COPD and Occupational Exposures: A Case-Control Study

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Objective: *Evidence demonstrates that occupational exposures are causally linked with chronic obstructive pulmonary disease (COPD). This case-control study evaluated the association between occupational exposures and prevalent COPD based on lifetime occupational history.* ***Methods:*** *Cases (*n *= 388) aged 45 years and older with COPD were compared with controls (*n *= 356), frequency matched on age, sex, and cigarette smoking history. Odds ratios for exposure to each of eight occupational hazard categories and three composite measures of exposure were computed using logistic regression.* ***Results:*** *Occupational exposures most strongly associated with COPD were diesel exhaust, irritant gases and vapors, mineral dust, and metal dust. The composite measures describing aggregate exposure to gases, vapors, solvents, or sensitizers (GVSS) and aggregate exposure to dust, GVSS, or diesel exhaust were also associated with COPD. In the small group of never-smokers, a similar pattern was evident.* ***Conclusion:*** *These population-based findings add to the literature linking occupational exposures to COPD.* (J Occup Environ Med. *2008;50:561–569*)

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The findings and conclusions in this report are those of the authors and do not necessarily represent the views of the National Institute for Occupational Safety and Health.

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Chronic obstructive pulmonary disease (COPD) poses a substantial economic burden to society through both the direct costs of health care services and the societal cost associated with lost productivity. The direct and indirect costs of COPD to the United States in 2007 were estimated at $42.6 billion,[1] and morbidity and mortality attributed to COPD are increasing in the United States and throughout the world.[2]

Although cigarette smoking is the dominant risk factor for COPD, many industry-based studies have shown that occupational exposure is a risk factor also.[3–5] Population-based studies suggest that a variety of employment settings and exposures can potentially lead to increased risk of COPD.[6] Hnizdo et al based on data from the 1988 to 1994 third National Health and Nutrition Examination Survey estimated that the fraction of COPD in the US adult population attributable to work is about 19% overall and 31% among never-smokers.[7] Occupational exposures thought to carry increased risk include dusts, gases, vapors, and fumes.[3–5]

Few population-based studies have been able to quantify the relationship between COPD and occupational exposure based on complete life-exposure. Rather, most population-based studies have focused on the longest-held job or current job to quantify exposure to one or more agents. We report on a case-control study designed to evaluate the association between prevalent COPD and occupational exposures assessed from lifetime occupational history.

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Materials and Methods

The participating institutions' human subjects committees approved the study protocol and recruitment procedures for this study.

Research Setting

Study participants were members of Kaiser Permanente Northwest (KPNW), a group model health maintenance organization based in Portland, OR. KPNW provides comprehensive, prepaid health care service, including occupational medicine, to about 460,000 members, whose demographics are representative of the Northwest Oregon/Southwest Washington community.[8] Most KPNW members receive coverage through their work or are included as part of a household member's work-related coverage. The membership also includes about 50,000 Medicare-eligible members. We used the KPNW's computerized medical records to identify study participants.

Subject Selection

Potential cases and controls were members of KPNW, aged 45 years and older, with continuous health care eligibility from January 2000 to December 2002. Selection of cases and controls was stratified by smoking status as documented in the electronic medical records; members without medical record information on cigarette smoking history were excluded from the selection (0.2% of potential cases and 2.8% of potential controls).

We searched the KPNW computerized medical records for years 2000 to 2002 and identified 16,718 subjects who had COPD diagnoses (defined as ICD-9: 490, 491, 492, 496) and met the age and membership criteria. From this group, cases were selected if FEV_1/FVC measured during January 2000 to December 2002 was below the lower limit of normal (LLN) (defined using National Health and Nutrition Examination Survey III prediction equations)[9] or if they met criteria for COPD based on an algorithm developed and validated for this study.

To develop the algorithm, we used the subset of 3033 individuals with COPD diagnoses in 2000 to 2002 for whom we had lung function measurements in the medical records during the study period. We used reverse stepwise logistic regression modeling to identify factors available in the medical records that were most predictive of spirometry-defined COPD (ie, FEV_1/FVC $<$LLN). Separate algorithms were developed for smokers and never-smokers. In smokers, the final algorithm considered COPD diagnosis, number of dispensings of drugs prescribed for COPD, use of home oxygen, and no diagnosis of congestive heart failure or asthma during the study period. In never-smokers, the algorithm considered similar but less stringent criteria. To validate the algorithms, we performed lung function tests on a randomly selected sample of 77 algorithm-identified potential cases who had no previous lung function testing; of these, 83% (82% of never-smokers and 83% of ever-smokers) had spirometry-defined COPD ($n = 64$).

