Cumulative Occupational Exposures and Lung-Function Decline in Two Large General-Population Cohorts

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Abstract

Rationale: Few longitudinal studies have assessed the relationship between occupational exposures and lung-function decline in the general population with a sufficiently long follow-up.

Objectives: To examine the potential association in two large cohorts: the ECRHS (European Community Respiratory Health Survey) and the SAPALDIA (Swiss Cohort Study on Air Pollution and Lung and Heart Diseases in Adults).

Methods: General-population samples of individuals aged 18 to 62 were randomly selected in 1991–1993 and followed up approximately 10 and 20 years later. Spirometry (without bronchodilation) was performed at each visit. Coded complete job histories during follow-up visits were linked to a job-exposure matrix, generating cumulative exposure estimates for 12 occupational exposures. Forced expiratory volume in 1 second (FEV1) and forced vital capacity (FVC) were jointly modeled in linear mixed-effects models, fitted in a Bayesian framework, taking into account age and smoking.

Results: A total of 40,024 lung-function measurements from 17,833 study participants were analyzed. We found accelerated declines in FEV1 and the FEV1/FVC ratio for exposure to biological dust, mineral dust, and metals (FEV1 = 215.1 ml, 214.4 ml, and 218.7 ml, respectively; and FEV1/FVC ratio = 20.52%, 20.43%, and 20.36%, respectively; per 25 intensity-years of exposure). These declines were comparable in magnitude with those associated with long-term smoking. No effect modification by sex or smoking status was identified. Findings were similar between the ECRHS and the SAPALDIA cohorts.

Conclusions: Our results greatly strengthen the evidence base implicating occupation, independent of smoking, as a risk factor for lung-function decline. This highlights the need to prevent or control these exposures in the workplace.

Keywords: spirometry; lung function; occupational exposure; occupational disease; longitudinal studies

Chronic obstructive pulmonary disease

(COPD) is an important cause of population morbidity and mortality, characterized by a low degree of lung function and persistent airflow limitation (1). The most well-recognized risk factor is tobacco smoking, which is associated with the majority

of COPD cases. Other environmental risk factors are also implicated in the pathogenesis of COPD (2), including occupational exposures (3). The ECRHS (European Community Respiratory Health Survey) has recently shown a higher incidence of COPD in workers exposed to biological dusts, gases, fumes, and pesticides, with a combined population-attributable fraction of 21% (4).

Lung function declines naturally with age, but an accelerated decline is a primary, although not obligatory, cause of COPD (5) and a long-term feature of asthma (6). Despite a large number of studies, including both population- and industry-based studies, demonstrating an association of asthma and COPD with occupational exposures (3, 7, 8), relatively few population-based longitudinal studies have examined the relationship between lung-function decline and occupational

exposures, as estimated by a job-exposure matrix (JEM) (9–11). A previous analysis from the first 10-year follow-up of the ECRHS did not show a steeper decline in lung-function in people exposed to vapors, gases, dusts, or fumes (9); the cohort, however, was fairly young then (30–55 yr at the time), and the follow-up time may have been too short to detect an association.

Therefore, our aim was to examine the association between occupational exposures and the rate of lung-function decline, given its potential relevance to COPD risk. To do so, we combined two large prospective cohorts participating in the Ageing Lungs in European Cohorts study (www.alecstudy.org): the ECRHS (12) and the SAPALDIA (Swiss Cohort Study on Air Pollution and Lung and Heart Diseases in Adults) (13). Both cohorts have accumulated two decades of follow-up with more participants over 50 years of age, thus allowing better and more precise estimates of the determinants of lung-function decline. In addition, we examined whether the association between occupation and lung-function decline is different between men and women and between smokers and nonsmokers.

Methods

The ECRHS is a multicenter longitudinal study initiated in 1991–1993 that enrolled random general-population samples of individuals aged 20–44 years in 55 centers from 23 countries (12). Participants at baseline

(ECRHS I) completed a detailed questionnaire via a face-to-face interview and underwent a clinical examination, spirometry, and other measurements. They were followed up between 1998 and 2002 (ECRHS II) and a second time between 2010 and 2012 (ECRHS III). SAPALDIA is also a multicenter longitudinal study with objectives, methods, and protocols very similar to those of the ECRHS, which was initiated in 1991 (SAPALDIA 1) and enrolled a random general-population sample of individuals aged 18–62 years from eight regions in Switzerland (13). SAPALDIA participants were also followed up in 2001 and 2011

(SAPALDIA 2 and 3). A flowchart of study participants from both cohorts can be found in the online supplement (see Figure E1 in the online supplement).

During both follow-ups, participants in both cohorts were asked to provide a detailed list of their occupations and industries from all jobs held since the last study visit; these were recorded in free text and subsequently coded in the International Classification of Occupations-88 (ISCO-88) standard by trained local coders who were blind to participant status. Ethical approval for each center was obtained from their respective competent bodies, and written informed consent was obtained from all participants.

