Airways Obstruction Among Older Construction and Trade Workers at Department of Energy Nuclear Sites

John M. Dement, PhD, CIH,[1]* Laura Welch, MD,[2] Knut Ringen, PH, MHA, MPH,[3] Eula Bingham, PhD,[4] and Patricia Quinn, BA[2]

Background *A study of chronic obstructive pulmonary disease (COPD) among 7,579 current and former workers participating in medical screening programs at Department of Energy (DOE) nuclear weapons facilities through September 2008 was undertaken.*

Methods *Participants provided a detailed work and exposure history and underwent a respiratory examination that included a respiratory history, respiratory symptoms, a posterior–anterior (P–A) chest radiograph classified by International Labour Office (ILO) criteria, and spirometry. Statistical models were developed to generate group-level exposure estimates that were used in multivariate logistic regression analyses to explore the risk of COPD in relation to exposures to asbestos, silica, cement dust, welding, paints, solvents, and dusts/fumes from paint removal. Risk for COPD in the study population was compared to risk for COPD in the general US population as determined in National Health and Nutrition Examination Survey (NHANES III).*

Results *The age-standardized prevalence ratio of COPD among DOE workers compared to all NHANES III data was 1.3. Internal analyses found the odds ratio of COPD to range from 1.6 to 3.1 by trade after adjustment for age, race, sex, smoking, and duration of DOE employment. Statistically significant associations were observed for COPD and exposures to asbestos, silica, welding, cement dusts, and some tasks associated with exposures to paints, solvents, and removal of paints.*

Conclusions *Our study of construction workers employed at DOE sites demonstrated increased COPD risk due to occupational exposures and was able to identify specific exposures increasing risk. This study provides additional support for prevention of both smoking and occupational exposures to reduce the burden of COPD among construction workers.* Am. J. Ind. Med. 2009. © *2009 Wiley-Liss, Inc.*

KEY WORDS: DOE; COPD; group-level exposures; asbestos; silica; welding; construction; trades; radiograph; parenchymal; pleural; surveillance

[1]Division of Occupational and Environmental Medicine, Duke University Medical Center, Durham, North Carolina
[2]The Center for Construction Research and Training, Silver Spring, Maryland
[3]Stoneturn Consultants, Seattle, Washington
[4]Department of Environmental Health, University of Cincinnati Medical Center, Cincinnati, Ohio

Contract grant sponsor: U.S. Department of Energy; Contract grant number: DE-FC01-06EH06004.

*Correspondence to: John M. Dement, Professor, Division of Occupational & Environmental Medicine, Department of Community & Family Medicine, Duke University Medical Center, 2200 West Main Street, Suite 400, Durham, NC 27710. E-mail: john.dement@duke.edu

Accepted 1 November 2009
DOI 10.1002/ajim.20792. Published online in Wiley InterScience (www.interscience.wiley.com)

INTRODUCTION

The American Thoracic Society [ATS, 1995b] defines chronic obstructive pulmonary disease (COPD) as the presence of airflow obstruction due to chronic bronchitis and emphysema. Chronic airflow limitation in COPD is caused by a combination of small airway disease (obstructive bronchiolitis) and lung parenchymal destruction (emphysema) and the relative contributions vary by person [GOLD, 2008]. Some researchers also include asthma (ICD-9 code 493) under the COPD rubric; however, detailed reviews have characterized asthma as inflammation with participation of complex cellular and chemical mediators, to be considered separate from COPD [ATS, 1995b]. Nonetheless, there is considerable overlap between asthma (diagnosed or undiagnosed) and the diseases classified as COPD.

COPD is a major public health problem with an estimated 8.5% of the US population reporting prevalent disease [Mannino et al., 2000]. In 1999 COPD ranked as the fourth leading cause of death with over 124,000 deaths [NCHS, 2001], and COPD is projected to become the third most common cause of death worldwide by 2020 [Chapman et al., 2006].

Cigarette smoking is a major risk factor for COPD [NHLBI/WHO, 2001]. The population attributable risk fraction (PAR) for COPD due to tobacco smoke is estimated to be 80–90%, with a higher fraction for men than women [ATS, 1995b]. While smoking is the primary cause of COPD, smoking alone does not explain all the variance in the development of COPD as only 15–20% of smokers developed COPD, an estimated 6% of persons who have COPD in the US are never smokers, and 10% of COPD-related mortality occurs in persons without a history of smoking [Barr et al., 2002; Mannino, 2002; ATS, 2003]. Hereditary deficiency in α_1-antitrypsin (ATT) has been documented as a risk factor; however, the fraction of COPD attributable to an ATT deficiency is generally estimated to be $<1\%$ [ATS, 1995b]. Other genotype–environmental interactions may play an important role in the development of COPD [Sandford and Silverman, 2002].

Occupational exposure to the general category of ''vapors, gases, dusts, and fumes'' (VGDF) has been associated with increased COPD risk [Becklake, 1989; NIOSH, 2002; ATS, 2003; Trupin et al., 2003; Balmes, 2005; GOLD, 2008; Blanc et al., 2009a,b]. These reviews and studies have concluded that occupational VGDF exposures can cause clinical bronchitis and clinically important loses in lung function in both smokers and nonsmokers, as well as marked COPD in smokers. COPD risk has been associated with occupational exposures to organic dusts, wood dusts, cadmium, coal dust, silica, welding fumes, cement dust, and isocyanates. An expert panel convened by the ATS [2003] reviewed data on the occupational burden of airway disease and concluded that a PAR of 15% was a reasonable estimate. Hnizdo et al. [2002] estimated a PAR for COPD attributable to work of 19% overall and 31% among never smokers. Blanc et al. [2009a] suggested that the occupational PAR for COPD might be higher due to joint effects of smoking and occupational factors.

Construction workers have been found to be at increased risk of COPD. Glencross et al. [1997] found that sheet metal workers followed over a 10-year period sustained significantly accelerated loss of FEV_1 if they were exposed to asbestos and smoked. Using spirometry data from the NHANES III for 1988–1994, workers in construction trades were observed to be at increased risk of COPD [Hnizdo et al., 2002], and Bergdahl et al. [2004] found an increased risk of COPD-related mortality among construction workers.

We report on the prevalence of airways obstruction among a sizable cohort of construction and trade workers formerly employed at Department of Energy (DOE) facilities. We also report on results of exploratory analyses of exposures associated with COPD risk among these workers.

MATERIALS AND METHODS

Medical Surveillance Programs at DOE Sites

In 1993 Congress added Section 3162 to the Defense Authorization Act, calling for the DOE to determine whether workers within the nuclear weapons facilities were at ''significant risk'' for work-related illnesses and if so, to provide them with medical surveillance. In 1996 and 1997, DOE established surveillance programs for construction workers at the Hanford Nuclear Reservation in Richland, Washington; the Oak Ridge Reservation in Oak Ridge, Tennessee; the Savannah River Site (SRS) in Aiken, South Carolina; and the Amchitka site in Alaska. The number of DOE sites has been considerably expanded and the surveillance programs for these sites consolidated to form the Building Trades National Medical Screening Program. These construction worker programs are conducted by a consortium which includes: The Center for Construction Research and Training (formerly The Center to Protect Workers' Rights); the University of Cincinnati; Duke University; and Zenith Administrators. We have previously reported on the prevalence of respiratory diseases, hearing loss, beryllium sensitivity, and mortality patterns among workers at these sites [Dement et al., 2003, 2005, 2009; Welch et al., 2004].

Participation in the medical screening programs is voluntary and without cost to workers. Workers participate in these programs only after signed informed consent. Details concerning worker outreach and enrollment have been previously published [Dement et al., 2003, 2005; Welch

et al., 2004]. Workers potentially eligible for participation are identified through multiple sources including union rosters, contractor records where available, media advertisement, and presentations at worker meetings. The Building Trades National Medical Screening Program operates a website (http://www.btmed.org) to provide workers with information about the program, instructions for participation, and health information. Ten staffed outreach offices are located in regions with covered DOE sites.

The screening programs use a two-step design with the initial step consisting of an intake questionnaire followed by a detailed work history interview. The intake questionnaire captures basic demographic information as well as DOE sites where worked and trades. The detailed work history provides information concerning; (1) performing or working near high-hazard work tasks, such as sand blasting or asbestos insulation application or removal, (2) working with or around high-hazard materials such as asbestos, silica, or beryllium, and (3) working in buildings or areas associated with potential exposures to hazardous materials or where known exposure incidents or emergencies occurred. The medical screening examinations are performed under contract with local clinical providers who meet certain credentialing requirements and are required to adhere to a detailed protocol. All data from the intake, work history, medical history, physical examination, and medical examination are entered into a quality-controlled database for purposes of reporting and statistical analyses.

The screening respiratory examination includes: a respiratory history and symptom questionnaire; a posterior–anterior (P–A) chest radiograph, classified by a B-reader according to International Labour Office (ILO) Classification of Radiographs of Pneumoconiosis [ILO, 1980, 2002]; and spirometry. The respiratory history and symptom questionnaire were adapted from the ATS DLD-78 questionnaire [Ferris, 1978].

All participating clinical facilities must agree to obtain spirometry according to ATS standards [ATS, 1995a, 2005]. An occupational health nurse, with training in review of spirometry, reviews all spirometry results and feedback is periodically given to the clinical provider about test results not meeting ATS standards. If necessary, workers are asked to repeat the spirometry at a later date if their initial test results are not interpretable. In addition, the surveillance program medical director reviews spirometry performance for all clinical facilities annually and provides a detailed report to each clinic on their spirometry performance. The medical director collaborates with the clinics to improve performance as needed, resulting in several clinics purchasing more updated equipment and sending technicians for additional spirometry training.