Using the spirometry criteria and the study algorithms, we identified 2454 potential cases; 64% of the potential cases had spirometry-defined COPD. Figure 1 shows in detail the case selection and recruitment process; 61 cases identified in the algorithm-validating study were also included in the main study. Study clinicians (Breen and Buist) reviewed the medical records of all 234 never-smoking potential cases to confirm study eligibility and excluded 108. We attempted to contact all 126 never-smoking cases, because the number in this group was small, together with a random sample of 684 ever-smoking cases. Potential control participants were randomly selected from the health plan population and were frequency matched 1:1 to the cases based on age, sex, and smoking status. Potential control participants had no visits for COPD-related diagnoses and no dispensings of COPD medications between 2000 and 2002. Participants who indicated in the telephone interview that they had worked fewer than 5 years total were also excluded.

Subject Recruitment

Study interviews were conducted by phone using trained interviewers blinded to case-control status. We were able to contact 78% of cases and 83% of controls. Of those contacted, 87% of cases and 88% of controls met preliminary study eligibility criteria (minimum work history requirement and ability to be interviewed in English by telephone). Of those eligible for the study, 61% of cases and 52% of controls agreed to participate, resulting in completed interviews on 391 cases and 358 controls. We reviewed the medical records for the few participants whose self-reported disease status differed from their disease status as determined by the case selection algorithm. As a result of this review, three participants initially classified as cases and two initially classified as controls were considered to be misclassified and were excluded from further analysis. Smoking status was reclassified for 5% of subjects based on self-report. The final study sample included 388 COPD cases (346 ever-smokers and 42 never-smokers) and 356 controls (298 ever-smokers and 58 never-smokers). Sixty-three percent of the final case group had spirometry-defined COPD, whereas the remainder had missing or, rarely, negative spirometry testing but satisfied the other criteria outlined above.

We compared the age and gender distributions of study participants and nonparticipants (refusers and those we could not contact). Among cases and controls, median ages of participant and nonparticipant groups were similar (67 and 66 respectively for cases; 67 and 65 respectively for controls); nevertheless, a smaller proportion of participants than nonparticipants was male (44% vs 49% respectively for cases; 41% and 51% respectively for controls).

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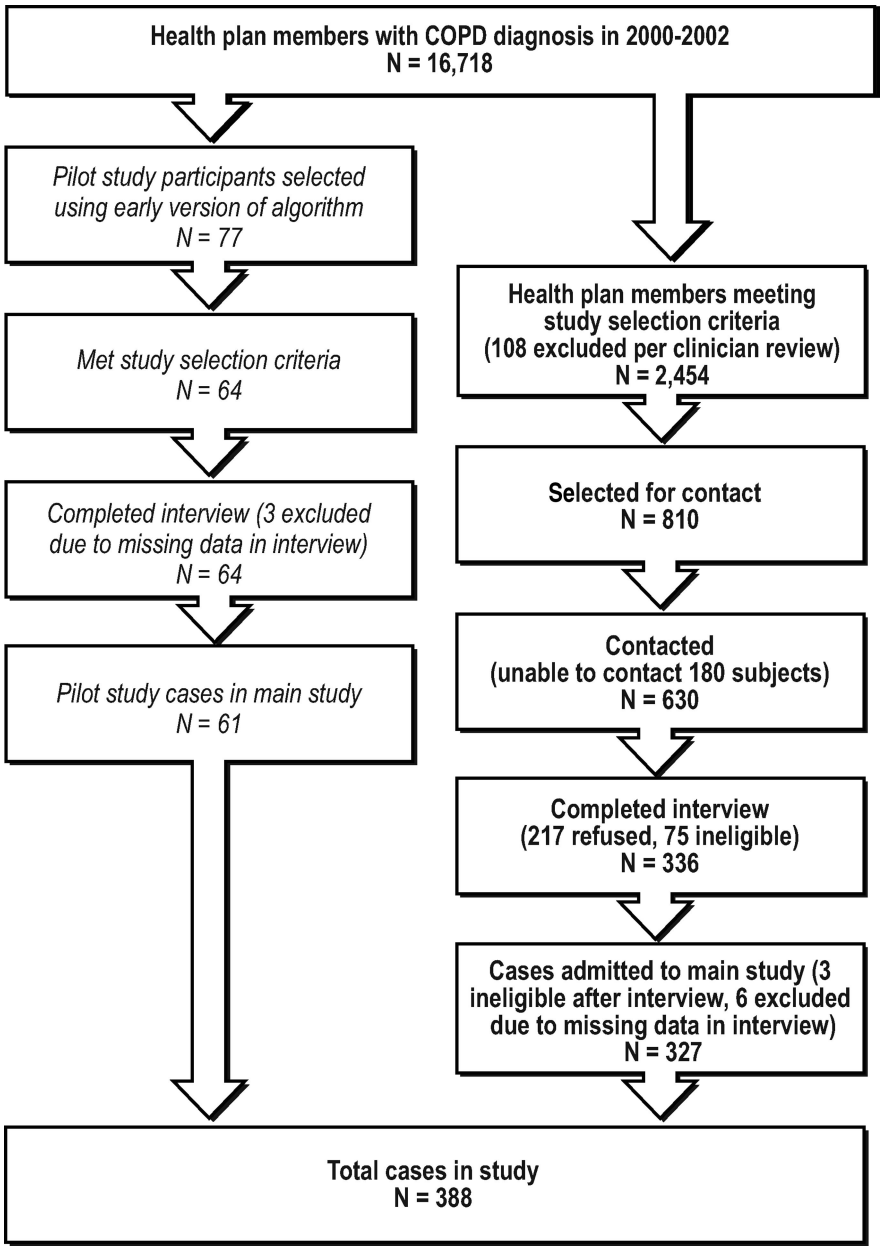

