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ORIGINAL ARTICLE

The association of forced expiratory volume in one second with occupational exposures in a longitudinal study of adults in a rural community in Iowa

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Abstract

Purpose The Keokuk County Rural Health Study (KCRHS) is a longitudinal population-based study conducted in rural Iowa. A prior analysis of enrollment data identified an association of airflow obstruction with occupational exposures only among cigarette smokers. The current study used spirometry data from all three rounds to investigate whether level of forced expiratory volume in one second (FEV_1) and longitudinal change in FEV_1 were associated with occupational vapor–gas, dust, and fumes (VGDF) exposures, and whether these associations were modified by smoking.

Methods This study sample comprised 1071 adult KCRHS participants with longitudinal data. A job-exposure matrix (JEM) was applied to participants' lifetime work histories to assign exposures to occupational VGDF. Mixed regression models of pre-bronchodilator FEV_1 (millimeters, ml) were fit to test for associations with occupational exposures while adjusting for potential confounders.

Results Mineral dust had the most consistent association with change in FEV_1, including ever/never (−6.3 ml/year) and nearly every level of duration, intensity, and cumulative exposure. Because 92% of participants with mineral dust also had organic dust exposure, the results for mineral dust may be due to a combination of the two. An association of FEV_1 level with fumes was observed for high intensity (−91.4 ml) among all participants, and limited to cigarette smokers with results of −104.6 ml ever/never exposed, −170.3 ml high duration, and −172.4 ml high cumulative.

Conclusion The current findings suggest that mineral dust, possibly in combination with organic dust, and fumes exposure, especially among cigarette smokers, were risk factors for adverse FEV_1 results.

Keywords Rural adults · Obstructive pulmonary disease · Longitudinal study · Lifetime work history · Job-exposure matrix

Introduction

Chronic obstructive pulmonary disease (COPD) is very common in the United States (US) and globally (Murray et al. 2012; WHO 2020). The overall age-adjusted prevalence of COPD among adults in the US was 6.2% in 2017 (Wheaton et al. 2017) and the mortality rate was an estimated 45.1/100,000 based on 2014 data (Dwyer-Lindgren et al. 2017). Cigarette smoking is the major preventable cause of COPD, but approximately one-fourth of cases in the US have never smoked (CDC 2012; Wheaton et al. 2017). Another preventable cause of COPD is occupational exposures, responsible for an estimated 14% of the total population burden and 31% of the burden among never smokers (Blanc et al. 2019). A recent review article concluded that experimental studies support the biological plausibility of occupational exposures contributing to the pathogenesis of COPD, most notably for inorganic dust but also for welding fumes, metals, and irritants (Murgia and Gambelunghe 2022).

Rural adults are at greater risk for COPD than their urban counterparts. From the National Health and Nutrition Examination Survey, the odds of airflow limitation as determined

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by spirometry was elevated for rural versus urban residents in the US, with an adjusted odds ratio (OR) 2.06, $p = 0.005$ (Raju et al. 2020). In another study that used national US data, rural residents had higher age-adjusted COPD prevalence and rates of COPD-related hospitalizations and deaths than residents in micropolitan and metropolitan locations (Croft et al. 2015).

The Keokuk County Rural Health Study (KCRHS) was a longitudinal population-based study that surveyed participants from a rural county in Iowa in three rounds during 1994–2011 (Merchant et al. 2002; Stromquist et al. 1997). We previously assessed occupational exposures for adult participants by applying a COPD-specific job-exposure matrix (JEM) to their most recent jobs (Doney et al. 2014; Doney et al. 2017). The COPD JEM was developed by scientists at the National Institute for Occupational Safety and Health (NIOSH), Centers for Disease Control and Prevention (CDC). The frequency of exposures relevant to COPD were more common in the rural KCRHS sample than in a sample of urban adults whose occupational exposures were determined using the same JEM (Doney et al. 2017). The contrast in frequency of adults with medium or high intensity of occupational exposures to vapor–gas, dust, and fumes (VGDF) was almost three-fold, with 43.2% for the rural residents and 15.0% for urban residents (Doney et al. 2017). We subsequently investigated the association of airflow obstruction based on cross-sectional spirometry with occupational VGDF exposures using enrollment data from KCRHS adults (Henneberger et al. 2020). While adjusting for potential confounders, high occupational VGDF exposure based on most recent job was a risk factor for airflow obstruction among ever-smokers, odds ratio $(OR) = 1.81$ (95% confidence interval (CI) 1.002–3.26), but not among never-smokers, $OR = 0.82$ (95% CI 0.32–2.12). However, this analysis was limited because it used only enrollment data and did not consider participants' entire work histories.

A lower level of forced expiratory volume in one second (FEV_1) or accelerated decline in FEV_1 over time is consistent with the development of COPD. Relatively few population-based studies have investigated the association of FEV_1 decline with occupational exposures, as evidenced by a recent systematic review and meta-analysis based on just 12 such articles (Rabbani et al. 2022). The two studies conducted in the United States reported accelerated longitudinal declines in FEV_1 associated with occupational exposures, specifically fumes (Harber et al. 2007) and dust (Liao et al. 2015), and both studies were centered in metropolitan areas. KCRHS data included high-quality spirometry and questionnaire data from three rounds of the study, and provided the opportunity to investigate the association of both FEV_1 level and change in FEV_1 with occupational exposures in a sample of US rural residents. The objectives of the current investigation were to answer the following questions: (1) Was cross-sectional FEV_1 level associated with occupational VGDF exposure? (2) Was longitudinal change in FEV_1 during the study associated with occupational VGDF exposure? and (3) Was the association of FEV_1 with occupational VGDF exposure modified by cigarette smoking status?