Study Population and Prevalence Analyses

Figure 1 presents a flow chart showing inclusion and exclusion of participants from this study. Data presented in this report are for 7,579 workers meeting the following criteria: (1) completed initial examinations with spirometry through September 2008; (2) not missing demographic data (age, race, sex, and height); and (3) spirometry meeting our inclusion criteria. Spirometry inclusion criteria included a minimum of three recorded expiratory efforts and reproducibility of FVC and FEV_1 of 0.2 L or less [ATS, 1995a].

Abnormal spirometry results were identified using the prediction equations of Hankinson et al. [1999], and the lower limits of normal associated with these equations. The severity of COPD was classified by stage based on the current Global Initiative for Chronic Obstructive Lung Disease (GOLD) working group criteria [NHLBI/WHO, 2001; GOLD, 2008]. GOLD classifications based on spirometry

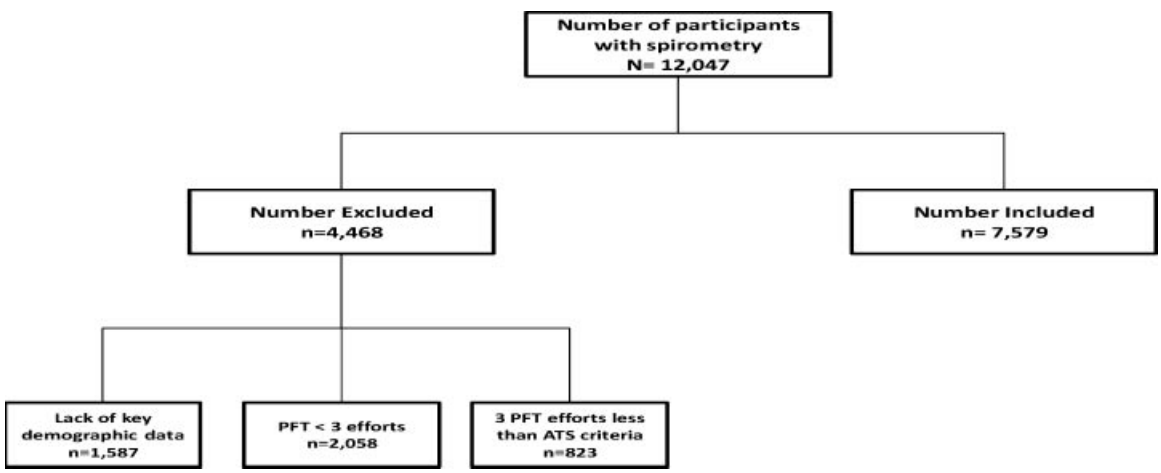

FIGURE 1. Selection of study population.

are: *Stage I* (mild): $FEV_1/FVC < 0.70$ but $FEV_1 \geq 80\%$ of predicted; *Stage II* (moderate): $FEV_1/FVC < 0.70$ and $50\% \leq FEV_1 < 80\%$ of predicted; *Stage III* (severe): $FEV_1/FVC < 0.70$ and $30\% \leq FEV_1 < 50\%$ of predicted; and *Stage IV* (very severe): $FEV_1/FVC < 0.70$ and $FEV_1 < 30\%$ of predicted.

For more detailed analyses of prevalence and risks for the COPD, a COPD case was defined by an FEV_1/FVC ratio of <0.70 and $FEV_1 < 80\%$ predicted, which corresponds to GOLD Stages II–IV (moderate to very severe COPD). This COPD case definition enabled us to compare our results with the COPD prevalence by occupation reported by Hnizdo et al. [2002] based on their analyses of data from the Third National Health and Nutrition Examination Survey (NHANES III).

Stratified analyses were used to explore COPD prevalence by trade and DOE site. Workers with and without COPD were compared for demographic characteristics and prevalence of respiratory symptoms, chest X-ray changes by ILO criteria, smoking history, and other respiratory diagnoses. Descriptive analyses include prevalence values (%) or mean values ± standard errors of the mean (SE) for continuous variables. Continuous variables were compared by analysis of variance (ANOVA) procedures using SAS Proc GLM. The Wilcoxon rank-sum test using SAS Proc NPARIWAY was employed for comparing continuous variables that departed significantly from a normal distribution. Dichotomous variables were compared using the chi-square test of general association. Ordinal categorical data were compared using the Cochran–Armitage test for trends or the Spearman correlation test for variables with more than two categories. In all tests *P*-values of 0.05 or less were considered statistically significant. Overall results for all DOE sites and trade groups included in the medical program are presented; however, site and trade-specific results are presented for groups with at least 100 participants.

Of the 7,579 workers included in the current analyses, 7,320 (96.6%) had a P–A chest radiograph, classified according to ILO criteria. For analyses presented in this report, a parenchymal abnormality was defined as a profusion score of 1/0 or greater for any shape or size of small opacity. Pleural abnormalities were defined as the presence of any notations of positive findings in Sections 3A–D of the NIOSH ILO coding form.

Alternate COPD Case Definition

Our COPD case definition (FEV_1/FVC ratio of <0.70 and $FEV_1 < 80\%$ of predicted) was chosen based on the predominate definition used in the published literature and for comparison with COPD prevalence data by occupation published by Hnizdo et al. [2002]. However, several investigators have suggested that use of a fixed FEV_1/FVC ratio to define airway obstruction may result in disease misclassification based on studies that show that the FEV_1/FVC declines with normal aging; resulting in underreporting of COPD in young workers and false-positive COPD classification for workers older than age 55 years [Hnizdo et al., 2006; Hansen et al., 2007; Enright et al., 2008; Swanney et al., 2008]. In order to address this possibility in our study, we performed several secondary analyses based on a COPD case definition of a FEV_1/FVC ratio below the lower limit of normal (LLN) using the prediction equations of Hankinson et al. [1999]. In this report we call this the alternate LLN analysis (or alternate LLN case definition). Our alternate LLN analyses included estimation of the overall prevalence of COPD, COPD risk by trade group, and exposure–response analyses, as previously described, but using the alternate LLN COPD case definition.

Exposure Assessment

We sought to develop exposure algorithms that would allow us to utilize worker reported exposures most efficiently, taking into account their correlation as well as variability. We first developed the exposure assessment methods and evaluated these methods by application to a known exposure–disease association (asbestos exposure and chest X-ray changes by ILO criteria). For the analyses of asbestos-related chest X-ray changes we defined a case based on a profusion score of 1/0 or greater *or* any pleural change as previously described. Exposure model development using asbestos-related chest X-ray changes allowed us to validate and refine our exposure assessment methods prior to their application to investigate exposures and COPD risks.

Exposure–response analyses were restricted to a subcohort of 5,013 workers who had worked five or fewer years of trade work outside of DOE sites and were not missing data on potential confounders including age, race, sex, years of DOE site work, and smoking. The exposure interview concentrated on exposures at DOE sites; therefore, restriction of the exposure analyses to workers with five or fewer years of trade work outside of DOE sites allowed us to use these data to better infer overall exposure frequencies.

Our qualitative exposure analyses are based on worker reported frequencies of performing tasks associated with exposures of interest. A certified industrial hygienist (J.D.) first reviewed all tasks reported by workers to identify those associated with exposures to the agents of interest. We chose tasks associated with exposures to asbestos (tasks = 8), silica (tasks = 8), welding and cutting (tasks = 13), cement dust (tasks = 4), solvents (tasks = 6), paints (tasks = 5), and dusts/fumes from paint scrapping or removal (tasks = 3) for more detailed analyses. For each job task, workers provided a qualitative estimate of the frequency of performing the task on an ordinal scale ranging from 0 to 5 as follows:

0—No reported performance of the task.
1—Rarely performs the task.
2—Performs the task a few times per month.
3—Performs the task a couple of times per week.
4—Performs the task daily or most days per week.
5—Performs the task nearly continuously.

Multiple tasks were associated with each exposure of interest. For example, asbestos exposures were associated with multiple tasks such as application or removal of pipe insulation; work with asbestos-cement products, gaskets, packings, etc. Additionally, some tasks such as work with asbestos–cement products (e.g., Transite) were associated with multiple exposures (e.g., asbestos, cement dust, silica).

For each task, we first assigned weights to the ordinal frequency categories to estimate the number of days per month that a worker performed the task in question. Monthly days of exposure assigned to the ordinal task frequency categories were as follows: 0 = 0 days/month; 1 = 1 day/month; 2 = 2 days/month; 3 = 8 days/month; 4 = 15 days/month; and 5 = 20 days/month. We then summed the estimated exposure days per month for tasks to form an overall exposure index for each agent. An example of asbestos-associated tasks and overall asbestos exposure index for a worker in our study is given below. In a similar manner, overall exposure indices were generated for each of the agents considered.

Task description	Ordinal task frequency	Exposure days per month
Drill, grind, cut, or apply asbestos containing insulation or Transite	3	8
Sand or refinish asbestos floor tiles	2	2
Finish or sand drywall	1	1
Overall asbestos exposure index		11

Given the nature of tasks typically performed by the various trades, task scores were correlated. For example, pipefitters typically reported working with asbestos-containing insulation as well as performing task with asbestos-containing gaskets and packings. In order to further examine task-associated risks by agent, principal component analysis (PCA) (with VARIMAX rotation) was used to derive exposure scores for the combination of tasks associated with each agent. PCA was used to identify independent factors that explained the maximum amount of mutual correlation of the individual task exposure scores [Burstyn, 2004; Vermeulen et al., 2004]. Inputs to the PCA were the reported exposure days per month for each task. PCA was used to transform a larger number of possibly correlated task exposure scores into a smaller number of uncorrelated variables or principal components. The first principal component accounted for as much of the variability in the data as possible, and each succeeding component accounted for as much of the remaining variability as possible. The output of principal component analyses was a set of weights or ''loadings'' that were then multiplied by each worker's task scores to derive a summary score for each exposure of interest. Principal components with eigenvalues >1 were selected for additional analyses. For each exposure, we also used scree plots (i.e., principal component number vs. eigenvalues) as an additional aid in determining the last principal component that made a significant contribution in explaining the multiple correlations among task scores. A useful property of the PCA method is that the extracted principal components are uncorrelated due to orthogonality of the eigenvectors. Because different factors are uncorrelated, they can simultaneously be chosen as independent variables in regression models without confounding each other [Hoffmann et al., 2004].