The population for this analysis includes all participants who underwent spirometry at baseline (ECRHS I/SAPALDIA 1) and were followed up at least once (at ECRHS II/SAPALDIA 2 and/or ECRHS III/SAPALDIA 3). All spirometric examinations were performed without bronchodilation and according to the American Thoracic Society/European Respiratory Society standards for reproducibility, using the maximum forced vital capacity (FVC) and forced expiratory volume in 1 second (FEV1) for each participant. Occupational exposures were determined by linking the

participants' ISCO-88–coded occupations to the semiquantitative ALOHA(1) JEM (10). This JEM assigns, for every ISCO-88 job code, three grades of exposure (none, low, high) to 12 agents (biological dusts, mineral dusts, gases/fumes, herbicides, insecticides, fungicides, aromatic solvents, chlorinated solvents, other solvents, and metals) including two composites of the above (all pesticides and vapors/gases/dusts/fumes

[VGDF]). For each participant, a cumulative exposure to each agent in intensity-years was calculated by multiplying the duration of each job with the intensity of exposure (0 for none, 1 for low, and 4 for high); these intensities reflect the lognormal distribution of occupational exposure concentrations when calculating cumulative exposures.

Covariates used for adjustments at each visit included age, sex, height (including its square, to allow for nonlinear associations), current asthma, current smoking, lifetime smoking pack-years, socioeconomic status (SES), and early-life disadvantage score; the latter is a composite variable that includes maternal smoking, maternal asthma, paternal asthma, childhood asthma (before age 10), and having a serious respiratory infection before age 5 (14). Current asthma was defined as a positive response to any of the following three questions: "Have you had an attack of asthma in the last 12 months?"; "Are you currently taking any medicines for asthma?"; and "Have you been woken by an attack of shortness of breath at any time in the last 12 months?" SES was defined according to the participants' age of completion of formal education and classified into three categories: high (under 19 yr), middle (16–19 yr), low (over 16 yr).

Associations between cumulative occupational exposures and lung function (FEV1, FVC, and the FEV1/FVC ratio) were assessed using linear mixed-effects models, providing the mean change in lung function per intensity-year of exposure. FEV1 and FVC were jointly modeled, and all models included participant level, random intercepts, and slopes, taking account

of the correlations between both random intercepts and slopes as well as FEV1 and FVC. For each ALOHA(1) exposure agent, we fitted two joint models, one using absolute FEV1 and FVC ("linear model") and one using their logarithms as the outcome ("log-linear model"); from the latter, we calculated the effects of exposures on the FEV1/FVC ratio as the difference between model parameters for log(FEV1)and log(FVC). In all instances, the comparison was between participants who were exposed and participants who were unexposed to the particular ALOHA(1) agent rather than between exposed participants and participants without any occupational exposure.

The models were fitted in a Bayesian framework with the JAGS software, setting noninformative priors for all parameters, and using four chains and 20,000 iterations per chain, discarding the first 2,000 as burn-in, and with a thinning interval of 5. Convergence was checked by visual inspection of the Markov chain Monte Carlo trace plots and by the Gelman-Rubin statistic. Furthermore, all models included a fully Bayesian imputation submodel for handling item (covariate) missingness, with hyperparameters set to noninformative priors (see online supplement for details). Uncertainty for the fixed effects was expressed with 95% credible intervals (95% CrIs).

In addition to the unstratified models, we fitted another set of models with added interaction terms for sex and smoking status (ever-/never-smoker), thereby calculating stratified estimates for the effect of occupational exposures in men and women and in ever-smokers and never-smokers. As a criterion to determine the presence of interaction (effect modification), we used the posterior probability distribution of the interaction term, at least 95% of which should lie above or below zero. As a sensitivity analysis, we also fitted all models to the data from each cohort (ECRHS and SAPALDIA) separately.

All analyses were performed with the R statistical environment, version 3.6.0 (15).

Results

Table 1 highlights the characteristics of the study population. We analyzed a total of 40,024 lung-function measurements from 17,833 study participants across 38 ECRHS and SAPALDIA centers, each of whom completed at least one follow-up visit after baseline, with a mean follow-up duration of 16.3 years (range, 4.3–22.6 yr). Of these participants, 10,803 (60.6%) completed both visits over a mean duration of 19.6 years (range, 15.7–22.6 yr); 5,793 (32.5%) participants completed the initial and the first follow-up visits only, whereas 1,237 (6.9%) completed the initial and the second follow-up visits only. Slightly less than half of our sample had never smoked, and about a third were current smokers at baseline, dropping almost by half to 18.3% at the second follow-up. A little less than half of all participants had been occupationally exposed to VGDF at some point during follow-up (39.8%), whereas fewer had been exposed to solvents (24.2%), metals (9.3%), or pesticides (3.3%). Men were overall more likely than women to be occupationally exposed to most agents, with the exception of biological dust (Table 2). In addition, many exposures showed substantial overlap with each other (Figure 1). A list of the most common jobs by exposure category can be found in the online supplement (Table E1); notably, “occupational cleaner” was the most frequent job title among those exposed to dusts, gases, and fumes (426 study participants).

Lifetime smoking pack-years were missing in 7.8% of all observations and had to be imputed in our models as described in the METHODS section; in addition, current smoking status was missing in 2.9%, current asthma status was missing in 0.5%, and SES was missing in 1.1% of all observations. Lung function in the study population naturally declined with advancing age across both follow-ups, and our Bayesian mixed-effects model was reliable in describing both mean lung function by age and the variability around the mean (Figure 2).

Table 3 summarizes the main results from our analysis, which included the effect of 25 intensity-years of occupational exposure to each ALOHA(1) agent on the three lung-function parameters (FEV1, FVC, and the FEV1/FVC ratio), both overall and stratified by sex and smoking status. A negative sign indicates reduced lung function as compared with no occupational exposure to the respective agent, given the same age, sex, and other covariates (i.e., an accelerated lung-function decline), whereas a positive number indicates a slower lung-function decline. As the numbers per year are very small, the effect per 25 intensity-years is presented rather than the effect per 1 intensity-year of exposure.