Methods

Human subjects review and approval

The Institutional Review Board (IRB) of the University of Iowa reviewed and approved the KCRHS protocol, and the NIOSH IRB reviewed and approved protocol 14-DRDS-01XP for the current investigation. Each KCRHS invitee provided written informed consent prior to participating.

Study sample

Details for KCRHS methods are available in earlier publications (Merchant et al. 2002; Stromquist et al. 1997). Keokuk County is in southeast Iowa and entirely rural. Households were selected at random from the sampling frame and all people within each household were invited to participate. A total of 1847 adults aged 18 years or older completed spirometry and questionnaires during at least one of the three rounds of testing. Participants who provided fewer than two acceptable spirometry curves ($n = 115$) or had missing data for smoking status, sex, age, body mass index (BMI), or asthma status ($n = 23$) were excluded from the sample. Additionally, ten nonwhite participants were excluded due to small numbers. These exclusions left 1,699 adult participants with spirometry data at enrollment, who were included in the earlier analysis of cross-sectional spirometry (Henneberger et al. 2020). However, 89 of these participants enrolled in Round 3 and had no opportunity for follow-up and contributing to longitudinal analyses. Of those enrolled in Round 1 or 2, 31% (498/1610) had no spirometry data in subsequent rounds, and 40 completed spirometry in at least one follow-up survey that did not pass NIOSH criteria for good quality (i.e., provided at least two acceptable curves that met repeatability criteria for FEV_1 and forced vital capacity, FVC) (CDC 2011). A final participant was excluded due to uncertain asthma status after enrollment. The remaining 1,071 participants with good data at enrollment and follow-up were included in the current investigation. They contributed a total of 2,678 observations from the three survey rounds.

Interviewing and testing KCRHS participants

The surveying of KCRHS participants occurred during 1994–2011 in three rounds: round 1, 1994–1998; round 2, 1999–2004; and round 3 2006–2011. Many questionnaire elements were from the American Thoracic Society (ATS) respiratory questionnaire and national studies such as the National Health Interview Survey and the Third National Health and Nutrition Examination Survey (Adams et al. 1999; CDC 1994; Ferris 1978). Spirometry was conducted without first administering a bronchodilator to participants.

Software for data management and analysis

We accomplished data management and analysis using SAS® 9.4 statistical software (SAS Institute Inc., Cary, NC, USA). Statistical significance was defined as $p \leq 0.05$, and borderline statistical significance as $0.05 < p \leq 0.10$.

Development of weights to use when modeling health outcomes

Loss to follow up in a longitudinal study can potentially yield a sample that is not representative of those enrolled and result in biased effect estimates (Kristman et al. 2004; Peytchev 2013). With this in mind, we generated weights based on the inverse probability of participating in follow-up rounds and applied these weights in regression models of health outcomes. A description of the calculation of weights is available in Supplement Methods for Calculating Weights. The weights had the range 1.20–5.97, interquartile range 1.50–1.92, median 1.68, and mean 1.78 (SD 0.49).

Occupational exposure variables

An individual's occupational exposure was assessed using their lifetime job history and the NIOSH COPD JEM (Doney et al. 2014). The KCRHS questionnaires collected a job history at each round and jobs were coded using the 2002 U.S. Census occupational codes (COCs). The COPD JEM used these COCs to assign one of three levels of exposure intensity (none or low, score = 0; medium, score = 1; high, score = 2) for the exposures vapor–gas, total dust, and fumes, and for the two subsets of total dust—organic dust and mineral dust.

Different characterizations of time-dependent occupational exposure were developed for each type of exposure: ever/never, duration in years, intensity expressed as an average level weighted by duration at each level, and cumulative exposure as the sum of the product of duration and intensity across a participant's jobs. Categories for level of duration, intensity, and cumulative exposure were created for each type of exposure. For vapor–gas, total dust, organic dust, and mineral dust, these categories (low, medium, high) were based on approximate tertiles of non-zero observations from all survey rounds. However, fumes exposure was much less common and non-zero values were divided at the median into only low and high levels. Each set of categories also included an unexposed reference group. The cut points for exposure categories are in Supplement Table S1.

Development of regression models for FEV_1

Analysis of the longitudinal FEV_1 data was performed using linear mixed models. Various covariates were considered when fitting a base model, with many of the same variables used to fit the model for participation (see Supplement Methods for Calculating Weights). Selected continuous variables were recoded as categorical variables. Pack-years of cigarettes was divided into four categories: never, low (> 0 and ≤ 7.5 pack-years), medium (> 7.5 and ≤ 24.0 pack-years), and high (> 24.0 pack-years). The cut-points were chosen to yield tertiles of observations among ever-smokers. BMI categories were defined as BMI < 18.5 underweight, 18.5 ≤ BMI < 25 normal, 25 ≤ BMI < 30 overweight, and BMI ≥ 30 obese. Time-independent covariates were age at enrollment (years), sex (male, female), height (inches), and ever farm work as a child (yes/no). Time-dependent covariates were smoking status (current, former, never), pack-years (categories), number of years since enrollment, ever asthma (yes/no), BMI category, and farming status as an adult (current, former, never) based on the work history.