Exposure Data Modeling

Our overall exposure scores as well as scores from the PCA analyses were based on worker self-reported exposure frequency; therefore, considerable variability was expected. Other investigators have generally found that exposure–response relationships are attenuated when based on individual versus group-level data [Tielemans et al., 1998; Teschke et al., 2004; Burstyn et al., 2006; McCracken et al., 2009]. We hypothesized that grouped exposure scores based on trade, site, and time period of DOE site work rather than individual exposure scores would produce stronger associations in our analyses. We developed linear statistical models to predict group-level overall task and PCA exposure scores and then used these predictive models to assign exposure scores to individuals in our study. Before modeling of exposure scores, we first examined probability plots of both the overall task scores and the PCA scores and found these to be generally significantly right skewed. In order to normalize our exposure score data for modeling, all exposure scores were log transformed (base e) after addition of constant to the PCA scores to eliminate negative values.

Our data are cross-sectional and did not include repeated exposure score assessments by worker; therefore, we were not able to model between and within-worker variance components. However, since some trade groups comprised several similar trades (e.g., Plumber, Steamfitter, Pipefitter), we initially explored within and between trade group variability in overall exposure scores and PCA scores in mixed models which were fit using the SAS MIXED procedure [SAS, 2004]. We first modeled the fixed effects (i.e., DOE site, trade group, time period of first DOE site work, sex, and race) and retained parameters with a likelihood ratio test with a P-value of 0.10 or less. We next included a random variable for specific trade in the models and found that addition of a specific trade random variable

did not significantly improve model fit by the Akaike's information criterion (AIC) nor did addition of this random variable change coefficients for the fixed effects in any important way; therefore, our final models included only fixed effects.

Peretz et al. [2002] have shown that ordinary multiple linear regression, which assumes independence, can be correctly applied when each worker has only a single measurement, as we have in our data. Given this observation and results of our exploratory analyses using mixed models, final linear models to predict group-level exposure scores were developed using the SAS GENMOD procedure [SAS, 2004], which uses maximum likelihood methods. Model predictors of log overall scores or PCA scores investigated for all exposures included trades nested within DOE site, time period of first DOE site work, sex, and race. Parameters were retained in the model for each exposure if the likelihood ratio test indicated a significance level of 0.10 or less. Each linear model to predict overall exposure scores or PCA scores then took the following general form:

$$\begin{aligned}\text{Log(exposure score)} &= \beta_0 + \beta_1(\text{trade} - \text{site}) \\ &+ \beta_2(\text{DOE work}) + \beta_3(\text{sex}) + \beta_4(\text{race}) + \varepsilon\end{aligned}$$

where log(exposure score) is the log of either overall exposure score or PCA score, trade-site is the trade group nested with DOE site, DOE work is the time period of first DOE site work ($\leq$1960, 1960–1979, 1980–1999, $\geq$2000), sex is the worker gender, race is the worker race (Caucasian, African-American, other), and ε is the error term.

Our population included a few workers with time periods of work in more than one trade or at more than one DOE site. Exposures for these workers were assigned based on the longest period of work by trade and DOE site.

Exposure–Response Analyses

Unconditional logistic regression was used to explore the risk of asbestos-related chest X-ray changes and COPD by qualitative exposure scores while controlling for age (continuous), sex, race (Caucasian, African-American, and other), cigarette smoking status (never, former, and current), and years of DOE site work (continuous). The primary outcome of interest was a statistically significant positive trend in the odds ratios by modeled log exposure scores. For comparison purposes, odds ratios and confidence intervals are presented as changes in risk of asbestos-related chest X-ray change or COPD associated with an increase of 1 standard deviation in predicted log PCA scores or overall task scores.

We explored COPD risks by trade group in a logistic model that controlled for age, sex, race, smoking, years of DOE site work, and DOE site. The reference category used for trade group odds ratios was workers classified as security, scientific/technical, or administrative support. We also explored the effect of BMI on the risk of COPD in trade and specific exposure models using a dichotomous variable for BMI based on a cut point of 38 as used by Hnizdo et al. [2002] in their analyses of NHANES III data.

SAS version 9.1.3 [SAS, 2004] was used for all analysis presented in this report.

All study procedures and materials were approved by the IRB of record for our study (Pacific Northwest National Laboratory Institutional Review Board).

RESULTS

Descriptive and Stratified Analyses

Demographics of the study population of 7,579 workers are presented in Table I. The study population was predominately male (93.4%) and Caucasian (86.7%); however, the proportion male was considerably lower at the Kansas City Site (87.8%) and the Savannah River Site (87.8%). Mean age at examination was 58.0 years with a range of means of 52.2–61.5 years by site. Workers had been employed DOE sites an average of 9.0 years (range 0.8–14.5 by site) and had an average duration of trade work of 24.5 years.

The overall prevalence of GOLD moderate to very severe COPD combined (Table II) was 15.0% and ranged from a low of 9.5% at Amchitka to 20.8% at Paducah. Mean values of FVC, FEV_1, and FEV_1/FVC ratio by site also are shown in Table II. The lower overall FEV_1/FVC ratio among workers at Paducah and Rocky Flats is consistent with the higher prevalence of COPD at these sites.

Workers with and without COPD, based on the definition of COPD used by Hnizdo et al. [2002] for their analyses of NHANES III data (i.e., GOLD categories II–IV), are compared in Table III. Workers with COPD were significantly older, more likely to be white males, and worked significantly longer at DOE sites and in the construction trades. The prevalence of respiratory symptoms (cough, phlegm, or dyspnea) was significantly higher in workers with COPD and, as expected, all spirometry parameters (% predicted FVC, FEV_1, FEV_1/FVC ratio) were significantly lower among those with COPD. Smoking is a very strong risk factor for COPD and our data are consistent with this observation as only 14.7% of workers with COPD reported never to have smoked cigarettes compared to 39.3% for workers without COPD. Workers with COPD were significantly more likely to report a prior physician's diagnosis of asthma, chronic bronchitis, or emphysema.

The study population included a wide range of trades with varied reported exposures. The prevalence of COPD [NIOSH NHANES III definition, Hnizdo et al., 2002] by trade (Table IV) ranged from 6.7% (95% CI = 4.0–10.5) among workers classified as Administrative, Scientific, or

TABLE I. Worker Demographic Summary by Site (DOE Construction and Craft Workers)*,**

DOE sites	Male (%)	Caucasian (%)	Mean age (SE)	Mean years at DOE (SE)	Mean years in trades (SE)[a]	Total workers
Amchitka	536 (92.3)	473 (81.4)	60.1 (0.4)	0.8 (<0.1)	—	581
Brookhaven Lab	135 (97.8)	131 (94.9)	60 (1.0)	2.6 (0.4)	31.2 (0.9)[b]	138
Fernald (FMPC)	700 (93.0)	672 (89.2)	52.2 (0.4)	3.8 (0.2)	23.6 (0.4)	753
Hanford	1,312 (97.9)	1,249 (93.2)	61.5 (0.4)	10.2 (0.3)	26.1 (0.4)	1,340
INEEL	325 (94.5)	329 (95.6)	58.6 (0.6)	6.9 (0.4)	25.4 (0.7)	344
Kansas City Plant	245 (87.8)	232 (83.2)	57.3 (0.7)	8.7 (0.6)	24.1 (0.7)	279
Mound	170 (97.7)	165 (94.8)	58 (0.8)	5.2 (0.6)	27 (0.9)	174
Oak Ridge	915 (96.1)	904 (95.0)	60.6 (0.4)	14 (0.4)	—	952
Paducah	379 (95.0)	389 (97.5)	61.1 (0.8)	5.4 (0.4)	25 (0.7)[b]	399
Portsmouth	233 (96.7)	236 (97.9)	61.4 (0.8)	7.7 (0.6)	17.1 (0.9)	241
Rocky Flats	274 (97.5)	245 (87.2)	60.5 (0.6)	10.2 (0.6)	28.7 (0.8)	281
Savannah River Site	1,660 (87.8)	1,351 (71.4)	54 (0.3)	11.5 (0.2)	22.5 (0.3)	1,891
All other sites	192 (93.2)	187 (90.8)	61 (0.7)	14.5 (0.9)	28.7 (0.9)	206
Overall	7,076 (93.4)	6,573 (86.7)	58.0 (0.1)	9.0 (0.1)	24.5 (0.2)	7,579

*Workers completing medical exams through September 2008.
**Demographics and other data in this report are for workers completing a PFT.
[a]Years in trades includes both DOE and non-DOE work.
[b]Total trade years not available for workers at Oak Ridge and Amchitka.

