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Restrictive Spirometry Pattern among Construction Trade Workers

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Short Title: Restriction Risks in Construction

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ABSTRACT

Background: Spirometry-based studies of occupational lung disease have mostly focused on obstructive or mixed obstructive/restrictive outcomes. We wanted to determine if restrictive spirometry pattern (RSP) is associated with occupation and increased mortality.

Methods: Study participants included 18,145 workers with demographic and smoking data and repeatable spirometry. The mortality analysis cohort included 15,445 workers with known vital status and cause of death through December 31, 2016. Stratified analyses explored RSP prevalence by demographic and clinical variables and trade. Log-binomial regression models explored RSP risk factors while controlling for important confounders such as smoking, obesity, and comorbidities. Cox regression models explored mortality risk by spirometry category.

Results:

Prevalence of RSP was very high (28.6%). Mortality hazard ratios for RSP were 1.50 for all causes, 1.86 for cardiovascular diseases, 2.31 for respiratory diseases, and 1.66 for lung cancer. All construction trades except painters, machinists and roofers had significantly elevated risk for RSP compared to our internal reference group. RSP was significantly associated with both parenchymal and pleural changes seen by chest x-ray.

Conclusions: Construction trade workers are at significantly increased risk for

RSP independent of obesity. Individuals with RSP are at increased risk for all-cause mortality as well as mortality attributable to respiratory diseases, cardiovascular diseases, and lung cancer. RSP deserves greater attention in occupational medicine and epidemiology.

KEY WORDS: restrictive spirometry pattern, construction trades, parenchymal, pleural, mortality.

INTRODUCTION

A restrictive respiratory defect is characterized by a reduction in total lung capacity (TLC) below the lower limit of normal (LLN) and a normal ratio of forced expiratory volume in one second (FEV_1) to vital capacity (VC) (FEV_1/VC).[1] Measurement of TLC by body plethysmography or other techniques (helium wash-in or nitrogen wash-out) is expensive and time consuming and not generally practical for large population-based surveillance programs or epidemiological studies. Additionally, slow VC determinations are not normally made during routine spirometry; therefore, forced vital capacity (FVC) is typically substituted for VC in the ratio estimate (FEV_1/FVC) to define spirometric restriction.[2] Spirometric restriction has been defined in various ways in the literature based on FEV_1, FVC, and FEV_1/FVC measurements.[3-7] A commonly used epidemiological definition of restriction is a FVC below LLN in the presence of a normal FEV_1/FVC. Restrictive spirometry pattern (RSP) has become the term of art to describe this condition.[8]

Estimated RSP prevalence in the U.S. based on NHANES data (2007-2010), range from 3.5% among those in the age category 20-29 years to a high of 9.0% among those 60-69 years of age.[9] Globally, RSP prevalence varies greatly, ranging from approximately 7 to 20% among adults in most population-based studies; however, prevalence as high as 48.7% has been observed among females living in The Philippines in the Burden of Disease Study.[3,7,10-17] Although not observed in all studies, common correlates and risk factors for RSP relative to those with normal spirometry include abnormal body mass index (BMI), older age, smoking, and a history of asthma, diabetes, hypertension, or cardiovascular disease.[7,12,15,18] RSP is associated with increased respiratory symptoms, especially dyspnea, and decreased health-related quality of life.[7,19] Individuals with RSP are at increased risk of mortality from all causes, respiratory diseases, and cardiovascular diseases compared to those with normal spirometry.[10,15,16,18] Strong evidence exists for an increased risk of lung cancer among those with RSP independent of smoking.[20,21]

Workplace exposures to substances causing fibrotic interstitial lung diseases (e.g. asbestos, silica, coal mine dust, and other organic and inorganic dusts) are associated with RSP.[9,22,23] Asbestos-related pleural plaque or diffuse pleural thickening are also associated with RSP.[23-27] Among ever smokers, the prevalence of interstitial lung abnormalities by computed tomography (CT) has been noted to be higher among those with RSP relative to those with normal spirometry.[28,29]

The current study investigated RSP in a population of predominately construction trade workers participating in a medical screening program spanning over 25 years. This worker population experienced significant but variable occupational exposures to vapors, gases, dusts, and fumes (VGDF) and has demonstrated increased risk of interstitial and pleural abnormalities by chest x-ray[30], chronic obstructive pulmonary disease (COPD) by spirometry[31,32], and mortality due to respiratory diseases and lung cancer.[33] While our prior studies have shown high risk from obstructive and mixed obstructive/restrictive airways disease, we have never examined RSP alone.