We used the SAS MIXED procedure with a RANDOM effect statement, yielding random slopes and intercept, and an unstructured covariance structure for this model to account for repeated measures from each subject. This covariance structure was selected because it had the smallest Akaike Information Criterion (AIC) value.

The variables included in the final base model of spirometry were chosen through an iterative backwards selection process based on the model's AIC. It is normal for FEV_1 to decline with age, and covariates for both age at enrollment and years since enrollment were forced into the model to adjust for the effects of time. The factors sex, height, smoking status, and pack-years category are also typically associated with pulmonary function and were forced into the model as well. We started with a full base model that included these six variables and four other variables—ever asthma, BMI category, ever farm work as a child, and farming status as an adult—that were tested for removal if each of their levels had a $p > 0.20$. None of the four candidate variables met the $p > 0.20$ criterion and all were retained in the final base model.

Time-dependent occupational exposure variables were added to the final base model to determine their association with level of FEV_1 and decline in FEV_1. Exposure-related average annual decline in FEV_1 was estimated by interacting the exposure covariate with the covariate for time since enrollment. The interaction coefficient estimated the exposure-related annual change in FEV_1, which was in addition to the coefficient for time since enrollment in the same regression model that estimated the annual change for the unexposed. The units for annual change in FEV_1 were ml/year (ml/yr).

Interaction of occupational exposure with cigarette smoking

We fit additional models of FEV_1 to investigate potential interactions of ever/never occupational exposure with ever/never cigarette smoking. This was accomplished by changing the smoking status covariate from three levels (current, former, never) to just two levels (ever, never). For any type of exposure that had an interaction that was at least borderline statistically significant, we also investigated the interaction of ever smoking with different levels of duration and intensity of exposure and cumulative exposure.

Results

Descriptive characteristics

Data were available from all three rounds for about half the sample (n = 536, 50%), and decreasing numbers from rounds 1 and 2 (n = 332, 31%), 2 and 3 (n = 193, 18%), and 1 and 3 (n = 10, 1%). Characteristics of the 1,071 KCRHS participants for the current study at enrollment and the final survey are presented in Table 1. The sample included more women (58%) than men, was middle-aged when enrolled (mean 52 years), and was followed a mean of 9.0 years. The percentages for former smokers (24–28%) and current smokers (12–9%) changed a few points during follow up, and mean pack-years increased from 21.1 to 23.1 among those who had ever smoked. By the final round, 72% (n = 771) of participants had ever conducted farm work in their lifetime, including one-third (34%) as a child and two-thirds as an adult (67%). The percentage currently farming declined from 23% at enrollment to 14% at the final survey. Mean FEV_1 in liters declined from 3.046 to 2.696 over the mean nine years of the study, for a crude mean annual decline of approximately 39 ml. See Table 1 for the distribution of participants by BMI level, alcohol consumption, marital status, and ever asthma.

Lifetime occupational VGDF exposure

The 1071 participants reported 7967 non-military jobs in their lifetime work histories. The COPD JEM assigned at least one occupational exposure to 3245 jobs held by 88% (n = 944) of the participants. The most common exposed occupation was in agriculture with 49% (n = 1600) of all exposed jobs. The next three occupational groups in descending frequency of exposed jobs were production, transportation, and material moving occupations (n = 487, 15%); building and grounds cleaning and maintenance occupations (n = 311, 10%); and construction and extraction occupations (n = 298, 9%). A final 549 exposed jobs (17%) were distributed across several other occupational groups.

Almost all 944 participants with any occupational exposure by the end of follow-up had been exposed to vapor–gas (99%) and total dust (96%) (Table 2). While organic dust was also experienced by a large majority of exposed participants (91%), mineral dust exposure was less common at 48%. Fumes exposure was the least common at 20% of those exposed. Exposed study participants typically had more than one type of occupational exposure. Summing the numbers exposed to vapor–gas, organic dust, mineral dust, and fumes (n = 2441) and dividing by the number of ever-exposed individuals (n = 944) yielded a mean 2.6 types of occupational exposure per exposed person. Vapor–gas, total dust, organic dust, and mineral dust had similar mean values for the characteristics of exposure duration (20.7 to 23.7 years) and intensity (1.3–1.5 level), and cumulative exposure (34.1–37.3 intensity-years) (Table 2). Fumes had the lowest mean values for all three metrics: 10.6 years, level 1.1, and 11.6 intensity-years, respectively. Most participants experienced their first occupational exposure before enrolling in the KCRHS. For example, those ever exposed to vapor–gas at work changed from n = 925 at enrollment to n = 934 at the final round, an increase of only 1.0% of the enrollment number. The percentage increase was similarly low for all other types of exposure, with 1.1% (893–903) total dust, 1.4% (851–863) organic dust, 3.4% (438–453) mineral dust, and 4.4% (183–191) fumes.