Security to 24.0% (95% CI = 15.2–31.1) among Cement Masons, Brick Masons, or Plasterers. The age-specific and age-standardized prevalence of COPD among DOE workers is compared to results from analyses of NHANES III [Hnizdo et al., 2002] in Table V. These analyses were restricted to 6,737 DOE workers 30–75 years of age for comparability to the published NHANES data. The age-specific prevalence ratio for DOE workers compared to all NHANSES III participants ranged from 0.8 to 2.1. Standardization of the DOE age-specific prevalence values to the NHANES III age distribution resulted in an age-standardized COPD prevalence of 9.3% for DOE workers compared to 7.1% for all

TABLE II. Spirometry Results and COPD Prevalence by GOLD Severity Criteria and DOE Site (DOE Construction and Craft Workers)

				GOLD COPD prevalence (%)[a]		
DOE sites	Mean % pred. FVC (SE)	Mean % pred. FEV_1 (SE)	Mean FEV_1/FVC ratio (SE)	Stage II: moderate COPD	Stage III: severe COPD	Stage IV: very severe COPD
Amchitka	84.5 (0.7)	88.8 (0.8)	0.79 (0.003)	32 (5.5)	18 (3.1)	5 (0.9)
Brookhaven Lab	85.0 (1.5)	87.8 (1.7)	0.78 (0.008)	9 (6.5)	4 (2.9)	1 (0.7)
Fernald (FMPC)	93.4 (0.6)	91.4 (0.6)	0.76 (0.003)	75 (10.0)	7 (0.9)	3 (0.4)
Hanford	91.5 (0.5)	89.9 (0.6)	0.74 (0.003)	166 (12.4)	48 (3.6)	18 (1.3)
INEEL	91 (0.9)	88.7 (1.0)	0.74 (0.005)	49 (14.2)	11 (3.2)	3 (0.9)
Kansas City Plant	88.1 (1.0)	88.1 (1.1)	0.77 (0.005)	21 (7.5)	6 (2.2)	1 (0.4)
Mound	91.1 (1.2)	88.8 (1.3)	0.74 (0.007)	21 (12.1)	3 (1.7)	0 (0.0)
Oak Ridge	79.7 (0.6)	79.9 (0.6)	0.76 (0.004)	102 (10.7)	57 (6.0)	14 (1.5)
Paducah	86.4 (0.9)	84.0 (1.1)	0.73 (0.006)	52 (13.0)	29 (7.3)	2 (0.5)
Portsmouth	82.6 (1.1)	83.9 (1.4)	0.76 (0.007)	23 (9.5)	12 (5.0)	4 (1.7)
Rocky Flats	96.4 (1.0)	91.7 (1.2)	0.72 (0.005)	35 (12.5)	8 (2.8)	2 (0.7)
Savannah River Site	83.2 (0.4)	82.7 (0.4)	0.77 (0.002)	181 (9.6)	58 (3.1)	25 (1.3)
All other sites	89.9 (1.2)	89.2 (1.4)	0.75 (0.006)	25 (12.1)	5 (2.4)	1 (0.5)
Overall	86.9 (0.2)	86.3 (0.2)	0.76 (0.001)	791 (10.4)	266 (3.5)	79 (1.0)

[a]COPD severity categories by GOLD [2008] criteria.

TABLE III. Comparison of Workers by COPD Case Status (DOE Construction and Craft Workers)

Parameter[a]	No COPD (N = 6,443)	COPD[b] (N = 1,136)	*P*-value
Mean age (SE)	56.9 (0.15)	64.6 (0.35)	<0.01
Male sex (%)	5,974 (92.7)	1,102 (97.0)	<0.01
Caucasian race (%)	5,511 (85.5)	1,052 (92.6)	<0.01
Years at DOE, mean (SE)	8.9 (0.11)	9.5 (0.30)	<0.05
Years in trades,[c] mean (SE)	23.9 (0.18)	27.8 (0.44)	<0.01
Spirometry, mean (SE)			
% Predicted FVC	89.4 (0.21)	72.7 (0.48)	<0.01
% Predicted FEV_1	91.3 (0.20)	57.5 (0.46)	<0.01
FEV_1/FVC ratio	0.79 (0.001)	0.59 (0.003)	<0.01
Respiratory symptom prevalence (%)[d]			
Cough (N = 6,258)	1,518 (28.4)	523 (56.7)	<0.01
Phlegm (N = 6,356)	1,579 (29.3)	564 (58.6)	<0.01
Dyspnea (N = 7,145)	1,785 (29.4)	679 (63.2)	<0.01
B-Reader prevalence (%)			
Pleural changes only	828 (12.9)	247 (21.7)	<0.01
Parenchymal changes only	101 (1.6)	34 (3.0)	
Both pleural and parenchymal	114 (1.8)	55 (4.8)	
No B-Read results available	209 (3.2)	50 (4.4)	
Cigarette smoking prevalence (%)			
Current	1,110 (17.2)	364 (32.0)	<0.01
Former	2,653 (41.2)	561 (49.4)	
Never smoked	2,529 (39.3)	167 (14.7)	
Smoking unknown	164 (2.4)	44 (3.9)	
Physician diagnosis (ever) (%)			
Asthma (N = 7,143)	489 (8.0)	217 (21.3)	<0.01
Chronic bronchitis (N = 7,053)	419 (6.9)	212 (21.2)	<0.01
Emphysema (N = 7,196)	173 (2.8)	259 (25.2)	<0.01
Mean BMI (N = 7,954) (SE)	29.9 (0.07)	28.4 (0.16)	<0.01
Hypertension prevalence (N = 7,560) (%)	2,107 (32.8)	416 (36.7)	0.02

[a]Results are based on workers without missing data. The number of responses available is shown for variables.
[b]COPD case definition: FEV_1/FVC ratio of <0.70 and FEV_1 <80% predicted.
[c]Total trade years not available for workers at Oak Ridge and Amchitka.
[d]*Cough*: "Yes" to "Do you usually have a cough?" and "Yes" to "Do you usually cough like this on most days for 3 consecutive months or more during the year?" *Phlegm*: "Yes" to "Do you usually bring up phlegm from your chest?" and "Yes" to "Do you bring up phlegm like this on most days for 3 consecutive months or more during the year?" *Dyspnea*: "Yes" to "Do you walk slower than people your age because of breathlessness?" or a positive answer to additional questions showing more severe shortness of breath.

NHANES III participants regardless of occupation. It should be noted that Hnizdo et al. [2002] used office workers as the referent population in their logistic models to investigate risks by occupation and this group had an overall COPD prevalence of 4.7%, considerably less than their 7.1% overall prevalence. These authors observed a COPD prevalence of 8.7% for construction workers included in the NHANES III data.

All but 259 (3.4%) of the study population had a P–A chest radiograph classified according to ILO criteria, and a cross tabulation of ILO reading results by COPD status is shown in Table VI. The prevalence of COPD was 12.6% among workers with a normal chest X-ray by ILO criteria but significantly higher among workers with positive ILO readings, with the highest prevalence (32.5%) observed among workers with both pleural changes and parenchymal changes (profusion score $\geq$1/0). A statistical test of association between chest X-ray changes and presence of COPD was highly significant ($P < 0.001$).

Using the alternate LLN COPD case definition of a FEV_1/FVC ratio below the LLN, the overall prevalence of COPD in our study population was 13.34% (95% CI = 12.58–14.13). For comparison, Swanney et al., [2008], using the same COPD case definition, reported an overall COPD prevalence of 5.5% among healthy non-smoking men using the NHANES III data.

TABLE IV. Crude Prevalence of COPD by Trade Groups: Trades With 100 or More Workers—All Sites Combined (DOE Construction and Craft Workers)

Trade group	Number examined	COPD[a] prevalence (%)	95% LCL	95% UCL
Administrative/scientific/security	254	6.7	4.0	10.5
Asbestos workers/insulator	219	18.7	13.8	24.5
Boilermaker	150	14.0	8.9	20.6
Carpenter	531	19.6	16.2	23.0
Cement mason/brick mason/plasterer	104	24.0	15.8	32.2
Electrician	1,298	14.0	12.1	15.9
Ironworker	389	16.2	12.7	20.2
Laborer	958	13.7	11.5	15.9
Millwright	153	19.6	13.6	26.7
Operating engineer	488	14.6	11.5	18.0
Painter	219	15.5	11.0	21.0
Plumber, steamfitter, pipefitter	1,431	15.6	13.7	17.6
Sheet metal worker	413	16.2	12.8	20.1
Teamster	278	16.1	12.1	21.1
All other workers	694	11.8	9.5	14.5
Overall	7,579	15.0	14.2	15.8

[a]COPD case definition: FEV_1/FVC ratio of <0.70 and FEV_1 $<80\%$ predicted. This corresponds to moderate to very severe COPD by GOLD [2008] criteria.

Multivariate Analysis by Trade

Logistic regression results for COPD risk by trade while adjusting for age, race, sex, smoking status, and years of DOE work are presented in Table VII. Results are presented for both our primary COPD case definition and the alternate case definition based on the LLN for the FEV_1/FVC ratio. For these analyses, the reference group consisted of workers classified as Security, Scientific/Technical, or Administrative Support. A dichotomous parameter for BMI ≥ 38 was not statistically significant and was thus dropped from the final model. The overall prevalence of COPD in the reference category was 6.69% (95% CI = 3.95–10.50) using our primary COPD case definition, a COPD prevalence very similar to that observed in the general population in NHANES III (Table V). The COPD prevalence in the reference group using the alternate LLN COPD case definition was 5.91% (95% CI = 3.34–9.55).

After controlling for confounders including cigarette smoking, increased COPD risks were noted for most trades. Trade groups with statistically significant odds ratios over 2.00 based on the primary COPD case definition included: asbestos workers/insulators (OR = 2.66, 95% CI = 1.46–4.97); carpenters (OR = 2.39, 95% CI = 1.37–4.19); cement/brick masons and plasterers (OR = 3.09, 95% CI = 1.53–6.22); and Millwrights (OR = 2.21, 95% CI = 1.13–4.30). Odds ratios for electricians, ironworkers, laborers, painters, plumbers/pipefitters, and sheet metal

TABLE V. COPD Prevalence Compared to NHANES III Data (DOE Construction and Craft Workers)

	NHANES III data[a]		DOE workers[b]		
Age category	Number	Prevalence (%)	Number	Prevalence (%)	Prevalence ratio
30–39	4,324	1.9	422	4.0	2.1
40–49	1,717	6.7	1,570	7.5	1.2
50–59	1,820	13.3	2,241	11.1	0.8
60–75	1,962	17.5	2,504	20.8	1.2
Crude overall prevalence	9,823	7.1	6,737	13.4	1.9
Age standardized prevalence[c]		7.1		9.3	1.3

[a]NHANES III data from Hnizdo et al. [2002].
[b]Data in this table were restricted to 6,737 DOE workers 30–75 years of age for comparison with NHANES III data. Twenty-seven workers were missing BMI.
[c]DOE overall prevalence directly standardized to NHANES III age distribution data by Hnizdo et al. [2002].