Fig. 1. Case selection, Kaiser Permanente Northwest, 2000 to 2002.

Data Collection

We interviewed participants using a questionnaire that included demographics, history of asthma and heart disease, family history of COPD and other respiratory conditions, smoking history, and detailed work history. For each job held for 6 months or longer, we recorded start and stop dates, tasks and activities on the job (open-ended question), and a check list with "yes or no" responses to whether the job involved activities with routine (at least once a week) exposure to dusts, fumes, diesel exhaust, gases, vapors, solvents, cleaning agents, adhesives or glues, paints or other coatings, compressed gases, cutting oils, or other chemicals. If the subject responded "yes" to any of the above exposures, we also asked the participant to provide more detail on the type of exposure (eg, "What kind of dust?"). We also collected information on the frequency of respirator use (always, sometimes, rarely, or never) and what the subject was doing when he or she used a respirator (open-ended question). Interviewers collected information on a maximum of eight distinct jobs, with jobs in the same industry and occupation categories treated as one job. If a subject had more than eight jobs, the interviewer collected information on the eight longest-held jobs. Participants were asked about exposure to environmental tobacco smoke (ETS) at each job and at home, history of pipe and cigar use, hobbies, comorbidities, respiratory symptoms, and family history of respiratory conditions.

Exposure Assessment

Information on work history was assessed by experienced certified industrial hygienists at KPNW and at the National Institute for Occupational Safety and Health (NIOSH) to evaluate the likelihood of exposure to specific hazards in the workplace. For each job reported by a study subject, an industrial hygienist assigned modified industry and occupation codes based on the 2000 Bureau of Census list. For each job, two industrial hygienists (one from KPNW; one from NIOSH) assigned a score for potential exposure to each of eight categories of occupational hazards likely to cause COPD: mineral dusts, metal dusts and fumes, organic dusts, irritant gases or vapors, sensitizers, organic solvents, diesel exhaust, and ETS. Our experts also assigned an overall score to each job, reflecting the likelihood that the participant was exposed to some significant occupational risk on that job. For exposure scoring, the experts used their knowledge of current and historical exposures in various jobs and industries, as well as the subject's response to a structured questionnaire. Expert exposure assessment based on subjects' self-reported exposure and job duty information have been previously used.[10,11] Expert assessment aided by self-report is usually somewhat better than self-report and generic job exposure matrices.[12]

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For all exposure categories except occupational ETS, exposure scores were assigned on a three-point scale of 0 (no or minimal exposure), 1 (moderate exposure), or 2 (high exposure). Occupational ETS was scored as 0 (no or minimal exposure) or 1 (moderate or high exposure). Despite detailed instructions developed to standardize the exposure coding, differences between exposure ratings by the KPNW and NIOSH industrial hygienists occurred. Kappa coefficients describing agreement on exposure scoring ranged from 0.46 to 0.86, depending on the exposure. For analysis, we used two algorithms to resolve differences. The "conservative" algorithm used the lower of the two hygienists' exposure ratings unless one hygienist coded 0 and the other coded 2, in which case a score of 1 was used. The "liberal" algorithm used the greater of the two ratings, even in cases where one coded 0 and the other coded 2. For primary analyses, these combined exposure measures were further collapsed into "ever-exposure" (a combined measure of 1 or 2) versus "no exposure" (score of 0). Scores based on the "conservative" algorithm with the collapsed ever (1–2) versus never (0) exposed categories constituted the primary outcome variables for this analysis, whereas scores based on the "liberal" algorithm and those that used the trilevel (0, 1, and 2) ratings were used as sensitivity analyses. Results of these sensitivity analyses were similar to those using the "conservative" coding.