The objectives of this study were to determine if RSP is associated with occupation and mortality. Secondarily, we evaluated if application of recently developed Global Lung Function Initiative (GLI) reference equations [34,35] provided a stronger basis for RSP associations with occupation and mortality than NHANES III prediction equations. [36] Analyses included cross-sectional estimates of RSP prevalence stratified by selected demographic and clinical characteristics and multivariate analyses that investigated associations and risk factors for RSP. Longitudinal analyses assessed associations of all-cause, respiratory disease, cardiovascular disease, and lung cancer mortality with RSP.

MATERIALS AND METHODS

Screening Program and Medical Protocol

Prior reports have described the origin and development of the Building Trades National Medical Screening Program (BTMed) as well as the work history and medical components.[30,37-40] Briefly, BTMed is an occupational medical screening program for construction trades workers previously employed in USA nuclear weapons facilities engaged in manufacturing, research and development, and more recently decontamination and demolition. The program started medical screening examinations at three large Department of Energy (DOE) sites in 1996 and 1997 and was subsequently expanded to 35 sites throughout the United

States. Participation in the BTMed is voluntary and without cost to workers. Workers potentially eligible for participation are identified through multiple sources including union rosters, contractor records where available, media advertisement, and presentations at worker meetings. BTMed operates a website (http://www.btmed.org) to provide workers with information about the program, instructions for participation, and health information. Ten outreach offices are located in regions with major DOE sites. In addition to the initial examination, workers are eligible for follow-up examinations every three years. Since inception BTMed has completed 44,000 medical screening examinations (61% initial and 39% follow-up examinations).

The BTMed protocol includes a detailed work history interview followed by medical examinations performed by local medical providers who meet credentialing requirements and adhere to a detailed protocol. The work history interview is conducted in person or by telephone by trained interviewers, most of whom are retired trade and craft workers. The occupational history is entered directly into the BTMed database by the interviewers. The work history documents periods of employment and jobs held at DOE sites and non-DOE sites, frequency of performing or working near high-hazard work tasks, such as sand blasting or asbestos insulation application or removal, frequency working with or around high-hazard materials, and work in buildings or areas associated with potential exposures to hazardous materials or where known exposure incidents or emergencies occurred.[38]

The BTMed 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;[41,42] and spirometry. The respiratory history and symptom questionnaire was adapted from the American Thoracic Society (ATS) DLD-78 questionnaire.[43] All participating medical facilities agreed to obtain spirometry according to ATS standards.[38]

While the medical examinations are performed by provider under contract to BTMed, the program has quality assurance procedures that apply to each exam: the providers' credentials are verified; providers follow a detailed protocol; and each exam is reviewed by a team of expert, trained nurses supported by occupational medicine specialists at the University of Maryland School of Medicine. Each spirometry test performed involves a minimum of three spirograms which are reviewed for reproducibility between efforts.

Study Populations, Case Definitions, and Risk Factors

Cross-sectional Analyses

The study population for cross-sectional analyses of RSP prevalence and risk factors consisted of 18,145 workers completing one or more BTMed examinations through March 2022. Each worker's most current examination meeting the following criteria was selected: 1) not missing demographic data (age, race, sex, height, weight, and smoking history); and 2) spirometry with a minimum of three recorded expiratory efforts and reproducibility of FVC and FEV_1 of 0.2 liters or less.[44]

While the focus of this study was RSP, cross-sectional prevalence of obstructive, restrictive, and mixed obstructive/restrictive spirometric patterns are presented to provide a full picture of respiratory impairment in this worker population. Spirometry results were classified based on spirometry without bronchodilation. The American Thoracic Society/European Respiratory Society (ATS/ERS) Task Force[45] recommends identification of obstruction based on an FEV_1/FVC ratio below the LLN to avoid age-related misclassification associated with use of a fixed FEV_1/FVC ratio.[46-49] In the main analyses, predicted spirometry measures used the prediction equations for the U.S. population based on NHANES III data consistent with recommendations for evaluation of occupational cohorts.[36,50,51] For Asian-Americans, a correction factor of 0.88 was applied to the reference values for Whites to calculate the predicted and LLN for FEV_1 and FVC.[52] In secondary analyses of RSP, Global Lung Function Initiative (GLI) reference equations were used to define predicted LLN thresholds for the FEV_1/FVC ratio and FVC.[34,35] Spirometry results were classified into the following mutually exclusive categories.[53]

- Obstruction: FVC ≥ LLN and FEV_1/FVC < LLN.
- Restriction: FVC < LLN and FEV_1/FVC ≥ LLN.
- Mixed Obstruction/Restriction: FVC < LLN and FEV1/FVC < LLN.