Association of FEV_1 with occupational VGDF exposure

We modelled FEV_1 using the 2678 observations from all rounds, starting with a base model that included covariates for potential confounders and other risk factors as described in the Methods (Supplement Table S2). We fit separate regression models of FEV_1 (ml) for each type of occupational exposure, first by including a covariate for ever-exposed (Model 1), followed by another model (Model 2) to estimate the association of annual change in FEV_1 (ml/yr) with exposure. The results for exposure-related annual changes in FEV_1 were over and above the changes related to aging. We repeated the pattern of fitting two models for each type of occupational exposure with the different levels of exposure duration and intensity and cumulative exposure (Table 3). The adverse effects associated with vapor–gas, total dust, and organic dust were most evident for high duration and high cumulative exposure. Vapor–gas had statistically significant results

Table 1 Sample characteristics and spirometry at enrollment and final round of testing for the 1,071 participants

Characteristic	Category or type of summary measurement	Timing	
		Enrollment	Final survey
Sex	Male	448 (42%)	–
	Female	623 (58%)	–
Age, years	Range	18, 87	19, 98
	Mean	52	61
	SD	14.8	15.0
Enrollment to final test, years	Range	–	1.8, 16.5
	Mean	–	9.0
	SD	–	3.6
Cigarette smoking status	Never	686 (64%)	674 (63%)
	Former	252 (24%)	303 (28%)
	Current	133 (12%)	94 (9%)
Pack-years for ever smokers	Range	0.5, 120	0.5, 120
	Mean	21.1	23.1
	SD	20.6	23.4
Body Mass Index, kg/m^2	Underweight, < 18.5	3 (0.3%)	11 (1%)
	Normal, 18.5 to < 25	251 (23%)	215 (20%)
	Overweight, 25 to < 30	415 (39%)	374 (35%)
	Obese, ≥ 30	402 (38%)	471 (44%)
Alcohol consumption[a]	None	335 (31%)	402 (38%)
	Light	711 (66%)	648 (61%)
	Heavy	25 (2%)	21 (2%)
Marital status	Never married	44 (4%)	30 (3%)
	Living together	11 (1%)	7 (0.7%)
	Divorced/Separated	63 (6%)	63 (6%)
	Widowed	85 (8%)	127 (12%)
	Married	868 (81%)	844 (79%)
Farm work as a child	No	711 (66%)	-
	Yes	360 (34%)	-
Farming status as an adult	Never	354 (33%)	349 (33%)
	Former	474 (44%)	567 (53%)
	Current	243 (23%)	155 (14%)
Ever asthma[b]	No	991 (92.5%)	977 (91.2%)
	Yes	80 (7.5%)	94 (8.8%)
Forced expiratory volume in one second (FEV_1), liters	Range	0.674, 6.091	0.575, 5.617
	Mean	3.046	2.696
	SD	0.901	0.890

SD standard deviation

[a]Heavy alcohol consumption is defined as having ≥ 5 drinks on the same occasion, on ≥ 5 of the last 30 days. Light alcohol consumption is defined as having reported drinking ≥ 1 drink on ≥ 1 day during the past 12 months, and not being classified as a heavy drinker

[b]Ever asthma was based on a positive response to the question, "Have you ever had asthma?"

for longitudinal change in FEV_1 of − 6.2 ml/yr for high duration and − 6.7 ml/yr for high cumulative exposure (Table 3, Part A). Total dust had one statistically significant association of − 105.4 ml in FEV_1 level with high duration of exposure, (Table 3, Part B). There was considerable overlap between vapor–gas and total dust exposure, such that 894 (95%) of the 943 participants with either exposure had both exposures, and few had vapor–gas (n = 40) or total dust (n = 9) without the other. Organic dust had no statistically significant results, but borderline significant results for both high duration and high cumulative exposure (Table 3, Part C).

Table 2 Distribution of participants by different types of occupational exposure at final round of testing and mean and standard deviation for exposure duration and intensity and cumulative exposure

Characterizations of exposure	Type of occupational exposure				
	Vapor–gas	Total dust	Organic dust	Mineral dust	Fumes
Ever exposure					
n participants	934	903	863	453	191
% of 944 with any exposure	99%	96%	91%	48%	20%
% of all 1,071 participants	87%	84%	81%	42%	18%
Duration, years					
Mean	23.7	22.6	20.7	22.2	10.6
SD	18.7	19.0	18.7	18.4	11.5
Intensity, level					
Mean	1.5	1.5	1.5	1.3	1.1
SD	0.5	0.5	0.5	0.5	0.5
Cumulative, intensity-years					
Mean	37.3	36.3	34.1	34.7	11.6
SD	34.8	35.6	35.2	34.6	13.8

SD standard deviation

The two less common types of exposure had their own distinct patterns of results. Mineral dust had statistically significant associations with FEV_1 change for ever exposure (−6.3 ml/yr) and all but one level of exposure duration and intensity, and cumulative exposure (Table 3, Part D). These results were in the range −5.1 to −9.7 ml/yr, with the maximum effect estimate for high intensity of exposure. Examining the overlap of the two types of dust, about half of those with organic dust exposure also had mineral dust exposure (415/863 = 48%), nearly everyone with mineral dust also had organic dust (415/453 = 92%), and only 38 had mineral dust exposure without organic dust as well. With the introduction of a covariate for the interaction of ever organic dust and ever mineral dust, we observed a statistically significant accelerated decline in FEV_1 for the combination of these two exposures with −5.4 ml/yr (95% CI −10.1, −0.007, $p = 0.02$), but not for mineral dust alone (−4.7 ml/yr, 95% CI −14.3, 4.9, $p = 0.34$) or organic dust alone (1.4 ml/yr, 95% CI −3.3, 6.1, $p = 0.55$). Unfortunately, the small number of participants (n = 38) exposed to mineral dust but not organic dust precluded a robust estimate of the effect of mineral dust alone. The subset of 479 jobs with both mineral dust and organic dust exposure was dominated by 458 jobs (96%) in agriculture. Fumes had a statistically significant association of -91.4 ml FEV_1 level with high intensity, but no associations with FEV_1 change (Table 3, Part E).