TABLE VI. COPD Prevalence by Chest Radiograph B-Reader Category (DOE Construction and Craft Workers)

Chest X-ray B-Reader classification[a]	Number with chest X-ray	COPD[b] prevalence (%)
Normal	5,941	750 (12.6)
Parenchymal changes only	135	34 (25.2)
Pleural changes only	1,075	247 (23.0)
Pleural and parenchymal changes	169	55 (32.5)
No chest X-ray available	259	50 (19.3)

[a]Parenchymal changes with profusion scores $\geq$1/0. Statistical test of association between COPD and X-ray category ($\chi^2 = 135.6$, df = 4, $P < 0.001$).
[b]COPD case definition: FEV_1/FVC ratio of <0.70 and FEV_1 <80% predicted. This corresponds to moderate to very severe COPD by GOLD criteria.

workers were statistically elevated but less than 2.00. Very similar patterns of excess risk were observed when these analyses were repeated using the alternate COPD case definition. The COPD risk among operating engineers was significantly increased using the alternate LLN COPD case definition and elevated but not statistically significant using our primary case definition. While we observed excess risk for most trades, the magnitude of these risks varied and our review of exposures by trade suggested differing patterns possibly related to the risk of COPD; therefore, additional analyses by reported exposures were undertaken to further explore these differences.

Exposure Model Validation for Asbestos Exposures and Chest X-Ray Changes

Results of the initial validation study based on the association between chest X-ray changes by ILO criteria (profusion score $\geq$1/0 or any pleural change) and reported asbestos exposures are presented in Table VIII. In all models, age, sex, race, and cigarette smoking were significantly associated with the risk of a positive chest X-ray change. Years of work at DOE sites was generally a weak predictor of chest X-ray changes but was retained in all models in order to allow more meaningful assessment of reported exposure frequency and disease risk. Total asbestos exposure scores, as measured by the sum of task scores, was significantly associated with the risk of an asbestos-related chest film changes. Increasing the sum of tasks score by 1 standard deviation was associated with an odds ratio of 1.166 (95% CI = 1.062–1.282). Models based on the predicted sum of task scores produced the largest odds ratio (OR = 1.348, 95% CI = 1.218–1.492) and the best fitting statistical model based on AIC criteria. Three principal components with eigenvalues greater than 1.0 were selected and the first two principal components were strongly associated with increased risk of asbestos-related chest X-ray changes. The odds ratio for the sum of task scores increased from 1.166 to 1.348 using the linear model predicted scores compared to the individual worker scores. Similar increases were observed

TABLE VII. Logistic Regression Model COPD Odds Ratios by Trade Groups: Trades With 100 or More Workers—All Sites Combined (DOE Construction and Craft Workers)

	Primary COPD case definition[a]			Alternate COPD case definition[b]		
Trade group	Prevalence odds ratio	95% LCL	95% UCL	Prevalence odds ratio	95% LCL	95% UCL
Administrative/scientific/security	1.00	Ref.	Ref.	1.00	Ref.	Ref.
Asbestos workers/insulator	2.66	1.42	4.97	2.10	1.08	4.08
Boilermaker	1.44	0.69	2.99	1.48	0.69	3.17
Carpenter	2.39	1.37	4.19	2.72	1.52	4.86
Cement mason/brick mason/plasterer	3.09	1.53	6.22	2.97	1.44	6.15
Electrician	1.73	1.01	2.96	2.15	1.23	3.76
Ironworker	1.99	1.11	3.57	1.85	1.00	3.42
Laborer	1.93	1.12	3.33	2.09	1.19	3.69
Millwright	2.21	1.13	4.30	2.20	1.09	4.46
Operating engineer	1.66	0.94	2.96	2.14	1.18	3.88
Painter	1.96	1.03	3.74	2.68	1.40	5.12
Plumber, steamfitter, pipefitter	1.83	1.07	3.11	1.93	1.10	3.36
Sheet metal worker	1.97	1.11	3.52	2.34	1.28	4.26
Teamster	1.79	0.96	3.31	1.69	0.88	3.23
All other workers	1.57	0.90	2.76	1.54	0.86	2.78

[a]COPD case definition: FEV_1/FVC ratio of <0.70 and FEV_1 <80% predicted. This corresponds to moderate to very severe COPD by GOLD criteria. Odds ratios control for age, sex, race, smoking, and years of DOE work.
[b]COPD cases defined based on an FEV_1/FVC ratio less than the lower limit of normal using the Hankinson et al. [1999].

TABLE VIII. Logistic Regression Models for Asbestos-Related Chest Film Changes: Validation of Principal Component and Linear Model Exposure Methods (DOE Construction and Craft Workers)*

Asbestos exposure variable[a]	Individual data or linear exposure model covariates[b]	Odds ratio[c]	95% LCL	95% UCL	Model AIC
Sum of asbestos task scores	Individual data	1.166	1.062	1.282	3,363
Linear model predicted sum of task scores	Linear model with trade (site), first DOE, and sex effects	1.348	1.218	1.492	3,339
Asbestos principal component #1[d]	Individual data	1.130	1.031	1.239	3,367
Asbestos principal component #2	Individual data	1.196	1.098	1.302	3,358
Asbestos principal component #3	Individual data	0.807	0.726	0.897	3,357
Linear model predicted asbestos principal component #1	Linear model with trade (site), first DOE, and sex effects	1.281	1.170	1.403	3,346
Linear model predicted asbestos principal component #2	Linear model with trade (site) effects	1.221	1.117	1.334	3,355
Linear model predicted asbestos principal component #3	Linear model with trade (site), first DOE, and sex effects	0.761	0.687	0.843	3,346

*Analyses based on sub-cohort of 4,758 workers having a chest radiograph read by ILO criteria, with five or fewer years of trade work outside of DOE sites, and data available for all other model covariates. A total of 695 workers had pleural abnormalities or parenchymal changes (profusion $\geq$ 1/0).

[a]The models were based on the linear model predictors for log of task or PC scores. A case in these models is either an ILO profusion of 1/0 or greater *or* any pleural change.

[b]Parameters found to be significant exposure predictors in the linear models are shown. "Trade (site)" indicates that trade is nested within site. "First DOE" is the year first employed at a DOE site.

[c]Odds ratios controlling for age, sex, race, smoking, and years of DOE work. The odds ratios represent changes in risk for an increase of 1 standard deviation in the given log of the exposure parameter. Confidence intervals are Wald limits.

[d]Principal components #1 and #2 were positively loaded (loadings >0.3) for asbestos–cement (Transite) work, pipe work including pipe insulation, drywall work, work with spray fireproofing or insulation, work with gaskets or packings, and building demolition. Principal component #3 was positively loaded for work with floor tiles and use of asbestos blankets or gloves.

for asbestos principal components #1 and #2. Factor loading for the three asbestos principal components were somewhat enlightening. Principal components #1 and #2 were positively loaded (loadings >0.3) for asbestos–cement (Transite) work, pipe work including pipe insulation, drywall work, work with spray fireproofing or insulation, work with gaskets or packings, and building demolition. The positive loading for principal component three included work with floor tiles and use of asbestos blankets or gloves; tasks normally associated with lower asbestos exposure levels compared to those tasks included in principal components #1 and #2.

In order to further explore trends in the risk asbestos-related chest X-ray changes, each exposure index found to be statistically significant was further analyzed by forming 10 categories for each exposure variable such that approximately equal numbers of cases were in each category. Since we had a total of 695 workers with positive chest X-ray changes, this resulted in about 70 cases in each group. We then re-ran our logistic models using these categorical

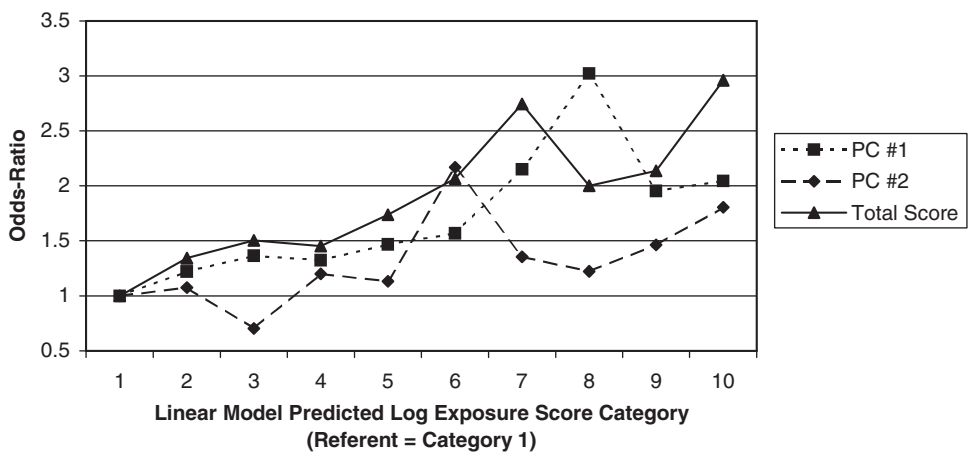

FIGURE 2. Odds ratios for asbestos-related chest X-ray changes (adjusted for age, sex, race, smoking, and years of DOE work).

variables with the lowest exposure category as the referent group for calculation of odds ratios. Figure 2 provides a plot of the resulting odds ratios by exposure category for the three exposure indices significantly associated with risk, demonstrating a strong positive increase in risk by exposure score category. This validation study provided some degree of confidence in the exposure assessment algorithms, including the use of linear models to generate group-level exposure estimates that were superior to individual measures.