For comparison with other studies, we constructed three composite measures for each individual, coded as described above: an overall measure of dust exposure, reflecting the individual's overall exposure to metal dust, mineral dust, or organic dust; an overall measure of gases, vapor, solvents, and sensitizers (GVSS) exposure; and a measure of exposure to either dust, GVSS, or diesel exhaust.

Statistical Analyses

We used unconditional logistic regression models to estimate odds ratios (ORs) for the association of COPD with each of the individual "ever or never" exposures, the two composite exposures (dust and GVSS), and the measure describing any exposure to dust, GVSS, or diesel exhaust, overall and stratified on smoking status. For each exposure measure, logistic regression models were adjusted for age and gender, as well as pack-years for ever-smokers and ever-smoking and pack-years for the overall models. We also evaluated the risk of COPD associated with duration of exposure, which was calculated as the total number of years worked in a job with the exposure, with each 40 hours worked considered a week of full-time work. We evaluated the associations for confounding and effect modification by other potential risk factors for COPD, including race or ethnicity (non-White or Hispanic vs White), history of asthma (yes or no), history of heart disease (yes or no), family history of asthma (yes or no), and family history of lung disease (yes or no). We also evaluated for effect modification by age, gender, current or former smoking status, and among smokers pack-years. Because only five cases and no controls reported a family history of alpha-1 antitrypsin deficiency, this potential confounder could not be evaluated. Individual exposure models were evaluated for confounding by specific hobbies (each yes or no) that also exposed the subject to the substance under investigation (eg, woodworking and organic dust exposure).

To examine the possibility of confounding among the different exposures, we constructed a multivariate model including the composite dust and GVSS measures, diesel exhaust, and ETS. Because of strong correlations among exposures, we could not include all individual exposures in a single multivariate model.

We evaluated the following combinations of occupational exposures for multiplicative effect modification: 1) diesel exhaust and sensitizers, 2) diesel exhaust and mineral dust, 3) diesel exhaust and ETS, and 4) metal dust and irritant gases and vapors. Interactions between some of these exposures were suggested by the literature.[5,13]

To estimate the proportion of COPD prevalence attributable to occupational exposures by ever-smoking status, the population-attributable risk percent (PAR%) was calculated according to the method for case-control studies described in Koepsell and Weiss (PAR% = [OR − 1]/OR × [Proportion of cases exposed]).[14] Confidence intervals (CIs) were calculated according to the method described by Greenland and Drescher.[15] The PAR% was estimated using the ORs from the logistic models, after adjustment for age, gender, smoking status, and pack-years (Table 2).

Results

Characteristics of the study sample are shown in Table 1. Cases were more likely than controls to report histories of asthma and heart disease and to report a family history of COPD, emphysema, or chronic bronchitis ($P < 0.05$, all).

Table 2 provides results of the logistic regression analyses of individual occupational exposures, as assessed by the industrial hygienists, in relation to COPD. In the basic models for all subjects adjusted for age, gender, and pack-years, the strongest associations between COPD status and occupational exposure occurred with exposure to diesel exhaust (OR = 1.9, 95% CI = 1.3, 3.0), mineral dust (OR = 1.7, 95% CI = 1.1, 2.7), irritant gases and vapors (OR = 1.6, 95% CI = 1.2, 2.2), and GVSS (OR = 1.7, 95% CI = 1.2, 2.4). Among never-smokers, OR estimates were similar to those of smokers for most measures, though confidence intervals were substantially wider because of the very small size of

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TABLE 1
Demographic and Clinical Characteristics of COPD Cases and Controls, Kaiser Permanente Northwest, 2000 to 2002