To provide perspective, we expressed the statistically significant exposure-related results for FEV_1 as a percentage of the study sample's decline of −37.3 ml/year since enrollment as estimated in the base regression model (Supplement Table S2). For exposure-related annual change in FEV_1, this percentage for the two vapor–gas results and most mineral dust results were in the range 14–19% with a median 17%, and for high intensity mineral dust it was 26% (data not shown). For exposure-related decrements in FEV_1 level, this percentage was 283% for high duration total dust and 245% for high intensity fumes, which can also be considered as approximately 2.8 and 2.5 years, respectively, of additional FEV_1 decline beyond normal aging.

Interaction of occupational exposure with cigarette smoking

Only ever fumes had evidence of an interaction with ever cigarette smoking, with a coefficient of −111.1 ml (95% CI −227.5, 5.3, $p = 0.06$) (Supplement Table S3). Stratified by smoking status, the effect estimates for ever fumes exposure were −104.6 ml (95% CI −193.0, −16.2, $p = 0.02$) in FEV_1 level for ever smokers and 6.5 ml (95% CI −81.2, 94.2, $p = 0.88$) for never smokers. The effect estimate for ever smokers was approximately 2.8 years of additional FEV_1 decline beyond the effect of normal aging, again using the study sample's decline of −37.3 ml/year from enrollment to follow-up as the reference. Longitudinal change in FEV_1 associated with ever fumes exposure among ever smokers was unremarkable: 1.3 ml/yr, 95% CI −7.1, 9.7, $p = 0.76$. Further testing with the outcome FEV_1 level revealed statistically significant interactions of ever smoke with high duration (−270.2 ml, 95% CI −416.6, −123.8, $p < 0.001$) and high cumulative (-219.9 ml, 95% CI −367.2, −72.7, $p = 0.003$) fumes exposure, but not high intensity or any low fumes exposure (Supplement Table S4). For the two exposures with significant interactions, effect estimates limited to ever smokers were −170.3 ml (95% CI −276.2, −64.3, $p = 0.002$) for high fumes duration and −172.4 ml (95% CI −276.9, −68.0, $p = 0.001$) for high fumes cumulative exposure. These results were both equivalent to the effect of

Table 3 Association of FEV_1 (ml) (Model 1) and longitudinal change in FEV_1 (ml/yr) (Model 2) with duration and intensity of exposure and cumulative exposure, for different types of occupational exposure[1]

Characterizations of exposure	n[2]	Model 1 FEV_1 (ml)			Model 2 Longitudinal change in FEV_1 (ml/yr)		
		Effect Estimate	95% CI	p value	Effect Estimate	95% CI	p value
Part A Vapor–gas							
Ever exposure							
No	137	0			0		
Yes	934	−42.3	−123.7, 39.1	0.31	−2.9	−7.6, 1.8	0.23
Duration, years							
None (reference)	352	0			0		
Low	773	−47.4	−130.1, 35.4	0.26	0.8	−4.6, 6.1	0.78
Medium	788	−22.0	−112.1, 68.2	0.63	−2.8	−8.1, 2.5	0.30
High	765	−62.9	−160.8, 35.0	0.21	**−6.2**	**−11.5, −0.8**	**0.02**
Intensity, level[3]							
None (reference)	352	0			0		
Low	767	−39.7	−122.1, 42.8	0.35	−2.0	−7.3, 3.4	0.48
Medium	781	−45.0	−137.2, 47.1	0.34	−3.2	−8.5, 2.1	0.24
High	778	−55.9	−152.0, 40.2	0.25	−3.6	−8.9, 1.8	0.19
Cumulative, intensity-years[4]							
None (reference)	352	0			0		
Low	765	−50.0	−132.1, 32.2	0.23	−0.1	−5.5, 5.2	0.97
Medium	793	−10.2	−102.8, 82.4	0.83	−2.3	−-7.5, 3.0	0.40
High	768	−27.0	−129.9, 75.9	0.61	**−6.7**	**−12.0, −1.4**	**0.01**
Part B Total dust							
Ever exposure							
No	168	0			0		
Yes	903	*−67.7*	*−146.7, 11.4*	*0.09*	−1.9	−6.3, 2.4	0.38
Duration, years							
None (reference)	429	0			0		
Low	770	*−67.6*	*−147.6, 12.4*	*0.10*	2.3	−2.7, 7.3	0.37
Medium	740	−62.8	−152.8, 27.1	0.17	−3.0	−8.1, 2.0	0.24
High	739	**−105.4**	**−203.8, −7.0**	**0.04**	*−4.6*	*−9.6, 0.5*	*0.07*
Intensity, level[3]							
None (reference)	429	0			0		
Low	742	*−67.4*	*−146.9, 12.2*	*0.10*	-1.5	-6.6, 3.6	0.56
Medium	763	−67.5	−161.4, 26.4	0.16	-1.4	-6.3, 3.6	0.59
High	744	−72.7	−172.3, 26.9	0.15	−3.1	−8.1, 2.0	0.24
Cumulative, intensity-years[4]							
None (reference)	429	0			0		
Low	779	*−68.2*	*−147.9,11.5*	*0.09*	1.9	−3.1, 6.9	0.45
Medium	729	−66.0	−159.9, 27.9	0.17	−3.0	−8.0, 2.0	0.24
High	741	−87.3	−192.6,17.9	0.10	*−4.7*	*−9.7, 0.3*	*0.07*
Part C. Organic dust							
Ever exposure							
No	208	0			0		
Yes	863	−57.8	−139.8, 24.2	0.17	−0.9	−4.9, 3.1	0.67