A decreased FEV1/FVC ratio was observed for biological-dust and mineral-dust exposure (20.52% and 20.43%, respectively) (Table 3), which was purely attributed to a FEV1 decline (215.08 ml and 214.42 ml, respectively), with no change in the FVC. A significant decline in FEV1 only was also observed for metal exposure

(218.73 ml; 95% CrI, 234.41 to 22.60 ml), and a lower FEV1/FVC ratio was observed for the composite VGDF exposure (20.34%; 95% CrI, 20.56 to 20.12%). On the other hand, smaller lung-function declines were seen for gases and fumes (27.35 ml in the FEV1 and 20.24% in the FEV1/FVC ratio) as well as for pesticides, especially in terms of the FEV1, although the results were very imprecise, with a wider 95% CrI than other exposures (Table 3). Among solvents, only exposure to chlorinated solvents was weakly associated with both lower FEV1 and lower FVC (216.98 ml and 214.59 ml). For comparison, as estimated in the model, 25 pack-years of smoking reduced FEV1 by an additional 211.07 ml (95% CrI, 222.27 to 2.49 ml), reduced FVC by 214.83 ml (95%CrI, 232.29 to 20.55 ml), and reduced the FEV1/FVC ratio by 20.21% (95% CrI, 20.44% to 0.03%). In addition,

current asthma was associated with an FEV1 that was 280.28 ml lower (95% CrI, 292.72 to 267.71 ml), an FVC that was lower by 213.60 ml (95% CrI, 227.44 to 20.05 ml), and an FEV1/FVC ratio that was 22.16%lower (95% CrI, 22.52% to 21.81%).

No effect modification by sex was detected for any occupational exposure or any lung-function parameter, with one exception: women exposed to aromatic solvents had a slower FVC decline than unexposed women (186.87 ml; 95% CrI, 13.80 to 161.25 ml), whereas no significant difference was found among men (27.84 ml; 95% CrI, 234.96 to 20.18 ml). In addition, no effect modification by smoking status was

Table 1. Characteristics of study participants by study wave detected, although in most cases, the effects of occupational exposures in ever-smokers tended to be slightly lower than in never-smokers (Table 3). In the sensitivity analysis, results were similar between the two cohorts and showed wide overlap; pesticide exposure resulted in greater FEV1 decline among ECRHS participants, whereas solvents resulted in slightly greater declines among SAPALDIA participants (Table E2).

Discussion

In this pooled analysis from two large longitudinal cohorts, we showed that certain groups of occupational exposures, namely biological dust, mineral dust, and metal exposure, were prospectively associated with accelerated lung-function decline, specifically with respect to FEV1 and the FEV1/FVC ratio. This loss of lung function is comparable with that associated with smoking, highlighting the importance of these occupational exposures in respiratory health. Our study provides significant new evidence on the topic, as few such studies have examined longitudinal lung-function decline in a general-population setting (10, 11, 16–18). In comparison with industry-based studies, studies of general-population cohorts can provide more generalizable information by including all types of exposures across all industries and by adjusting for SES and other covariates. Previous analyses from both ECRHS and SAPALDIA have shown an increased asthma risk for certain occupational exposures (19), an increased incidence of COPD in participants occupationally exposed to biological dust and mineral dust (4, 20), and an increased incidence of chronic cough and chronic phlegm symptoms in those exposed to mineral dust and metals (21). Our current analysis corroborates previous findings for biological dust in a much larger study population with additional follow-up. It also indicates that mineral dust and metal exposure are associated not only with chronic bronchitis symptoms but also with lung-function decline. The latter result is in agreement with recent findings from the smaller Tasmanian longitudinal health study cohort (22) and with a systematic review of exposure to welding fumes and lung-function decline (23). We also found cleaner to be a frequent jobtitle among exposed occupations, one that was recently associated with an accelerated decline in lung function (24).

A striking finding is the very small absolute effect sizes observed, only a few milliliters (or a fraction of a percentage point) of lung-function decline after 25 intensity-years of exposure, which, for many workers, may represent their entire lifetime exposure. At first glance, such reductions could not plausibly account for an increased COPD risk, as has been seen in previous analyses (4, 8, 20); however, these are average subject-specific effects over an exposure group, and small average reductions can mask a larger effect for certain individuals inside the group (25), especially if one also considers the sizable individual variation in lung function

(Figure 2). In addition, the comparator is not a fully occupationally unexposed group but is rather composed of participants unexposed to the agent under consideration (who may have other occupational exposures). Furthermore, nondifferential misclassification is the main limitation

in using JEMs in population-based occupational epidemiology studies, mostly stemming from the variability in job tasks and actual exposures between workers belonging in the same JEM exposure category (26). Grouping exposures in a JEM does not in itself bias regression coefficients toward the null but rather results in imprecision because of Berkson-type error (27); nevertheless, regression-dilution bias can be introduced if the estimated group mean is different from the true group mean (28). Intraindividual variability in exposure over time is another consideration, which is particularly relevant when calculating a cumulative exposure estimate on the basis of job duration and a JEM classification, which was, in this case, calculated over a long period of 20 years (29). All of these factors mean that the small average declines observed in our analysis should not be used for prediction, as they are unlikely to represent the actual magnitude of the effect of these exposures on lung function in any particular individual. For the same reasons, our results cannot be used to definitively rule out an effect of occupational solvent exposure on lung function, as recently observed in the Tasmanian longitudinal health study cohort (22), nor can they be used to rule out an effect of pesticide exposure (4, 10). Especially regarding pesticides, the small percentage of exposed participants (less than 5%) (Table 2) has substantially reduced precision, as reflected in the wider CrIs of the lung function–decline estimates.