Posterior-anterior (P-A) chest radiographs, classified according to ILO criteria using NIOSH B-readers, were available for 17,988 (99.1%) workers included in the cross-sectional analyses. A parenchymal abnormality was defined as a profusion score of 1/0 or greater for any shape or size of small opacity. Any pleural abnormality was defined as presence of unilateral or bilateral pleural thickening consistent with asbestos exposure. Severity of both parenchymal and pleural abnormalities was further defined for more detailed analyses. Parenchymal abnormalities were further classified into profusion score categories (<1/0, 1/0 - 2/2, and > 2/2) and pleural abnormalities were classified by severity of pleural plaque and diffuse pleural thickening using a scoring system previously described and adapted for use within this worker population.[54,55] Circumscribed pleural thickening and localized pleural thickening, with or without calcification, were classified as pleural plaque. Separate severity indices for pleural plaque and diffuse pleural thickening were calculated. The possible severity scores for these indices ranged from 0 (none) to 44 for pleural plaque and 0 (none) to 38 for diffuse pleural thickening.

BMI (weight in kilograms divided by height in meters squared) was calculated using height and weight measurements recorded at examination. Histories of physician-diagnosed hypertension, cardiovascular disease, diabetes, asthma, chronic bronchitis, or emphysema were taken from the medical history.

Respiratory symptoms of cough, phlegm, dyspnea, and wheeze were defined using the respiratory symptom questionnaire data based on the following criteria:

- Chronic Cough -- “Yes” to “Do you usually have a cough?” and “Yes” to “Do you usually cough like this on most days for three consecutive months or more during the year?”
- Chronic 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.
- Wheeze - “Yes” to “Does your chest sound wheezy or whistling most days or nights”.

In addition to dichotomous classification for dyspnea, the Modified Medical Research Council (mMRC) dyspnea scale was used to classify dyspnea by severity, with a range of 0 (none) to 4 (severe dyspnea).[56]

Smoking status and pack-years were taken from the participant reported medical and respiratory histories. A history of having smoked was based on a ‘Yes’ response to the question – ‘Have you ever smoked cigarettes? (NO means less than 20 packs of cigarettes or 12 oz. of tobacco in a lifetime or less than 1 cigarette a day for 1 year.)’.

Exposures to asbestos, silica, welding and cutting, and organic solvents are frequently reported by construction trade workers in this population. Using data from the occupational history, qualitative exposure indices were developed based on worker reported frequencies of performing tasks associated with exposures of interest using methods and procedures previously described.[38] Additional information concerning development of the exposure indices is provided in the Supplemental Materials.

Mortality by Spirometry Baseline Category

Longitudinal analyses investigated all-cause, cardiovascular disease, respiratory disease, and lung cancer mortality in relation to spirometry category (normal, restriction, obstruction, mixed) at baseline BTMed examination. The mortality study population included workers with an initial BTMed examination through December 30, 2016 meeting the following criteria: 1) not missing demographic data (age, race, sex, height, weight, and smoking history); and 2) spirometry with a minimum of three recorded expiratory efforts and reproducibility of FVC and FEV_1 of 0.2 liters or less.[44] Spirometry classifications and risk factors for these analyses were the same as previously described for the cross-sectional analyses. Vital status and causes of death from the most recent mortality update of this population were used.[33] The final mortality analysis cohort included 15,445 workers with known vital status and cause of death through December 31, 2016. Causes of death were coded according to the tenth revision of the International Classification of Diseases (ICD-10). ICD-10 codes I00–I99 were classified as cardiovascular diseases, ICD-10 codes J00-J99 were classified as respiratory diseases, and ICD-10 codes C33-C34 were classified as lung cancer.

Statistical Analyses

Cross-sectional Analyses

Demographic and clinical characteristics of the study population by spirometry category were described and compared. Risk factor prevalence values (%) or mean values ± standard errors of the mean (SE) for continuous variables were calculated. Continuous variables were compared by Analysis of Variance (ANOVA). Wilcoxon rank-sum tests were employed for comparing continuous variables that departed significantly from a normal distribution. Categorical variables were compared using a chi-square test of general association.

Stratified analyses were used to explore RSP prevalence by demographic and clinical risk factors.