Table 3 (continued)

Characterizations of exposure	n[2]	Model 1 FEV$_1$ (ml)			Model 2 Longitudinal change in FEV$_1$ (ml/yr)		
		Effect Estimate	95% CI	p value	Effect Estimate	95% CI	p value
Duration, years							
None (reference)	529	0			0		
Low	778	−53.6	−136.9, 29.6	0.21	3.7	−0.9, 8.4	0.12
Medium	675	−69.0	−161.5, 23.6	0.14	−2.9	−7.7, 2.0	0.25
High	696	*−86.5*	*−188.3, 15.4*	*0.10*	*−4.0*	*−8.8, 0.8*	*0.10*
Intensity, level[3]							
None (reference)	529	0			0		
Low	696	−58.7	−141.3, 23.9	0.16	−0.8	−5.6, 4.1	0.76
Medium	746	−51.7	−148.1, 44.7	0.29	−0.2	−4.9, 4.6	0.95
High	707	−65.8	−168.7, 37.2	0.21	−1.8	−6.6, 2.9	0.45
Cumulative, intensity-years[4]							
None (reference)	529	0			0		
Low	728	−58.8	−141.1, 23.6	0.16	2.2	−2.6, 6.9	0.36
Medium	710	−53.6	−152.5, 45.3	0.29	−0.2	−5.0, 4.6	0.94
High	711	−85.5	−193.9, 23.0	0.12	*−4.5*	*−9.3, 0.3*	*0.06*
Part D Mineral dust							
Ever exposure							
No	618	0			0		
Yes	453	−30.1	−93.1, 32.9	0.35	**−6.3**	**−9.5, −3.1**	**0.0001**
Duration, years							
None (reference)	1554	0			0		
Low	387	−10.6	−77.9, 56.8	0.76	**−5.9**	**−10.7, −1.1**	**0.02**
Medium	365	−51.3	−125.4, 22.8	0.17	**−5.9**	**−10.9, −0.9**	**0.02**
High	372	*−76.8*	*−162.5, 8.9*	*0.08*	**−6.3**	**-11.0, -1.6**	**0.01**
Intensity, level[3]							
None (reference)	1554	0			0		
Low	372	−34.2	−107.7, 39.3	0.36	**−5.8**	**−10.5, −1.1**	**0.02**
Medium	381	−22.1	−97.2, 53.0	0.56	*−3.9*	*−8.5, 0.7*	*0.10*
High	371	−34.2	−117.6, 49.2	0.42	**−9.7**	**−14.5, −4.9**	**<.0001**
Cumulative, intensity-years[4]							
None (reference)	1554	0			0		
Low	372	−12.3	−79.8, 55.3	0.72	**−5.1**	**−9.9, −0.3**	**0.04**
Medium	380	*−64.2*	*−138.9, 10.6*	*0.09*	**−6.5**	**−11.4, −1.7**	**0.008**
High	372	−42.4	−131.0, 46.3	0.35	**−7.2**	**−11.9, −2.5**	**0.003**
Part E. Fumes							
Ever exposure							
No	880	0			0		
Yes	191	−47.6	−113.7, 18.4	0.16	−0.7	−4.9, 3.5	0.74
Duration, years							
None (reference)	2211	0			0		
Low	234	−52.0	−130.0, 26.0	0.19	0.1	−5.9, 6.0	0.98
High	233	−42.9	−123.0, 37.2	0.29	−1.5	−7.1, 4.0	0.58
Intensity, level[3]							
None (reference)	2211	0			0		
Low	234	−0.7	−84.4, 82.9	0.99	−4.3	−9.9, 1.4	0.14

Table 3 (continued)

Characterizations of exposure	n[2]	Model 1 FEV_1 (ml)			Model 2 Longitudinal change in FEV_1 (ml/yr)		
		Effect Estimate	95% CI	p value	Effect Estimate	95% CI	p value
High	233	**−91.4**	**−172.0, −10.0**	**0.03**	2.4	−3.2, 8.1	0.40
Cumulative, intensity-years[4]							
None (reference)	2211	0			0		
Low	238	−28.3	−103.0, 46.5	0.46	−1.5	−7.4, 4.3	0.61
High	229	*−73.3*	*−154.0, 7.3*	*0.07*	0.8	−4.9, 6.4	0.79

Bold values indicate $p \leq 0.05$

Italic values indicate $0.05 < p \leq 0.10$

[1]Regression models included covariates to adjust for age at enrollment, sex, height, cigarette smoking status, pack-years, time since enrollment, ever asthma, BMI category, farm work as a child, and farming status as an adult

[2]n is the number of participants (1,071 total) for ever exposure and the number of observations (2,678 total) for the duration and intensity of exposure and cumulative exposure

[3] Mean intensity across work history of each participant, weighted by number of years at each job

[4]Cumulative was the product of intensity level times years of duration at that level, summed across a participant's work history

approximately 4.6 years of additional FEV_1 decline beyond the effect of normal aging.