COPD Exposure–Response Analyses

Our COPD exposure–response analyses included 4,935 workers and 603 COPD cases. Based on the validation study with asbestos, analyses of tasks and exposures associated with COPD were based on the linear model predicted scores for the sum of tasks and the principal components derived from the tasks. All models were adjusted for age, sex, race, smoking, and years of DOE work. We also include a dichotomous variable for BMI $\geq$38; however, this parameter was not statistically significant in any of the models and was thus excluded from the final models. Cigarette smoking was a strong risk factor for COPD in all models. Statistically significant positive associations with COPD risk were observed for asbestos, welding, silica, and cement dusts based on the sum of task scores for these exposures (Table IX). Asbestos principal component #2 for was statistical significance. The association between COPD and asbestos exposure remained statistically significant (OR = 1.111, 95% CI = 1.005–1.229) in a model which included a categorical variable for chest X-ray parenchymal changes of profusion 1/0 or greater by ILO criteria.

A different pattern of positive association was observed for exposures to solvents, paints, and fumes/dusts from paint removal. For these exposures, the exposure metric based on the sum of tasks scores was not statistically significant; however, one of the principal components derived for these tasks was significantly associated with COPD risk. A review of the positive loadings on these principal components was interesting. For solvent principal component #3, positive loadings (loadings >0.3) were observed for tasks associated with fueling trucks and equipment. Paint principal component #3 (not shown in Table IX) was of borderline significance ($P = 0.06$), and this principal component had a strong positive loading for the general task of mixing and applying paints but without specification of the types of paint. Positive loading of paint removal principal component #3 was obtained for tasks associated with flame cutting, burning, or welding lead paint coated surfaces and grinding or scraping paints or coatings.

Glencross et al. [1997] found that sheet metal workers followed over a 10-year period sustained significantly accelerated loss of FEV_1 if they were exposed to asbestos and smoked, suggesting an interactive effect on COPD risk. We investigated the possibility of interaction of smoking and asbestos exposures in our logistic models by inclusion of an interactive term. The interaction term was significant ($P = 0.039$) suggesting possible interactive effects of smoking and asbestos in the etiology of COPD in this population.

The medical history questionnaire asked about hobbies and activities done outside of work. We investigated these as potential confounders in logistic models that controlled for age, sex, race, years of DOE work, and smoking with the activity entered as a dichotomous variable. Hobbies or tasks

TABLE IX. Logistic Regression Models for COPD Prevalence by Linear Model Exposures DOE Construction and Craft Workers*

Statistical model predicted exposure scores	Linear exposure model covariates[a]	Odds ratio[b]	95% LCL	95% UCL	Model AIC
Asbestos task total	Trade (site), first DOE, sex	1.115	1.010	1.230	3,289
Asbestos principal component #2[c]	Trade (site)	1.100	1.006	1.203	3,289
Welding task total	Trade (site), first DOE, sex	1.055	1.001	1.114	3,290
Silica task total	Trade (site), first DOE, sex	1.123	1.017	1.241	3,288
Cement task total	Trade (site), first DOE, sex	1.132	1.025	1.250	3,288
Solvent principal component #3[c]	Trade (site), first DOE, race	1.166	1.057	1.285	3,284
Paint remove principal component #1[c]	Trade (site), first DOE, sex	1.102	1.004	1.209	3,289

*Analyses based on sub-cohort of 4,935 workers with five or fewer years of trade work outside of DOE sites and data available for all other model covariates. Only exposures significantly associated with COPD risk ($P < 0.05$) are shown.

[a]Parameters found to be significant exposure predictors in the linear models are shown. "Trade (site)" indicates that trade is nested within site. "First DOE" is the year first employed at a DOE site.

[b]Odds ratios controlling for age, sex, race, smoking, and years of DOE work. The odds ratios represent changes in risk for an increase of 1 standard deviation in the given log of the exposure parameter. COPD case definition: FEV_1/FVC ratio of <0.70 and FEV_1 <80% predicted.

[c]Principal component positive loadings (loadings >0.3) were as follows: asbestos PC #2: asbestos–cement (Transite) work, pipe work including pipe insulation, drywall work, work with spray fireproofing or insulation, work with gaskets or packings, and building demolition. Solvent PC #3: tasks associated with fueling trucks and equipment. Paint removal PC #1: tasks associated with flame cutting, burning, or welding lead paint coated surfaces and grinding or scraping paints or coatings.

analyzed included melting or working with metals, house painting, jewelry making, operating farm machinery, woodworking, cutting with a chain saw, furniture refinishing, operating motorcycles, paint removal, pottery or ceramics, stained glass work, and volunteer firefighter work. None of the odds ratios were statistically significant; however, the odds ratios for melting or working with metals (OR = 1.13, 95% CI = 0.91–1.41), stained glass work (OR = 1.16, 95% CI = 0.43–3.12), and volunteer firefighter work (OR = 1.20, 95% CI = 0.72–1.99) were greater than 1.0. Inclusion of covariates for hobby activities with an odds ratio greater than 1.0 in the exposure–response models did not change the results presented in Table IX in any meaningful way.

All COPD exposure–response models were re-run but using the alternate LLN COPD case definition based on values for the FEV_1/FVC ratio below the LLN and these results are presented in Table X. Results were very similar to those obtained using our primary COPD case definition. For most exposures, the odds ratios based on the alternate LLN of normal COPD case definition were higher than those found using the fixed FEV_1/FVC ratio definition. This was especially true for solvent principal component #3. Additionally, the overall exposure score for paint, silica principal component #1, and cement principal component #1 were statistically significant based on the alternate LLN case definition. The statistically significant silica and cement principal components demonstrated positive loadings (loadings >0.3) for tasks associated cutting or drilling Transite, cutting or drilling concrete, and building demolition.

DISCUSSION

Our study included a wide variety of construction trades working at multiple DOE sites across the US, thus providing a good opportunity to explore risks not only by trade but also by risks associated with common task-related exposures across trades. The overall prevalence of moderate to very severe COPD in this cohort was high (15.0%). Comparisons with published analyses of NHANES III data [Hnizdo et al., 2002] using the same COPD case definition provided further support for increased COPD risk among DOE workers. A very similar pattern of overall excess risk and risk by trade group was observed when analyses were repeated using the alternative LLN COPD case definition.

Our study population included workers whose spirometry meet ATS criteria for reproducibility. There is evidence that the failure to perform reproducible spirometry may itself be an indicator of lung disease, with test failure as likely to reflect the poor health as it is to reflect poor cooperation, poor effort, or the incompetence of the technician [Becklake, 1990]. Eisen et al. [1984, 1985] have shown that selection of occupational cohorts based on meeting ATS spirometry standards may bias epidemiologic findings by the exclusion of many subjects with accelerated loss of lung function. To determine if our decision to include only workers who met the ATS reproducibility criteria excluded workers with COPD, we performed additional analyses including workers not meeting ATS reproducibility criteria. Inclusion of workers whose spirometry did not meet ATS reproducibility criteria had negligible impact on COPD prevalence,

TABLE X. Logistic Regression Models for COPD Prevalence by Linear Model Exposures: Alternate COPD Case Definition Based on Lower Limit of Normal for FEV_1/FVC Ratio (DOE Construction and Craft Workers)*

Statistical model predicted exposure scores	Linear exposure model covariates[a]	Odds ratio[b]	95% LCL	95% UCL	Model AIC
Asbestos task total	Trade (site), first DOE, sex	1.135	1.028	1.252	3,351
Asbestos principal component #2[c]	Trade (site)	1.151	1.056	1.254	3,348
Welding task total	Trade (site), first DOE, sex	1.122	1.019	1.237	3,352
Silica task total	Trade (site), first DOE, sex	1.170	1.059	1.293	3,348
Silica principal component #1[c]	Trade (site), first DOE, sex, race	1.150	1.046	1.264	3,349
Cement task total	Trade (site), first DOE, sex	1.193	1.079	1.319	3,345
Cement principal component #1[c]	Trade (site), first DOE, sex	1.142	1.043	1.252	3,350
Solvent principal component #3[c]	Trade (site), first DOE, race	1.322	1.186	1.473	3,330
Paint task total	Trade (site), first DOE	1.087	1.002	1.180	3,354

*Analyses based on sub-cohort of 4,935 workers with five or fewer years of trade work outside of DOE sites and data available for all other model covariates. Only exposures significantly associated with COPD risk ($P < 0.05$) are shown.

[a]Parameters found to be significant exposure predictors in the linear models are shown. "Trade (site)" indicates that trade is nested within site. "First DOE" is the year first employed at a DOE site.

[b]Odds ratios controlling for age, sex, race, smoking, and years of DOE work. The odds ratios represent changes in risk for an increase of 1 standard deviation in the given log of the exposure parameter. COPD cases defined based on an FEV_1/FVC ratio less than the lower limit of normal using the Hankinson et al. [1999].

[c]Principal component positive loadings (loadings >0.3) were as follows: Asbestos PC #2: asbestos–cement (Transite) work, pipe work including pipe insulation, drywall work, work with spray fireproofing or insulation, work with gaskets or packings, and building demolition. Silica PC #1 and cement PC #1: cutting or drilling Transite, cutting or drilling concrete, and building demolition.

increasing the overall prevalence from 15.0% to 15.2%. Given these results, selection bias based on meeting ATS criteria does not appear to be an important factor in explaining our results.

Smoking is an important risk factor for COPD and construction workers as a whole have generally smoked more than the general population [Bang and Kim, 2002; Lee et al., 2007]. However, our internal analyses by trade, which controlled for smoking and other confounders, found COPD odds ratios to range from 1.57 to 3.09 by trade. Using the same COPD case definition as our study, Hnizdo et al. [2002] observed an increased risk of COPD among workers in the construction industry (OR = 1.3, 95% CI = 0.8–2.3) and among construction trades (OR = 1.2, 95% CI = 0.6–2.5). Our study population included 7,579 construction and trade workers and 1,136 COPD cases, thus we had good statistical power to investigate trade-specific risks while controlling for important confounders.