Risk factors for RSP relative to normal spirometry were investigated using multivariate log-binomial regression.[57,58] Regression analyses were restricted to 15,699 workers with normal spirometry or RSP and data for all model covariates. Model covariates included age, gender, race/ethnicity (Caucasian, African American, Hispanic, All Other), BMI category (underweight, normal, overweight, obese), smoking status (current, former, never), smoking pack-years, chest x-ray parenchymal profusion category (< 1/0, 1/0-1/2, and ≥ 2/1), pleural plaque severity index category (none, ≤6, and >6), diffuse pleural thickening severity index category (none, none, ≤4, and >4), and indicator variables for comorbidities (hypertension, diabetes, and cardiovascular disease).

RSP prevalence for all construction trade groups (i.e. all construction trades collectively) and prevalence by specific trade group were estimated. Workers were classified by the trade longest held, and only 3.8% worked in more than one trade. Trade-specific results were estimated only for construction trade groups with at least 100 participants *and* a minimum of 10 RSP cases for statistical stability of point estimates.

Multivariate analyses explored RSP risks for all construction trades and by construction trade group using an internal reference group of individuals employed in administrative, scientific, or security jobs. Prevalence odds-ratios for RSP relative to normal spirometry were estimated using log-binomial models that adjusted for age, sex, race/ethnicity, BMI, and smoking (status and pack-years), and comorbidities (hypertension, diabetes, and cardiovascular disease). Respiratory symptoms and chest radiograph covariates were not included in the models for risk by construction trade as these covariates are likely in the causal pathway between construction trade exposures and RSP.

In addition to analyses of all RSP by construction trade, additional analyses investigated the risk of moderate to severe restriction. Moderate to severe restriction was defined as having an FVC < LLN, FEV1/FVC ≥ LLN, and FEV_1 < 70% predicted.[9,50]

Mortality by Spirometry Category

Cox proportional hazard models were used to investigate mortality from all causes, respiratory diseases, cardiovascular disease, and lung cancer for workers with obstruction, restriction, or mixed obstruction/restriction relative to workers with normal spirometry. All Cox models used age as the time scale and adjusted for sex, race/ethnicity, baseline BMI category, smoking category at baseline (current, former, and never), smoking pack-years at baseline, baseline spirometry category, and baseline comorbidities (hypertension, diabetes, and cardiovascular disease). Cause-specific competing risk models were used for cardiovascular diseases, respiratory diseases, and lung cancer.[59] Cox model proportionality was assessed using regression diagnostics available in SAS Version 9.4 based on Schoenfeld residuals.

Sensitivity Analyses

We conducted several sensitivity analyses to evaluate robustness of our findings, the results of which are discussed and presented in the Supplemental Materials.

To determine RSP risk factors independent of BMI, we conducted sensitivity analyses by restricting the models to only those with normal BMI or overweight. To determine if presence of parenchymal changes could impact relative risk estimates for pleural plaque and diffuse pleural thickening, we performed sensitivity analyses wherein workers with parenchymal changes with profusion score ≥ 0/1 were omitted. To determine if use of our reference group as the baseline to establish relative risks led to an underestimate of relative risk because of elevated RSP prevalence in the reference group, we conducted sensitivity analyses wherein we limited the reference population to a much smaller group of 208 workers (33 RSP cases) in administrative/support occupations, likely our least occupationally exposed group. Finally, sensitivity analyses were conducted using each individual's initial examination rather than the most recent examination.

All statistical analyses were performed using SAS Version 9.4.[59] P-values < 0.05 were considered statistically significant, without adjustment for multiple comparisons.

Ethics Review and Approval

All study procedures and materials were reviewed and approved by the Central Department of Energy Institutional Review Board (CDOEIRB). All participants provided informed consent. Use of data for the current analyses was approved by the CDOEIRB (DOE000826, approved December 14, 2022).

RESULTS

Cross-sectional Analyses

A total of 18,145 workers were included in the cross-sectional analyses with the following spirometry classifications: 1251 (6.9%) obstruction, 5063 (27.9%) restriction, and 1195 (6.6%) mixed obstruction/restriction. Characteristics of the study population by spirometry category are provided in Table 1 as well as statistical comparisons of those with RSP to those with normal spirometry. Workers with RSP were older than those with normal spirometry, although the absolute difference (2.2 years) was relatively small. Compared to workers with normal spirometry, workers with RSP were significantly more likely to be Caucasian (86.4%) and male (93.4%). Workers with RSP were significantly more likely to have respiratory symptoms of cough (33.4%), phlegm (30.6%), dyspnea (49.7%), and wheeze (29.8%) compared to individuals with normal spirometry. Participants with RSP reported significantly more frequent histories of asthma (15.2%), chronic bronchitis (11.5%), and emphysema (7.0%); and a history of physician diagnosed hypertension (64.6%), diabetes (30.2%), and cardiovascular disease (48.7%) compared to those with normal spirometry. Mean BMI was significantly increased among those with RSP (31.5) compared to participants with normal spirometry (29.6). Smoking, both current and former), was significantly more prevalent among those with RSP compared those with normal spirometry. The distribution of chest x-ray ILO B-reader categories was significantly different for those with RSP versus those normal, with a higher prevalence in each category of abnormality (pleural 13.6%, parenchymal 2.2%, and both pleural and parenchymal 3.2%) among those with RSP. Absolute differences in mean years of DOE work or work in construction trades across spirometry categories were relatively small and, on average, workers had spent about half their working careers on DOE sites.