Smoking is known to induce inflammation and impair the host-defense mechanisms of the lung (30, 31) and has been reported to increase the adverse effect of occupational exposures on lung-function decline and COPD risk (32–34). However, in our analyses, we found little evidence of effect modification by smoking after tightly adjusting both for current smoking status and cumulative pack-years. This indicates that all workers may be at risk of airway obstruction because of these occupational exposures, even though this may be more clinically significant for smokers, who represent the majority of patients with COPD in most countries, who already have lower levels of lung function, such that any additional loss or acceleration of decline may push them over the diagnostic cut off. Similarly, we found little difference between men and women on the effect of occupational exposures, even though the distribution of jobs for each exposure category was different between men and women. This may partially be explained by the lower proportion of occupationally exposed women in our cohorts, particularly for exposures like metals, pesticides, and solvents. Future occupational epidemiology studies should try to recruit more women to investigate effect modification by sex.

Strengths of the current study include its prospective population-based design and long follow-up of 20 years. Full job histories were collected for the study period, and cumulative occupational exposures were calculated using a JEM instead of self-report; the latter could be vulnerable to recall bias, especially given the long follow-up involved. Lung function was modeled in great detail using a mixed-effects model with random intercepts and slopes and accounting for the correlation between FEV1 and FVC; joint modeling of both spirometric parameters is important, as we identified positive correlations not only between the participant-level random intercepts and slopes for FEV1 and FVC but also between the intercepts for FEV1 and FVC and the slopes for FEV1 and FVC (data not shown). In addition, we controlled for multiple confounders, including SES, current asthma, and, especially, lifetime smoking pack-years, to minimize confounding by intensity of smoking. The sample size was very large, thanks to the pooling of two large cohorts, facilitating the detection of associations of very small magnitude.

On the other hand, there are certain limitations to our study. Spirometric examinations were performed without bronchodilation, and the results should be interpreted accordingly. Accelerated lung-function decline in and of itself does not equate with COPD risk; in particular, occupation can also be a risk factor for asthma, and it is thus not possible to distinguish lung-function decline due to new-onset occupational asthma from that contributing to increased COPD incidence. The application of a JEM may ensure more objective exposure estimates, which are free from exposure-specific recall but can introduce both imprecision because of Berkson-type error and some bias toward the null; therefore, despite its large size, the sample may not have always been sufficient to detect an association (e.g., the effects of pesticides or identification of an effect modification). For the same reason, we cannot disentangle the effect of multiple overlapping exposures, which would require a large number of small subgroup analyses. We also could not assess the heterogeneity of the results across study centers or countries because the necessary inclusion of participant-level random effects left almost no variance to be explained by study center. Finally, residual confounding cannot be completely ruled out, despite the detailed model adjustments, and may have affected the observed associations, given their small magnitude. As this is an observational study, some degree of selection and response bias also cannot be definitely ruled out.

In conclusion, long-term occupational exposure to biological dust, mineral dust, and metals over two decades of follow-up was associated with an accelerated decline in FEV1 and the FEV1/FVC ratio, which would potentially translate to an increased risk of airway obstruction and COPD. This decline was comparable with that associated with smoking and was similar between men and women as well as between smokers and nonsmokers. These results strengthen the case for occupation as a modifiable risk factor for asthma and COPD, in agreement with previous studies. And they make the workplace, or controlling them with appropriate protective measures, to protect the respiratory health of workers.

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Table 1. Characteristics of study participants by study wave

	ECRHS I/SAPALDIA 1	ECRHS II/SAPALDIA 2	ECRHS III/SAPALDIA 3
Number of participants	17,833 (9,765/8,068)	16,596 (8,725/7,871)	12,040 (6,013/6,027)
Men, %	48.0 (48.0/47.9)	48.1 (48.1/48.0)	47.7 (47.9/47.5)
Mean age	37.2 (34.0/41.0)	47.2 (42.8/52.0)	56.9 (54.1/59.7)
Current asthma, %	6.4 (7.9/4.7)	7.9 (9.9/5.6)	7.6 (11.2/4.1)
Never-smokers, %	46.0 (44.8/47.4)	45.9 (45.5/46.4)	48.5 (49.0/48.1)
Current smokers, %	33.3 (34.5/31.9)	27.7 (29.0/26.3)	18.3 (18.1/18.5)
Mean cumulative smoking pack-years	8.4 (7.2/10.0)	11.1 (9.7/12.7)	11.7 (10.9/12.3)
Participants exposed, %			
Biological dust	—	22.0 (26.6/17.0)	26.7 (30.7/22.6)
Mineral dust	—	17.6 (21.1/13.8)	20.9 (23.9/18.0)
Gases & fumes	—	31.7 (37.4/25.4)	37.4 (41.3/33.5)
Vapors, gases, dusts & fumes	—	35.8 (41.9/29.2)	42.0 (46.1/37.9)
Herbicides	—	1.7 (1.5/1.9)	2.2 (1.8/2.6)
Insecticides	—	2.1 (2.3/1.9)	2.8 (2.9/2.6)
Fungicides	—	2.2 (2.4/2.0)	3.1 (3.4/2.8)
All pesticides	—	2.7 (3.2/2.1)	3.6 (4.3/3.0)
Aromatic solvents	—	11.4 (13.1/9.6)	13.5 (14.9/12.1)
Chlorinated solvents	—	9.1 (10.3/7.7)	10.9 (12.2/9.6)
Other solvents	—	19.4 (23.0/15.3)	23.6 (26.9/20.4)
Metals	—	7.9 (9.5/6.1)	9.7 (11.4/8.0)
Mean cumulative exposures since previous follow-up, intensity-years			
Biological dust	—	2.2 (2.2/2.1)	4.1 (4.7/3.6)
Mineral dust	—	2.3 (2.4/2.2)	4.1 (4.7/3.5)
Gases & fumes	—	3.6 (3.9/3.3)	6.6 (7.7/5.4)
Vapors, gases, dusts, and fumes	—	5.1 (5.3/4.8)	9.2 (10.6/7.9)
Herbicides	—	0.2 (0.1/0.3)	0.4 (0.3/0.6)
Insecticides	—	0.4 (0.3/0.6)	0.8 (0.6/1.1)
Fungicides	—	0.3 (0.3/0.4)	0.6 (0.6/0.6)
All pesticides	—	0.5 (0.4/0.6)	0.9 (0.7/1.1)
Aromatic solvents	—	1.0 (1.0/1.0)	1.7 (1.9/1.6)
Chlorinated solvents	—	1.2 (1.2/1.2)	1.9 (2.1/1.7)
Other solvents	—	1.7 (1.8/1.6)	3.2 (3.7/2.7)
Metals	—	1.2 (1.3/1.1)	2.0 (2.3/1.7)