The investigations of exposures associated with COPD risks among these DOE workers were exploratory. The exposure assessment was based on self-reported frequency scores for tasks associated with exposures of interest. We recognized this limitation and sought to maximize the utility of these data through the use of linear statistical models to assign group-level exposure scores for exposure–response analyses. Our validation study, which investigated the association between asbestos-related chest X-ray changes and reported asbestos exposures, demonstrated both the utility of our self-reported exposures as well as advantages of group-level exposure assignments using linear statistical models. Our observations with regard to advantages of group-level exposure assessments are thus consistent with other published results [Tielemans et al., 1998; Teschke et al., 2004; Burstyn et al., 2006; McCracken et al., 2009].

Exposure–response analyses found several statistically significant associations between exposures experienced by construction workers and COPD risk. For asbestos, silica, cement dust, and welding, the strongest associations were observed using the exposure index representing the sum of task-specific scores, thus suggesting a general effect of total exposures rather than from any specific set of tasks represented in the principal component analyses.

The association between asbestos exposure and COPD risk remained significant in a model that adjusted for presence of parenchymal changes consistent with radiological asbestosis (ILO profusion $\geq$1/0). The role of asbestos as a risk factor for obstructive airway disease has been debated; however, there is general consensus that asbestos exposure is associated with an obstructive physiological abnormality [ATS, 2004]. Epidemiological studies have shown an association between asbestos exposures or asbestosis and reduction in FEV_1 and the FEV_1/FVC ratio and chronic airflow obstruction has been observed among subjects without radiological evidence of asbestosis who were lifelong nonsmokers [ATS, 2004]. An interactive effect of asbestos exposure and smoking has been previously reported [Glencross et al., 1997] and we observed interaction between asbestos exposure and smoking in our logistic models. Our results thus support an association between asbestos exposure and obstructive lung impairment consistent with the published literature [Ohar et al., 2004; Meldrum et al., 2005], perhaps with an interaction with smoking. This conclusion must be tempered with the observation that many trades in our study with significant exposure to asbestos also had exposures to several other agents found to be associated with COPD in our study (e.g., silica and welding/cutting).

We observed an association between silica exposures and COPD risk. Recent reviews have concluded that exposure to silica is a cause of COPD independent of presence of radiological evidence of silicosis [Ruston, 2007]. In their review Hnizdo and Vallyathan [2003] concluded that exposure to levels of silica dust not expected to cause disabling silicosis may cause chronic bronchitis, emphysema, and/or small airways disease. Much of this evidence has come from studies of mining and milling and mineral processing populations; however, increased airways disease has been observed among construction workers doing highway and tunnel work and exposed to silica [Oliver and Misracle-McMahill, 2006].

Consistent with our results, a number of studies have found significantly increased risk of COPD among welders and other workers performing welding tasks [Mastrangelo et al., 2003; Meldrum et al., 2004; Balmes, 2005; Hunting and Welch, 1993]. We also observed a positive association between exposure to cement dust and COPD; however, other studies have produced mixed results relative to cement dusts exposures and COPD [Abrons et al., 1998; Fell et al., 2003; Fell et al., 2003; Mwaiselage et al., 2004; Ruston, 2007]. Ruston [2007] noted that sizable differences in cement dust exposure levels across these studies could partially account for differences in results. Since the predominate cement dust exposure among our workers resulted from cutting and sawing finished cement rather than from production of Portland cement, the predominate exposure in the literature, our workers may have had important differences in exposure. In addition workers in our study with significant exposures to cement dust also experienced significant silica exposures; therefore, attribution of either exposure alone is not possible.

We observed positive associations with some tasks associated with exposures to solvents, paints, and fumes/dusts from paint removal. For solvents, a positive association was only observed for tasks associated with fueling of trucks and equipment. Few studies have associated COPD with exposures to specific solvents. Hart et al. [2008] observed increased COPD mortality among railroad workers exposed to diesel exhaust. An increased risk of COPD-related hospitalization has been observed for male taxi and bus drivers [Tüchsen and Hannerz, 2000]. Workers reporting

refueling trucks and equipment in our study are more likely to have experienced exposures to engine exhausts in addition to fumes from fuels; therefore, our task may be serving as a surrogate for general vehicle-related exposures.

The association between paint tasks and COPD risk in our study was of borderline significance for tasks involving mixing and applying paints without specification of the types of paints. Mastrangelo et al. [2003] observed a significant association between COPD and painting. It may be the case that specific paints confer the risk of COPD; Pronk et al. [2007] observed an association between COPD-like symptoms and exposure to spray paints containing hexamethylene diisocyanate, and a significantly increased risk of physician-diagnosed COPD (OR = 3.73, 95% CI = 1.27–11.0) was observed by Hammond et al. [2005] in their cross-sectional study of automotive workers doing painting. We were not able to evaluate isocyanate-based paint exposures separately in our analyses due to the low frequency of this reported exposure in our population (0.8% of workers).

Lastly, we observed a positive association with paint removal task such as flame cutting, burning, or welding lead paint coated surfaces or grinding/scraping paints or coatings. We are not aware of similar findings in the literature relative to this specific exposure; however, other studies have consistently shown increased COPD risks among workers exposures to VGDF as previously described.

CONCLUSIONS

Our study of a diverse population of construction workers employed at DOE sites demonstrated increased COPD risk due to occupational exposures, and also identified specific exposures that confer risk. The age-standardized COPD prevalence ratio for this population compared to NHANES III results was 1.3 and further internal analyses using relatively unexposed workers as the reference category found COPD odds ratios to range from 1.57 to 3.09 by trade, after adjustment for age, race, sex, smoking, and duration of DOE work. The diversity of reported exposures and the large number of COPD cases among our study population allowed us to explore task-related exposures associated with the risk of COPD. Increased COPD risk was observed for exposures to asbestos, silica, welding, cement dust, and some tasks with exposures to solvents, paints, and dust/fumes from paint removal. All of our statistical models found smoking to be a powerful risk factor for COPD. This study provides additional support for the importance of preventing both smoking and occupational exposures in order to reduce the burden of COPD among construction workers.

ACKNOWLEDGMENTS

Funding for this work is provided through cooperative agreement number DE-FC01-06EH06004 from the U.S. Department of Energy. The Amchitka, Hanford, Oak Ridge, and Savannah River construction workers medical screening program have rolled into the Building Trades National Medical Screening Program still operated by CPWR and its consortium and funded by DOE. We have received guidance and support from the Central Washington, Augusta, and Knoxville Building and Construction Trade Councils. We received assistance from a numerous people at the Hanford Reservation, Savannah River Site, and the Oak Ridge Reservation. These programs were reviewed by the Pacific Northwest National Laboratory Institutional Review Board at Hanford (Sherry Davis, administrator); Savannah River Site (Karen Brown, administrator); and Oak Ridge (Shirley Fry and Elizabeth Ellis, chairs). The Oak Ridge program was coordinated by Dr. Eula Bingham and Bill McGowan at the University of Cincinnati. The coordinating office and data center are administered at Zenith Administrators, Seattle, under the supervision of Don Davies, Sue Boone, Anna Chen, and Kim Cranford.

REFERENCES

Abrons HL, Petersen MR, Sanderson WT, Engelberg AL, Harber P. 1998. Symptoms, ventilatory function, and environmental exposures in Portland cement workers. Br J Ind Med 45:368–375.

American Thoracic Society. 1995a. Standardization of spirometry: 1994 update. Am Rev Respir Dis 152:1107–1136.

American Thoracic Society. 1995b. Standards for the diagnosis and care of patients with chronic obstructive pulmonary disease. Am J Respir Crit Care Med 152:S77–S121.

American Thoracic Society. 2003. American Thoracic Society Statement: Occupational contribution to the burden of airway disease. Am J Respir Crit Care Med 167:787–797.

American Thoracic Society. 2004. American Thoracic Society Statement: Diagnosis and initial management of nonmalignant diseases related to asbestos. Am J Respir Crit Care Med 170:691–715.

American Thoracic Society. 2005. ATS/ERS Task Force: Standardisation of lung function testing. Eur Respir J 26:319–338.

Balmes JR. 2005. Occupational contribution to the burden of chronic obstructive pulmonary disease. J Occup Environ Med 47:154–160.

Bang KM, Kim JH. 2002. Prevalence of cigarette smoking by occupation and industry in the United States. Am J Ind Med 40:233–239.

Barr RG, Herbstman J, Speizer FE, Camargo A. 2002. Validation of self-reported chronic obstructive pulmonary disease in a cohort of nurses. Am J Epidemiol 155(10):956–971.

Becklake MR. 1989. Occupational exposures: Evidence for a causal association with chronic obstructive pulmonary disease. Am Rev Respir Dis 140:S85–S91.

Becklake MR. 1990. Epidemiology of spirometric test failure. Br J Ind Med 47:73–74.

Bergdahl IA, Torėn K, Eriksson K, Hedlund U, Nilssonz T, Flodin R, Järvholm B. 2004. Increased mortality in COPD among construction workers exposed to inorganic dust. Eur Respir J 23:402–406.

Blanc PD, Iribarren C, Trupin L, Earnest G, Katz PP, Balmes J, Sidney S, Eisner MD. 2009a. Occupational exposures and the risk of COPD: Dusty trades revisited. Thorax 64:6–12.

Blanc PD, Eisner MD, Earnest G, Trupin L, Balmes JR, Yelin EH, Gregorich SE, Kratz PP. 2009b. Further exploration of the links between occupational exposure and chronic obstructive pulmonary disease. J Occup Environ Med 51:804–810.

Burstyn I. 2004. Principal component analysis is a powerful instrument in occupational hygiene inquiries. Ann Occup Hyg 38:655–661.

Burstyn I, Kim HM, Cherry N, Yasui Y. 2006. Metamodels of bias in Cox proportional-hazards and logistic regressions with heteroscedastic measurement error under group-level exposure assessment. Ann Occup Hyg 50:271–279.

Chapman KR, Mannino DM, Soriano JB, Vermeire PA, Buist AS, Thun MJ, Connell C, Jemal A, Lee TA, Miravitlles M, Aldington S, Beasley R. 2006. Epidemiology and costs of chronic obstructive pulmonary disease. Eur Respir J 27:188–207.