Characteristic	Current or Former Cigarette Smokers		Never Smokers of Cigarettes		All Subjects	
	Cases (*N* = 346)	Controls (*N* = 298)	Cases (*N* = 42)	Controls (*N* = 58)	Cases (*N* = 388)	Controls (*N* = 356)
Age (yr)	66 (9)	65 (9)	73 (11)	69 (9)	67 (9)	66 (9)
Male sex	158 (46)	123 (41)	14 (33)	24 (41)	172 (44)	147 (41)
Non-White race or Hispanic ethnicity	14 (4)	12 (4)	3 (7)	4 (7)	17 (4)	16 (4)
Personal history of asthma	199 (58)	33 (11)	25 (60)	7 (12)	224 (58)	40 (11)
Personal history of heart disease	110 (32)	72 (24)	15 (36)	11 (19)	125 (32)	83 (24)
Family history of COPD/emphysema/ chronic bronchitis	122 (35)	63 (21)	11 (26)	10 (17)	133 (34)	73 (21)
Cigarette smoking history						
Never	0 (0)	0 (0)	42 (100)	58 (100)	42 (11)	58 (16)
Former	282 (82)	265 (89)	0 (0)	0 (0)	282 (73)	265 (74)
Current	64 (19)	33 (11)	0 (0)	0 (0)	64 (16)	33 (9)
Cigarette pack-yr	42 (33)	23 (22)	NA	NA	38 (34)	20 (22)
Pipe or cigar smoking history						
Never	243 (70)	203 (68)	39 (93)	53 (91)	282 (73)	256 (72)
Former	98 (28)	90 (30)	3 (7)	5 (9)	101 (26)	95 (27)
Current	5 (1)	5 (2)	0 (0)	0 (0)	5 (1)	5 (1)

Continuous data expressed as mean (SD).
Categorical data expressed as number (%).

TABLE 2
Logistic Regression Models for Single Exposure Measures in Relation to Prevalent COPD Overall and by Smoking Status, Adjusted for Age, Sex, and Pack-Years, Kaiser Permanente Northwest, 2000 to 2002

Exposure	Ever-Smokers			Never-Smokers			All Subjects	
	Cases (*N* = 346) No. (%)	Controls (*N* = 298) No. (%)	OR (95% CI)*	Cases (*N* = 42) No. (%)	Controls (*N* = 58) No. (%)	OR (95% CI)†	OR (95% CI)‡	PAR% (95% CI)
Metal dust	73 (19)	45 (15)	1.5 (0.93, 2.3)	8 (19)	9 (16)	1.8 (0.56, 5.8)	1.5 (0.98, 2.3)	7 (0, 14)
Mineral dust	77 (22)	46 (15)	1.5 (0.95, 2.5)	8 (19)	5 (9)	3.5 (0.94, 13.3)	1.7 (1.1, 2.7)	9 (2, 16)
Organic dust	97 (28)	85 (24)	0.98 (0.67, 1.4)	11 (26)	15 (26)	1.0 (0.41, 2.6)	0.99 (0.70, 1.4)	0
Irritant gases and vapors	194 (56)	132 (44)	1.7 (1.2, 2.4)	18 (43)	23 (40)	1.4 (0.59, 3.2)	1.6 (1.2, 2.2)	21 (8, 32)
Organic solvents	100 (29)	68 (23)	1.3 (0.86, 2.0)	8 (19)	12 (21)	1.1 (0.36, 3.2)	1.3 (0.88, 1.9)	7 (0, 15)
Sensitizers	72 (21)	69 (23)	0.96 (0.64, 1.4)	8 (19)	5 (9)	2.7 (0.80, 9.4)	1.1 (0.74, 1.6)	2 (0, 9)
Diesel exhaust	89 (26)	51 (17)	1.7 (1.1, 2.7)	7 (17)	3 (5)	6.4 (1.3, 31.6)	1.9 (1.3, 3.0)	12 (5, 19)
Environmental tobacco smoke	288 (83)	227 (76)	1.3 (0.86, 2.0)	21 (50)	29 (50)	0.91 (0.40, 2.1)	1.2 (0.85, 1.8)	15 (0, 36)
Dust composite measure	159 (46)	124 (42)	1.1 (0.76, 1.6)	18 (43)	22 (38)	1.4 (0.58, 3.3)	1.2 (0.86, 1.7)	8 (0, 20)
GVSS composite measure	231 (67)	165 (55)	1.5 (1.0, 2.1)	24 (57)	26 (45)	2.3 (0.96, 5.6)	1.7 (1.2, 2.4)	27 (12, 40)
Any dust, GVSS, or diesel exhaust exposure	246 (71)	186 (62)	1.4 (0.95, 2.0)	28 (67)	29 (50)	2.4 (0.99, 5.6)	1.5 (1.1, 2.1)	24 (5, 39)

*Adjusted for age, sex, and cigarette pack-years.
†Adjusted for age and sex.
‡Adjusted for age, sex, ever-smoking (yes/no), and cigarette pack-years.
GVSS indicates irritant gases or vapors, sensitizers, organic solvents.

the group. Of note, OR estimates for never-smokers were markedly larger than those for ever-smokers for diesel exhaust, mineral dust, sensitizers, and the GVSS combination measure.

When the three-category exposure measures were evaluated in a secondary analysis, ORs for the high exposure group tended to be larger than those for the moderate group (Fig. 2); this analysis was hampered by the small numbers of subjects in the high exposure group, and confidence intervals were wide.