Definition of abbreviations: ECRHS = European Community Respiratory Health Survey; SAPALDIA = Swiss Cohort Study on Air Pollution and Lung and Heart Diseases in Adults
N = 17,833 ECRHS and SAPALDIA participants followed up at least once. Data are shown as data for the entire cohort (data for ECRHS/data for SAPALDIA).

Table 2. Proportion of participants with any occupational exposure during follow-up, stratified by sex

	Men Exposed (%)	Women Exposed (%)
Biological dust	22.2 (25.5/18.2)	27.7 (32.5/22.0)
Mineral dust	28.8 (33.6/23.1)	11.8 (13.4/10.0)
Gases & fumes	42.7 (47.9/36.4)	29.0 (33.2/23.8)
Vapors, gases, dusts & fumes	46.3 (51.8/39.7)	33.8 (38.2/28.4)
Herbicides	2.8 (2.5/3.1)	1.2 (1.0/1.5)
Insecticides	3.5 (3.8/3.1)	1.6 (1.6/1.5)
Fungicides	4.1 (4.7/3.4)	1.5 (1.4/1.6)
All pesticides	4.9 (5.9/3.7)	1.7 (1.8/1.6)
Aromatic solvents	21.5 (23.6/18.8)	5.0 (5.9/3.8)
Chlorinated solvents	16.8 (18.7/14.5)	4.5 (5.2/3.7)
Other solvents	25.5 (28.4/22.0)	18.9 (22.7/14.4)
Metals	17.3 (20.1/13.9)	1.8 (2.4/1.0)

N = 17,833 ECRHS (European Community Respiratory Health Survey) and SAPALDIA (Swiss Cohort Study on Air Pollution and Lung and Heart Diseases in Adults) participants that followed up at least once. Data are shown as data for the entire cohort (data for ECRHS/data for SAPALDIA).