Dement JM, Welch LW, Bingham E, Cameron B, Rice C, Quinn P, Ringen K. 2003. Surveillance of respiratory diseases among construction workers at Department of Energy nuclear sites. Am J Ind Med 43:559–573.

Dement JM, Ringen K, Welch L, Bingham E, Quinn P. 2005. Surveillance of hearing loss among older construction and trade workers at Department of Energy nuclear sites. Am J Ind Med 48:348–358.

Dement JM, Ringen K, Welch LS, Bingham E, Quinn P. 2009. Mortality of older construction and craft workers employed at Department of Energy (DOE) nuclear sites. Am J Ind Med 52(9): 671–682.

Eisen EA, Robins JM, Greaves IA, Wegman DH. 1984. Selection effects of repeatability criteria applied to lung spirometry. Am J Epidemiol 120:734–742.

Eisen EA, Oliver LC, Christiani DC, Robins JM, Wegman DH. 1985. Effects of spirometry standards in two occupational cohorts. Am Rev Respir Dis 132:120–124.

Enright P, Skloot G, Herbert R. 2008. Standardization of spirometry in assessment of responders following man-made disasters: World Trade Center Worker and Volunteer Medical Screening Program. Mt Sinai J Med 75:109–114.

Fell AKM, Thomassen TR, Kristensen P, Egeland T, Kongerud J. 2003. Respiratory symptoms and ventilatory function in workers exposed to portland cement. J Occup Environ Med 45:1008–1014.

Ferris BG. 1978. Epidemiology standardization project. Am Rev Respir Dis 118:1–53.

Glencross MP, Weinberg JM, Ibrahim JG, Christiani DC. 1997. Loss of lung function among sheet metal workers: Ten-year study. Am J Ind Med 32:460–466.

GOLD. 2008. Global Strategy for the Diagnosis, Management, and Prevention of Chronic Obstructive Pulmonary Disease, Global Initiative for Chronic Obstructive Lung Disease (GOLD), Updated 2008, www.goldcopd.com.

Hammond SK, Gold E, Baker R, Quinlan P, Smith W, Pandya R, Balmes J. 2005. Respiratory health effects related to occupational spray painting and welding. J Occup Environ Med 47:728–739.

Hankinson JL, Odencrantz JR, Fedan KB. 1999. Spirometric reference values from a sample of the general U.S. population. Am J Respir Crit Care Med 159:179–187.

Hansen JE, Xing-Guo S, Wasserman K. 2007. Spirometric criteria for airway obstruction. Chest 131:349–355.

Hart JE, Laden F, Eisen EA, Smith TJ, Garshick E. 2009. Chronic obstructive pulmonary disease mortality in railroad workers. Occup Environ Med 66:221–226.

Hnizdo E, Vallyathan V. 2003. Chronic obstructive pulmonary disease due to occupational exposure to silica dust: A review of epidemiological and pathological evidence. Occup Environ Med 60:237–243.

Hnizdo E, Sullivan PA, Bang KM, Wagner G. 2002. Association between chronic obstructive pulmonary disease and employment by industry and occupation in the US Population: A study of data from the Third National Health and Nutrition Examination Survey. Am J Epidemiol 156:738–746.

Hnizdo E, Glindmeyer HW, Petsonk EL, Enright P, Buist AS. 2006. Case definitions for chronic obstructive pulmonary disease. J Chronic Obstructive Pulm Dis 3:95–100.

Hoffmann K, Schulze MB, Schienkiewitz A, Nöthlings U, Boeing H. 2004. Application of new statistical method to derive dietary patterns in nutritional epidemiology. Am J Epidemiol 159:935–944.

Hunting KL, Welch LS. 1993. Occupational exposure to dust and lung disease among sheet metal workers. Br J Ind Med 50:432–442.

International Labour Office (ILO). 1980. Guidelines for the use of the ILO International Classification of Radiographs of Pneumoconiosis. Geneva: International Labour Office.

International Labour Office (ILO). 2002. Guidelines for the Use of the ILO International Classification of Radiographs of Pneumoconioses, revised edition 2000 (Occupational Safety and Health Series, No. 22). Geneva: International Labour Office.

Lee DJ, Fleming LE, Arheart KL, LeBlanc WG, Caban AJ, Chung-Bridges K, Christ SL, McCollister KE, Pitman T. 2007. Smoking rate trends in U.S. occupational groups: The 1987 to 2004 National Health Interview Survey. J Occup Environ Med 49(1):75–81.

Mannino DM. 2002. Epidemiology, prevalence, morbidity and mortality, and disease heterogeneity. Chest 121(Suppl):121S–126S.

Mannino DM, Gagnon RC, Petty TL, Lydick E. 2000. Obstructive lung disease and low lung function in adults in the United States: Data from the National Health and Nutrition Examination Survey, 1988–1994. Arch Intern Med 160(11):1683–1689.

Mastrangelo G, Tartari M, Fedeli U, Fadda E, Saia B. 2003. Ascertaining the risk of chronic obstructive pulmonary disease in relation to occupation using a case–control design. Occup Med 53:165–172.

McCracken JP, Schwartz J, Bruce N, Mittleman M, Ryan LM, Smith KR. 2009. Combining individual and group-level exposure information: Child carbon monoxide on the Guatemala woodstove randomized control trial. Epidemiology 20:127–136.

Meldrum M, Rawbone R, Curran AD, Fishwick D. 2005. The role of occupation in the development of chronic obstructive pulmonary disease (COPD). Occup Environ Med 62:212–214.

Mwaiselage J, Bratveit M, Moen B, Mahalla Y. 2004. Cement dust exposure and ventilatory function impairment: An Exposure Response Study. J Occup Environ Med 46:658–667.

NCHS. 2001. National Vital Statistics Report, Vol. 49, No. 11, Centers for Disease Control and Prevention, National Center for Health Statistics, October 12, 2001.

Ng'Ang'a LW, Ernst P, Jaakkola MS, Gerardi G, Hanley JH, Becklake MR. 1992. Spirometric lung function. Distribution and determinants of test failure in a young adult population. Am Rev Respir Dis 145:48–52.

NHLBI/WHO. 2001. Global Strategy for the Diagnosis, Management, and Prevention of Chronic Obstructive Pulmonary Disease, NHLBI/WHO Global Initiative for Chronic Obstructive Lung Disease (GOLD) Workshop Summary. Am J Respir Crit Care Med 163:1256–1276.

NIOSH. 2002. NIOSH hazard review. Health effects of occupational exposure to respirable crystalline silica. Cincinnati, OH: US Department of Health and Human Services, Centers for Disease Control and

Prevention, National Institute for Occupational Safety and Health, DHHS (NIOSH). Publication No. 2002-129.

Ohar J, Sterling DA, Bleeker E, Donohue J. 2004. Changing patterns of asbestos-induced lung disease. Chest 125:744–753.

Oliver LC, Misracle-McMahill H. 2006. Airway disease in highway and tunnel construction workers exposed to silica. Am J Ind Med 49:983–996.

Oxman AD, Muir DCF, Shannon HS, Stock SR, Hnizdo E, Lange HJ. 1993. Occupational dust exposure and chronic pulmonary disease. Am Rev Respir Dis 148:38–48.

Peretz C, Goren A, Smid T, Kromhout H. 2002. Application of mixed-effects models for exposure assessment. Ann Occup Hyg 46:69–77.

Pronk A, Preller L, Raulf-Heimsoth M, Jonkers IC, Lammers JW, Wouters IM, Doekes G, Wisnewski A, Heederik D. 2007. Respiratory symptoms, sensitization, and exposure response relationships in spray painters exposed to isocyanates. Am J Respir Crit Care Med 176:1090–1097.

Ruston L. 2007. Chronic obstructive pulmonary disease and occupational silica exposure. Rev Environ Health 22:255–272.

Sandford AJ, Silverman EK. 2002. Chronic obstructive pulmonary disease 1: Susceptibility factors for COPD the genotype–environment interaction. Thorax 57:736–741.

SAS Institute, Inc. 2004. SAS, Version 9. Cary, NC: SAS Institute, Inc.

Swanney MP, Ruppel G, Enright GPL, Pedersen OF, Crapo RO, Miller MR, Jensen RL, Falaschetti E, Schouten JP, Hankinson JL, Stocks J, Quanjer PH. 2008. Using the lower limit of normal for the FEV_1/FVC ratio reduces the misclassification of airway obstruction. Thorax 63:1046–1051.

Teschke K, Spierings J, Marion SA, Demers PA, Davies HW, Kennedy SM. 2004. Reducing attenuation in exposure–response relationships by exposure modeling and grouping: The relationship between wood dust exposure and lung function. Am J Ind Med 46:663–667.

Tielemans E, Kupper LL, Kromhout H, Heederik D, Houba R. 1998. Individual-based and group-based occupational exposure assessment: Some equations to evaluate different strategies. Ann Occup Hyg 42:115–119.

Trupin L, Earnest G, San Pedro M, Balmes JR, Eisner MD, Yelin E, Katz PP, Blanc PD. 2003. The occupational burden of chronic obstructive pulmonary disease. Eur Respir J 22:462–469.

Tüchsen F, Hannerz H. 2000. Social and occupational differences in chronic obstructive lung disease in Denmark, 1981–1993. Am J Ind Med 37:300–306.

Vermeulen R, Li G, Lan O, Dosemeci M, Rappaport SM, Bohong X, Smith MT, Zhang L, Hayes RB, Linet M, Mu R, Wang L, Xu J, Yin S, Rothman N. 2004. Detailed exposure assessment for a molecular epidemiology study of benzene in two shoe factories in China. Ann Occup Hyg 48:105–116.

Welch L, Ringen K, Dement J, Takaro T, McGowan W, Chen A, Quinn P. 2004. Screening for beryllium disease among construction trade workers at Department of Energy nuclear sites. Am J Ind Med 46:207–218.