Occupations that were sources of exposure associated with decrements in FEV_1 level or longitudinal declines in FEV_1 during follow-up

Various occupational groups were responsible for exposures associated with lower FEV_1 levels and declines in FEV_1during follow-up. As noted above, statistically significant lower FEV_1 levels were associated with high total dust duration and high fumes intensity. The 316 participants in the high total dust duration category had 1260 jobs that the COPD JEM assigned to total dust exposure (Supplement Table S5). Almost three-quarters of these jobs were agriculture occupations (71%, n = 895) and another 12% (n = 145) were in construction and extraction occupations. A total of 191 participants had 318 jobs with fumes exposure, including a little over half in production, transportation, and material moving occupations (n = 184, 58%), one-fifth in installation, maintenance, and repair (n = 67, 21%), and none in agriculture (Supplement Table S5). The three most common occupations with fumes exposure were in production: welding, soldering, and brazing workers (42 jobs), electrical, electronics, and electromechanical assemblers (40 jobs), and miscellaneous assemblers and fabricators (39 jobs).

Statistically significant longitudinal declines in FEV_1 were associated with high vapor–gas duration and cumulative exposure and with nearly all characterizations of mineral dust exposure. The 329 participants with high duration of vapor–gas had 1445 jobs assigned to this type of exposure, with two-thirds of the jobs (n = 900, 65%) in agriculture and the rest scattered across other occupational groups. The JEM assigned 866 jobs worked by 453 participants to mineral dust exposure. The distribution of these jobs by occupation included approximately half (n = 458, 53%) in agriculture, one-fourth (n = 232, 27%) in construction and extraction, and 12% (n = 105) in production, transportation, and material moving (Supplement Table S5).

Discussion

Summary of findings

We applied a COPD JEM to the work histories of a sample of adults living in a rural county in the state of Iowa to yield estimates of occupational VGDF exposure. A large majority of participants (88%) had ever experienced occupational exposures, and those exposed had a mean 2.6 different types of occupational exposure. Associations of FEV_1 were explored separately for each type of agent, and the character of the comparison group varied by type of exposure. The more common exposures (i.e., vapor–gas, total dust, and organic dust) had comparison groups that were smaller and with fewer participants who had another type of exposure. In contrast, the less common exposures (i.e., mineral dust and fumes) had comparison groups that were larger and with more participants who had another type of exposure. The statistically significant associations with the three common exposures included declines in FEV_1 with high duration and high cumulative exposure of vapor–gas, and level of FEV_1 with high duration of total dust. Ninety-five percent of those with either vapor–gas or total dust exposure had experienced both exposures, which suggests that the effects for each individually may be, in fact, effects of some combination of the two. For mineral dust, accelerated declines in FEV_1 were associated with ever/never exposure (−6.3 ml/yr) and nearly all levels of duration, intensity, and cumulative exposure. Because 92% of those with mineral dust exposure also had some organic dust exposure, the results for mineral dust could be due to some combination of mineral and organic dusts, and the occupations with this combination of exposures were overwhelmingly in agricultural. Level of FEV_1 was associated with high fumes intensity, and fumes was the only exposure type that had an interaction with cigarette smoking. Ever smokers had associations of FEV_1 level with ever vs. never, high duration, and high cumulative fumes exposure that were not observed for never smokers.

Results across the different types of exposure suggest that duration rather than intensity was a more consistent risk factor for an adverse FEV_1 outcome. This was especially true for exposure to vapor–gas and total dust (Table 3). However, both characterizations of mineral dust exposure were risk factors, and fumes had positive results for intensity in the full study sample and for duration in the subset of participants who smoked (Supplement Table 4).

Findings for mineral dust

In contrast to the current findings for mineral dust, results for agricultural workers in other studies have often implicated organic rather than mineral dust. For example, a large study of Norwegian farmers reported similar levels of association for both organic and mineral dust with COPD and FEV_1, but only the results for organic dust were statistically significant (Eduard et al. 2009). A Danish cross-sectional study found an association of COPD with organic dust but not mineral dust in the agriculture subset of participants (Wurtz et al. 2015). However, a large national study in Denmark reported no association of incident COPD with organic dust exposure among workers in the agriculture and wood industry (Vested et al. 2019). Findings from general population studies are mixed. From an analysis of data from two large general population cohorts, longitudinal decline in FEV_1 was associated with both mineral and organic dust (Lytras et al. 2021). At the same time, a recent meta-analysis of data from several longitudinal studies reported a statistically significant association of FEV_1 decline with cumulative exposure to organic dust but not mineral dust (Rabbani et al. 2022). A general population study in the United States found airflow obstruction associated with JEM-assigned high exposure to a combination of mineral and organic dust, as well as with high mineral dust and medium organic dust exposure (Doney et al. 2019).

Jobs with fumes exposure and the interaction with cigarette smoking

As is likely in many rural communities, agricultural occupations were responsible for about half of all exposed jobs in the current cohort. Fumes was an outlier among the different types of exposure because none of the fumes-exposed jobs were in agriculture. As noted in the Results, 58% of jobs with fumes exposure were in production, transportation, and material moving occupations (Supplement Table S5).