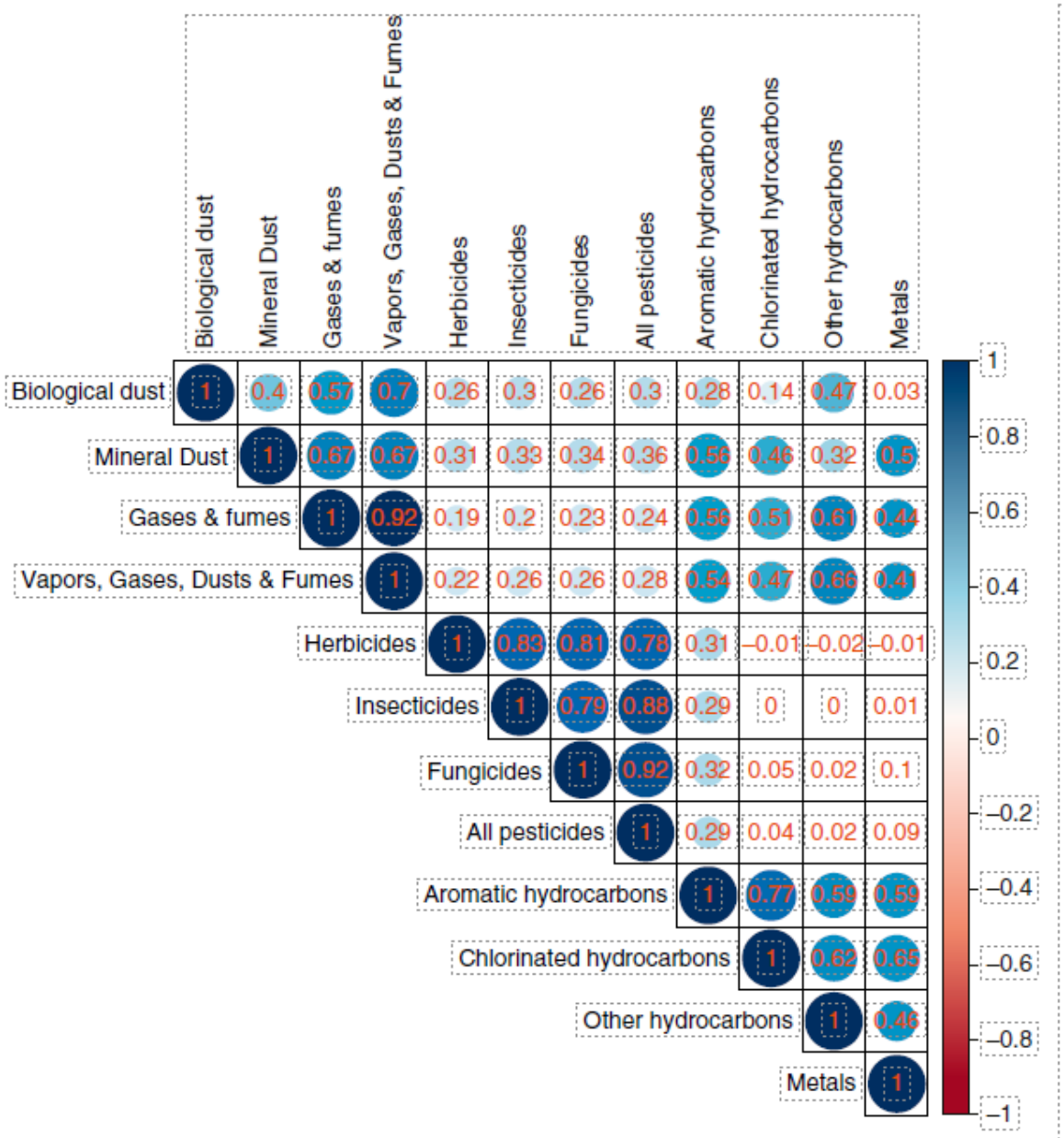

Figure 1. Correlation matrix (Spearman rho) between cumulative occupational exposures (intensity-years) in the study population, as estimated by the ALOHA(+) job-exposure matrix. ($n = 17,833$; European Community Respiratory Health Survey and Swiss Cohort Study on Air Pollution and Lung and Heart Diseases in Adults participants).