Other than asthma, measured covariates did not confound individual or composite exposure measures. History of asthma was strongly associated with COPD and with most of the occupational exposures. The association between COPD and occupational exposures was similar in those with and without asthma history (Fig. 3). We did not detect

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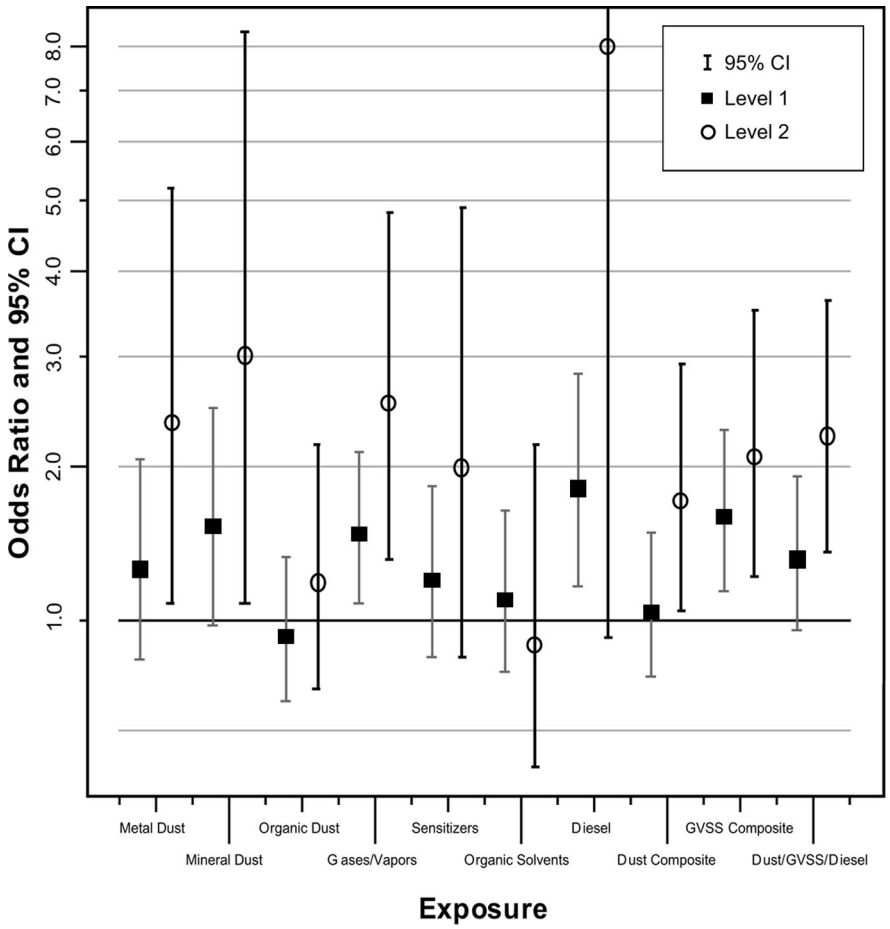

Fig. 2. Odds ratio estimates for association of COPD with occupational exposure levels 1 (moderate) and 2 (high) among ever-smokers, Kaiser Permanente Northwest, 2000 to 2002. Odds ratios adjusted for age, gender, and cigarette pack-years. GVSS indicates irritant gases or vapors, sensitizers, organic solvents.

exposure interactions with age, sex, pack-years, race or ethnicity, history of heart disease, or family history of COPD. Categorical or linear measures of exposure duration did not contribute significantly to these models.

Some specialized hobbies involving exposure to agents studied in the occupational analysis were more common among subjects with those occupational exposures than among subjects without such exposures. Examples included woodworking (32% of those with and 14% of those without occupational organic dust exposure), auto work (44% with and 13% without occupational diesel exhaust exposure), and metal work (13% with and 3% without occupational metal dust exposure). When evaluated in logistic regression models, participation in these hobbies did not confound the association between COPD and the related occupational exposures.

To investigate possible confounding among the occupational exposures, we included dust, GVSS, diesel exhaust, and ETS in a multivariate logistic regression model along with age, gender, ever-smoking status, and pack-years. Results were similar to those for single exposure models. The diesel exhaust and GVSS measures had the strongest associations for both smokers and never-smokers (data not shown). Among all subjects combined, ORs for the diesel exhaust and GVSS measures were 1.8 (95% CI = 1.1, 2.8) and 1.7 (95% CI = 1.2, 2.5), respectively, whereas the OR for the composite dust measure was 0.85 (95% CI = 0.57, 1.3) and the OR for ETS was 1.2 (95% CI = 0.79, 1.7). Of the four pairs of occupational exposures examined, none of the tests for interaction reached statistical significance.