We detected an association of FEV_1 level with high fumes duration and high cumulative exposure among smokers but not non-smokers. Associations of decrements in FEV_1 level and longitudinal declines in FEV_1 with welding fumes have been reported in several studies, and some but not all studies have identified a greater effect among smokers. For example, one group of investigators reported statistically significant lower levels of FEV_1 for welders versus controls among only smokers (Ozdemir et al. 1995), while another group reported an adverse effect of welding on FEV_1 level regardless of smoking status (Rastogi et al. 1991). A review article that summarized results from five studies reported that the pooled estimate for the difference in annual longitudinal decline in FEV_1 between welders and control subjects was greater for smokers (−13.7 ml/yr, 95% CI −33.6, 6.3) than nonsmokers (−3.8 ml/yr, 95% CI −20.2, 12.6), although the confidence intervals for these results overlapped (Szram et al. 2013). One study cited in this review reported an especially strong accelerated decline in FEV_1 associated with welding fumes for smokers (−123.0 ml/yr, 95% CI −224.2, −21.7) but not nonsmokers (80.2 ml/yr, 95% CI 0.5, 159.8) (Erkinjuntti-Pekkanen et al. 1999), while another study reported an effect of welding fumes for both smokers and non-smokers (Chinn et al. 1990).

Limitations and strengths

The current study has several limitations. Regarding the broader applicability of findings, results of this analysis are based on a study of adult rural residents in one county in Iowa and do not represent the experience of all US rural residents. The overwhelming bulk of lifetime occupational exposure in this cohort was due to workers who were already exposed by enrollment and may have experienced additional exposure during follow-up. The results would potentially differ in a cohort of rural workers who experienced most occupational exposures during the study follow-up period. The COPD JEM assigned more than one type of occupational exposure to many participants as dictated by their lifetime work histories. Consequently, it was difficult with some types of exposure to say with certainty that associations with

FEV_1 level or decline were associated exclusively with a single exposure of interest. This phenomena of workers with exposure to multiple agents has been reported before. For example, a published review of studies that investigated the association of COPD with occupational exposures observed that adults who had worked in industrial settings were likely to have experienced a combination of different agents rather than a single agent (Sadhra et al. 2017). The current analyses were based on data for KCRHS participants who completed at least two surveys. Those who completed only the enrollment survey were not represented, although we compensated for this deficit to some extent by applying weights in regression models based on the inverse probability of participating in surveys beyond enrollment. Individual participants may have avoided certain exposed jobs or left exposed jobs because they already had respiratory problems, and this situation in which a respiratory disease influenced the extent of exposure could have distorted effect estimates. The COPD JEM likely contributed to nondifferential misclassification of exposure, resulting in wider confidence intervals for effect estimates. A potential criticism of the current study is the failure to adjust for multiple comparisons. This issue is based on the premise that what is observed in a study is due entirely to random processes, what is commonly referred to as a universal null hypothesis (Goldberg and Silbergeld 2011; Rothman 1990; Savitz and Olshan 1995). However, this conflicts with reasonable suspicions about causal exposure–response relationships, such as those that underly the objectives of the current study. Given the hypothesis-driven nature of the study, adjusting for multiple comparisons was not necessary.

This study also has many strengths. The estimates of occupational exposure were based on participants' entire work history which is appropriate given the outcome. In contrast, a recent review article reported that studies of occupational COPD were twice as likely to estimate exposure for most-recent or longest held job rather than estimate lifetime occupational exposure (Sadhra et al. 2017). The characterization of occupational exposure was based on a JEM and unlikely to have been influenced by the disease status of the individual, thus avoiding information bias that can occur with self-reported exposure. Spirometry was performed using recommended equipment and protocols and was unlikely to have been influenced by occupational exposure status. The availability of demographic and personal information related to respiratory health meant we were able to adjust for potential confounders while examining the association of FEV_1 with occupational exposures. The availability of large numbers of participants ($n = 1071$) and observations ($n = 2678$) meant we had adequate power to address many research questions.

Conclusion

Results from the current study suggest adverse FEV_1 outcomes were associated with mineral dust, possibly in combination with organic dust, and fumes exposure, especially among cigarette smokers. These findings could help inform strategies for preventing work-related obstructive respiratory disorders among adults living in rural communities. Future analyses of KCRHS data could examine the relationship of other spirometry-based outcomes such as FEV_1/FVC ratio, airflow obstruction, FVC, and restrictive patterns with occupational exposures.

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Author contributions KM Kelly contributed to the design and implementation (including data collection) of the Keokuk County Rural Health Study, which was the source of the data used in the current study. PK Henneberger, MJ Humann, X Liang, BC Doney, and KM Kelly made substantial contributions to the concept and design of the current study. All authors made substantial contributions to the implementation of the current study. SM Rollins, X Liang, and ML Humann conducted data management and analyses. PK Henneberger drafted the manuscript, assisted by all other authors. All authors contributed to interpretation of results, provided critical review of the manuscript, and approved the final version that was submitted for publication.

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Availability of data and materials Data are participant-level and cannot be shared publicly.

Declarations

Conflict of interest The authors have no competing interests to report.

Ethical approval The Institutional Review Board (IRB) of the University of Iowa approved the KCRHS study protocol, and the current analysis is part of a project approved by the National Institute for Occupational Safety and Health IRB. Each KCRHS participant provided written informed consent before taking part in the study.

Disclaimer The findings and conclusions in this report are those of the authors and do not necessarily represent the official position of the National Institute for Occupational Safety and Health, Centers for Disease Control and Prevention.

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