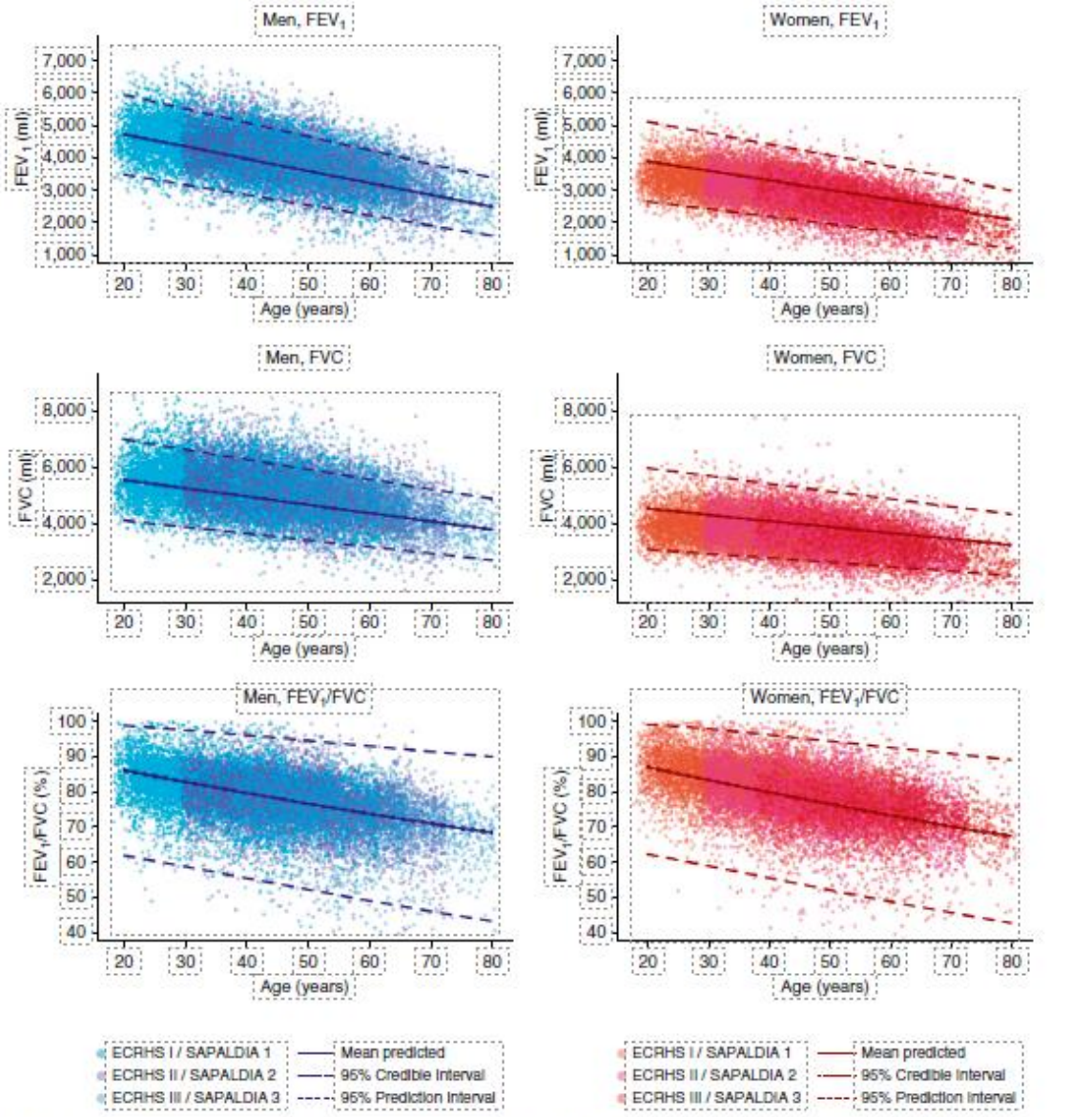

Figure 2. Lung function by age and sex in the study population, including observed and model-predicted lung function (n = 40,024 measurements in 17,833 ECRHS and SAPALDIA participants). The height is set to the cohort mean by sex; smoking pack-years and cumulative vapors/gases/dusts/fumes exposure are set to the cohort mean by age and sex. ECRHS = European Community Respiratory Health Survey; FEV_1 = forced expiratory volume in 1 second; FVC = forced vital capacity; SAPALDIA = Swiss Cohort Study on Air Pollution and Lung and Heart Diseases in Adults.

Table 3. Effect of occupational exposures on lung-function decline, per 25 intensity-years of exposure, compared with being unexposed to the respective agent, overall and stratified by sex and smoking status

	FEV_1 (*ml*)	FVC (*ml*)	FEV_1/FVC (%)
Biological dust	−15.08 (−28.66 to −0.88)	2.68 (−12.68 to 18.28)	−0.52 (−0.88 to −0.16)
Never-smokers, men/women	−3.23 (−26.67 to 20.22)/−14.38 (−45.32 to 15.59)	13.44 (−12.79 to 39.41)/8.35 (−25.83 to 43.27)	−0.28 (−0.95 to 0.41)/−0.52 (−1.35 to 0.36)
Ever-smokers, men/women	−15.86 (−33.93 to 2.09)/−27.11 (−53.91 to −1.19)	−0.47 (−20.80 to 19.98)/−5.59 (−35.49 to 24.14)	−0.52 (−1.02 to −0.02)/−0.76 (−1.46 to −0.04)
Mineral dust	−14.42 (−26.41 to −2.50)	0.12 (−12.99 to 13.10)	−0.43 (−0.75 to −0.10)
Never-smokers, men/women	−9.38 (−28.04 to 9.65)/5.55 (−29.53 to 39.95)	10.96 (−10.24 to 31.96)/15.54 (−22.24 to 53.37)	−0.56 (−1.10 to −0.02)/−0.31 (−1.23 to 0.61)
Ever-smokers, men/women	−20.83 (−35.33 to −6.25)/−6.15 (−37.68 to 24.57)	−7.12 (−23.55 to 9.48)/−2.42 (−37.19 to 33.52)	−0.44 (−0.84 to −0.03)/−0.18 (−1.01 to 0.65)
Gases & fumes	−7.35 (−17.99 to 3.15)	3.46 (−8.66 to 15.25)	−0.24 (−0.53 to 0.04)
Never-smokers, men/women	4.22 (−12.83 to 21.44)/−10.01 (−39.00 to 19.03)	14.43 (−4.90 to 33.41)/11.31 (−22.02 to 43.81)	−0.14 (−0.64 to 0.35)/−0.38 (−1.16 to 0.43)
Ever-smokers, men/women	−10.22 (−23.34 to 3.14)/−24.37 (−51.63 to 3.81)	−2.14 (−16.77 to 12.32)/−5.52 (−36.24 to 25.02)	−0.24 (−0.59 to 0.11)/−0.48 (−1.24 to 0.24)
Vapors, gases, dusts & fumes	−7.42 (−15.93 to 1.03)	6.02 (−3.04 to 15.42)	−0.34 (−0.56 to −0.12)
Never-smokers, men/women	−1.44 (−14.83 to 11.91)/−6.21 (−28.65 to 16.31)	11.89 (−2.73 to 26.67)/14.92 (−10.55 to 39.96)	−0.27 (−0.65 to 0.11)/−0.47 (−1.06 to 0.13)
Ever-smokers, men/women	−9.45 (−19.62 to 0.97)/−14.20 (−35.47 to 7.03)	1.76 (−9.68 to 13.41)/5.14 (−18.42 to 28.40)	−0.33 (−0.61 to −0.06)/−0.52 (−1.06 to 0.01)
Herbicides	−14.69 (−49.54 to 20.57)	−8.57 (−47.42 to 29.56)	−0.34 (−1.28 to 0.59)
Never-smokers, men/women	−19.16 (−85.70 to 43.26)/35.35 (−51.37 to 122.19)	−23.73 (−96.58 to 48.69)/22.63 (−73.97 to 120.70)	−0.28 (−2.17 to 1.65)/0.55 (−1.85 to 3.00)
Ever-smokers, men/women	−33.13 (−77.76 to 11.56)/21.78 (−46.93 to 91.26)	−20.84 (−72.01 to 28.90)/26.82 (−50.71 to 104.30)	−0.67 (−1.88 to 0.55)/0.12 (−1.71 to 2.05)
Insecticides	−7.24 (−29.73 to 15.04)	−2.43 (−27.68 to 23.16)	−0.23 (−0.83 to 0.38)
Never-smokers, men/women	−7.72 (−47.54 to 32.36)/22.94 (−28.06 to 74.16)	3.48 (−40.41 to 46.91)/35.24 (−22.53 to 92.33)	−0.50 (−1.60 to 0.65)/−0.21 (−1.64 to 1.20)
Ever-smokers, men/women	−20.10 (−51.00 to 10.02)/10.06 (−31.78 to 52.25)	−18.67 (−53.26 to 15.24)/12.87 (−34.21 to 58.71)	−0.24 (−1.06 to 0.60)/0.04 (−1.07 to 1.17)
Fungicides	−13.68 (−41.81 to 14.97)	−11.45 (−43.33 to 20.68)	−0.17 (−0.97 to 0.61)
Never-smokers, men/women	−22.51 (−72.85 to 28.73)/28.10 (−41.07 to 98.08)	−12.06 (−67.76 to 43.25)/38.65 (−39.70 to 114.70)	−0.46 (−1.98 to 1.03)/0.03 (−1.88 to 1.96)
Ever-smokers, men/women	−28.9 (−66.48 to 8.72)/21.89 (−36.93 to 79.10)	−29.25 (−69.81 to 12.87)/21.37 (−45.18 to 87.03)	−0.26 (−1.31 to 0.77)/0.23 (−1.37 to 1.85)
All pesticides	−10.74 (−32.37 to 10.90)	−6.60 (−31.35 to 18.95)	−0.20 (−0.78 to 0.39)
Never-smokers, men/women	−16.23 (−55.54 to 22.68)/17.02 (−34.02 to 66.51)	−7.92 (−52.14 to 36.53)/27.85 (−26.88 to 84.30)	−0.42 (−1.50 to 0.69)/−0.18 (−1.58 to 1.25)
Ever-smokers, men/women	−22.87 (−52.79 to 7.68)/10.42 (−30.63 to 51.27)	−21.70 (−55.53 to 11.46)/14.28 (−32.80 to 59.60)	−0.23 (−1.00 to 0.58)/0.01 (−1.05 to 1.12)
Aromatic solvents	0.28 (−22.53 to 23.42)	3.90 (−21.95 to 29.65)	0.01 (−0.61 to 0.63)
Never-smokers, men/women	−12.82 (−49.46 to 24.15)/40.35 (−32.52 to 113.02)	−13.70 (−53.99 to 25.40)/79.39 (−1.55 to 159.07)	−0.08 (−1.18 to 1.02)/−0.17 (−2.14 to 1.82)
Ever-smokers, men/women	−2.34 (−30.95 to 26.43)/51.06 (−15.10 to 117.27)	−3.31 (−36.96 to 28.35)/89.92 (14.99 to 162.53)	0.07 (−0.71 to 0.84)/−0.02 (−1.77 to 1.81)
Chlorinated solvents	−16.98 (−34.20 to 0.43)	−14.59 (−33.52 to 4.42)	−0.18 (−0.64 to 0.29)
Never-smokers, men/women	−13.31 (−42.06 to 14.73)/5.43 (−61.00 to 72.39)	−10.47 (−40.24 to 21.30)/31.80 (−42.25 to 106.20)	−0.19 (−1.01 to 0.64)/−0.14 (−2.00 to 1.79)
Ever-smokers, men/women	−20.45 (−40.67 to 0.17)/−1.38 (−67.59 to 65.47)	−20.98 (−43.51 to 1.47)/21.02 (−51.04 to 93.25)	−0.19 (−0.73 to 0.37)/−0.14 (−1.89 to 1.67)
Other solvents	−6.05 (−23.61 to 11.37)	7.65 (−11.39 to 27.28)	−0.24 (−0.70 to 0.24)
Never-smokers, men/women	3.67 (−28.12 to 36.60)/−11.05 (−46.12 to 24.35)	22.33 (−14.03 to 58.55)/17.37 (−22.07 to 55.83)	−0.32 (−1.25 to 0.61)/−0.56 (−1.53 to 0.39)
Ever-smokers, men/women	−0.76 (−26.90 to 26.20)/−15.35 (−43.67 to 12.26)	5.32 (−23.18 to 36.10)/−0.01 (−32.23 to 32.14)	−0.06 (−0.73 to 0.63)/−0.29 (−1.04 to 0.44)

