline slows down or even catches up with the decline of those who were not exposed during their active working life. To investigate this finding more explicitly, longitudinal studies and complete job histories are required.

**Strength and Limitations**

In the current study, we included a substantial number of subjects ( $N = 55,631$ ) in the analyses on baseline lung function level and 13,761 subjects in the analyses on annual lung function decline. We used a general-population JEM to categorize exposure level based on self-reported current or last-held job at baseline, and this eliminates recall or differential misclassification bias of the investigated exposures (44). A disadvantage of using a JEM is that it does not assess exposure at the individual chemical or biological agent level, which leads to imprecision. Also, not

having a full job history and being unable to estimate cumulative occupational exposure throughout somebody’s entire career is a big limitation and might have resulted in noninformative analyses of rate of lung function decline. Furthermore, some of the occupational exposures are strongly correlated (e.g., fungicides with insecticides or herbicides and gases and fumes with biological dust or mineral dust). This strong correlation complicates the investigation of the effect of the separate exposures on lung function. Finally, we adjusted for well-known covariates (also covariates that are available in the Lifelines cohort study) to overcome confounding effects. We did not adjust for other potential confounders such as stress or physical workload. So, we cannot rule out the effect of these unmeasured confounders in our analysis.

**Conclusions**

In the current study, we found that occupational exposures are related to a

**Table 3.** Association between occupational exposures and annual lung function decline

Occupational Exposure	Exposure Level	Main Analyses*				Interaction with Male Sex <sup>†</sup>				Interaction with Current Smoking <sup>‡</sup>			
		FEV <sub>1</sub>	FVC	FEV <sub>1</sub> /FVC	FEF <sub>25-75</sub>	FEV <sub>1</sub>	FVC	FEV <sub>1</sub> /FVC	FEF <sub>25-75</sub>	FEV <sub>1</sub>	FVC	FEV <sub>1</sub> /FVC	FEF <sub>25-75</sub>
Biological dust	Low												
	High	↓								↓		(↓)	↓
Mineral dust	Low			↑	(†)								
	High		↓	↑							(↓)		
Gases and fumes	Low	(↓)	↓							(↓)		(↓)	
	High			↑									
Insecticides	Low									↓	↓	(↓)	
	High												
Herbicides	Low							(↓)					
	High				↑								
Fungicides	Low									↓			(↓)
	High												
Aromatic solvents	Low												
	High							(†)	↑				
Chlorinated solvents	Low									(↓)			
	High												
Other solvents	Low												
	High									(↓)			
Metals	Low												
	High							(†)					

*Definition of abbreviations:* FEF<sub>25-75</sub> = forced expiratory flow, midexpiratory phase; FEV<sub>1</sub> = forced expiratory volume in 1 second; FVC = forced vital capacity. The linear regression was adjusted for age, sex, height, pack-years, smoking, education, and monthly income. The FEF<sub>25-75</sub> model was additionally adjusted for FVC.

\*No exposure as reference group.

<sup>†</sup>Females as reference group.

<sup>‡</sup>Never-smokers as reference group.

↑Positive associations or interactions.

↓Negative associations or interactions.

↑/↓ =  $P < 0.05$ .

(↑/↓) =  $0.05 \leq P < 0.10$ .

lower lung function level at baseline, which is obstructive in nature. Males and smokers are at higher risk of having a lower lung function after occupational exposures than females and nonsmokers, respectively. Future studies should consider the total

duration of exposure, cumulative exposure, age of first exposure, and time since last exposure to detect the effects over the life course of occupational exposures on lung function level and the rate of decline over time. ■

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