For all subjects combined, the estimated proportion of COPD prevalence attributable to individual occupational exposures was highest for irritant gases and vapors, ETS, and diesel exhaust (Table 2). Using the "any exposure to dust, GVSS, or diesel exhaust" measure as the definition of occupational exposure yielded a PAR% of 24% (95% CI = 5, 39) overall, 19% (95% CI = 0, 37) for ever-smokers, and 43% (95% CI = 0, 68) for never-smokers.

Discussion

In this population-based sample of adults with comprehensive health care coverage, we observed positive associations between several occupational exposures and prevalent COPD. These individual exposures were selected based on their potential to induce inflammatory processes in the lung that can lead to increased risk of COPD.[5] When we evaluated these eight exposures individually, the strongest associations were found for diesel exhaust, irritant gases and vapors, and mineral dust. Both ever-smokers and never-smokers had elevated ORs for these exposures, as well as for the GVSS composite measure and the measure describing any exposure to dust, GVSS, or diesel exhaust.

The magnitudes of the ORs for the variable describing any dust, GVSS, or diesel exhaust were similar to those in other reports for any exposure to dust, vapors, gases, and fumes, which ranged from 1.3 to 3.1 in several population-based studies.[16–23] Results for gases and fumes in previous studies have been variable, with some studies[17,20,23–25] but not others[26] finding elevated risk. Other population-based studies found positive associations with exposure to any dust[17,20,21,25,27] and mineral dust.[24,26,28] Positive results for organic dust were found in some studies[24,26] but not others.[28] This may reflect a difference in the dusts

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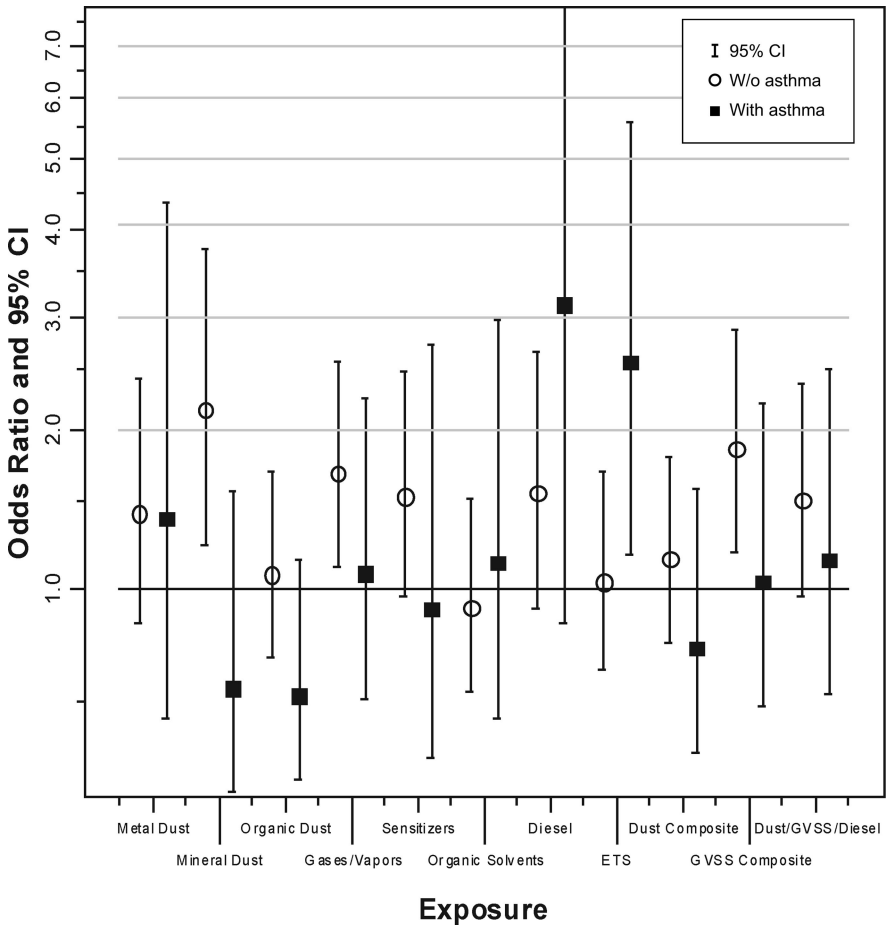

Fig. 3. Odds ratio estimates for association of COPD with occupational exposure among ever-smokers with and without self-reported history of asthma diagnosis, Kaiser Permanente Northwest, 2000 to 2002. Odds ratios adjusted for age, gender, and cigarette pack-years. GVSS indicates irritant gases or vapors, sensitizers, organic solvents.