(Continued)

Table 3. (*Continued*)

	FEV_1 (*ml*)	FVC (*ml*)	FEV_1/FVC (%)
Metals	−18.73 (−34.41 to −2.60)	−10.17 (−27.46 to 7.85)	−0.36 (−0.79 to 0.07)
Never-smokers, men/women	−11.75 (−37.20 to 14.07)/−30.34 (−110.04 to 48.64)	0.82 (−27.55 to 29.57)/−36.03 (−123.98 to 50.88)	−0.47 (−1.20 to 0.26)/−0.43 (−2.59 to 1.81)
Ever-smokers, men/women	−21.37 (−40.42 to −2.68)/−39.73 (−118.34 to 35.47)	−13.01 (−34.08 to 8.36)/−49.46 (−135.45 to 35.93)	−0.30 (−0.84 to 0.21)/−0.24 (−2.38 to 1.91)

Definition of abbreviations: FEV_1 = forced expiratory volume in 1 second; FVC = forced vital capacity.
N = 17,833 ECRHS (European Community Respiratory Health Survey) and SAPALDIA (Swiss Cohort Study on Air Pollution and Lung and Heart Diseases in Adults) participants that followed up at least once. Results are posterior medians with 95% credible intervals in parentheses. Numbers represent the absolute change in milliliters for FEV_1 and FVC and represent the relative percentage change for the FEV_1/FVC ratio. A negative sign indicates a lower value than that of participants who were fully unexposed to the respective agent. Data are adjusted for age, sex, current smoking, cumulative smoking pack-years, socioeconomic status, and early-life disadvantage score. All lung-function measurements are without bronchodilation.