to which individuals in the different studies were exposed because the response depends on the nature and size of the inhaled particles.[29] A study of railroad workers found a positive association between COPD mortality and occupational exposure to diesel exhaust.[30]

Although we found associations between COPD and ever-exposure to some occupational factors, there was no clear relationship with exposure duration. It may be that our duration variable, based on groups of self-reported jobs combined, poorly reflects actual duration of exposure. This result may also be due in part to the "healthy worker survivor effect," in which susceptible persons would be more likely to leave high exposure jobs early than workers more able to tolerate the environment.[31] This effect may be substantial; four percent of a large international sample attributed previous job change to breathing problems at work.[23] Among other population-based studies, few have attempted to evaluate the duration of exposure; Korn[32] reported increased prevalence of COPD symptoms with duration of occupational dust exposure but not with duration of occupational exposure to gases or fumes, though both categories of exposure were associated with COPD symptoms when coded as ever-never. Xu[20] found similar results with a measure combining duration and intensity of exposure. Another study did not find increased risk of chronic nonspecific lung disease with increasing duration of exposure to dust,[21] though the ever-never exposure variable was associated, and higher risk was associated with high dust exposure compared with intermittent dust exposure. Similarly, for dust and other measures, our study also found the suggestion of higher risk with high-intensity exposure compared with moderate exposure.

In our logistic models examining multiple exposures simultaneously, exposures to diesel exhaust and GVSS were the strongest occupational predictors of COPD, whereas exposure to the composite dust variable was not associated with elevated risk. In contrast to our results, four previous studies examining dust and fumes variables in multivariate models found dust to be the more important occupational exposure: dust but not gases or fumes[20,32]; inorganic dust but not wood dust, gases or irritants, or fumes[28]; mineral and biological dust but not gases or fumes.[26] Two studies[21,25] evaluated exposure to solvents and dust in multivariable models and found that both exposures were associated with the respiratory outcome. In our study, the number of individuals with high dust exposure was probably small compared with other studies, as our subjects included very few miners. Also, occupational exposures in the United States are likely lower than in some other countries, so these studies may be comparing exposures of differing intensity.

The estimated proportion of COPD prevalence attributable to occupational exposures in this population (24% for any exposure to dust, GVSS, or diesel exhaust) was within the range of those reported by other studies: 12% to 55% (median 18%) for lung function impairment in smokers and never-smokers combined,[33] and 4% to 24% (median 15%) for chronic bronchitis.[6] For never-smokers, compared to our 43% estimate for any exposure to dust, GVSS, or diesel exhaust, two much larger studies reported 31% for COPD prevalence[7] and 53% for COPD mortality[28]; the 95% confi-

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dence intervals around our estimate (0, 68) were very wide.

This study had several limitations. Study cases were selected using an automated algorithm to search a medical record database rather than using standard pulmonary function assessments, so our case group probably had more severe COPD than if we had identified cases through lung function testing. Differentiation between COPD and asthma can be difficult, and, although we attempted to exclude asthma cases, some cases may have had asthma rather than COPD. Therefore, we also examined occupational exposures as risk factors in those without asthma diagnosis. Because asthma may be on the biologic pathway to development of COPD in some people[34] and occupational exposure can cause occupational asthma or exacerbate preexisting asthma, we chose not to adjust for asthma. Aside from COPD, all medical history was self-reported in the interview. Response rates for cases and controls, though similar, were relatively low and could introduce bias. Because subjects were interviewed retrospectively, COPD cases may have been more likely than controls to remember and report occupational exposures or jobs with occupational exposure. Information on occupational exposures relied on industrial hygienists' assessment of job title, years of employment, and subjects' report of exposures to categories of respiratory exposure. Our use of all lifetime jobs in the data analysis also may have attenuated the association between COPD and ever-exposure to occupational factors, as cases may have avoided "dirty" jobs after COPD diagnosis, whereas controls would not have this incentive to avoid such employment. Because of the types of employer groups contracting with this health plan, the number of persons exposed to some potentially hazardous substances, such as agriculture and mining, was small. Statistical power was poor, as expected, for analysis of exposure-disease relationships in the small group of never-smokers. Finally, although we followed a prespecified analysis plan, we fitted a large number of models without adjusting significance levels or the size of our confidence intervals for multiple comparisons.

In conclusion, this population-based study found several occupational exposure measures, including diesel exhaust, irritant gases and vapors, mineral dust, a composite measure of any GVSS exposure, and a measure of exposure to any of seven workplace pollutants to be positively associated with prevalent COPD among both ever-smokers and never-smokers.

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