Prevalence of RSP stratified by demographic and clinical characteristics is provided in Table 2. RSP prevalence was relatively high (20.5%) among those ≤45 years of age, increased through the age category 60-74 years (30.1%) and decreased slightly among workers older than 75 years (29.8%). The prevalence among males (28.4%) was higher than females (22.6%). The highest prevalence of RSP by race/ethnicity was 28.2% among Hispanics and lowest among African-Americans (23.6%). Prevalence of RSP among current smokers, former smokers, and never smokers was 26.8%, 29.9%, and 25.9%, respectively. By BMI category, RSP prevalence was highest among those underweight (35.6%) or obese (35.2%) compared to 19.6% among workers with normal BMI. RSP prevalence increased with increasing B-read parenchymal profusion category, pleural plaque severity index, and diffuse pleural thickening index. Among those with a parenchymal profusion score 2/1 or greater, the prevalence of RSP was 54.6% and workers with a diffuse pleural thickening index >4 had a RSP prevalence of 59.7%.

Table 2 also provides results of the multivariate log-binomial model showing associations with RSP compared to normal spirometry. Statistically significant reduced prevalence-ratios (PR) were observed for females relative to males (PR=0.90, 95% CI=0.81-0.99) and among African-Americans (PR=0.83, 95% CI=0.76-0.90) compared to Caucasians. Increasing age was associated with significantly increased risk, with the highest PR of 1.28 (95% CI=1.14-1.43) among those 60-74 years of age compared to those ≤ 45 years of age. Significantly increased RSP risk was observed for BMI underweight (PR=1.84, 95% CI=1.56-2.05) or obese (PR=1.37, 95% CI=1.27-1.47) compared to normal BMI. Cigarette smoking was associated with increased risk among current smokers (PR=1.28, 95% CI=1.19-1.38) and former smokers (PR=1.07, 95% CI=1.02-1.14), with increasing risk by increasing smoking pack-years. RSP was significantly associated with a reported physician diagnosis of hypertension (PR=1.10, 95% CI=1.05-1.16), diabetes (PR=1.35, 95% CI=1.28-1.41), and cardiovascular disease (PR=1.27, 95% CI=1.21-1.33). The PR for a B-read parenchymal profusion category ≥ 2/1 was significantly increased (PR=1.22, 95% CI=1.08-1.31). Severity indices for pleural plaque and diffuse pleural thickening were significantly associated with RSP.

RSP prevalence and model adjusted PR by construction trade are presented in Table 3, wherein workers in construction trades are compared to a lesser occupationally exposed reference population of workers in administrative, scientific, and security jobs. Data for both all RSP and moderate-severe RSP are provided in this table. While the prevalence of RSP in the reference category was high (21.5%), prevalence among most individual construction trades, ranged from 21.3% among machinists to 35.3% among asbestos workers/insulators. The log-binomial model found significantly increased risk of all RSP among all construction trades combined (PR=1.32, 95% CI=1.17-1.51) and for 11 of 16 individual construction trade groups; with the highest risk among asbestos workers/insulators (PR=1.61, 95% CI=1.37-1.88). The PRs for moderate to severe RSP were even higher for each construction trade with over a 2-fold risk among asbestos workers/insulators. Figures 1 and 2 provide forest plots of all RSP and moderate-severe RSP prevalence-ratios and 95% confidence intervals by construction trade ranked from highest to lowest.

Construction trade workers experience many common exposures either by directly performing tasks or while working in the vicinity of tasks being performed by other crafts. Qualitative exposures indices by trade group for asbestos, silica, welding/cutting, and organic solvents are provided in the Supplemental Materials (Figures S10-S13). While trades vary with regard to specific exposures, all experience significant mixed VGDF exposures compared to our internal reference population of individuals in administrative, scientific, or security jobs.

Mortality by Spirometry Category

The mortality analyses included 15,455 workers with a median follow-up time of 7.5 years (interquartile range 3.7-10.8). The mean duration of construction trade work was 21.5 (SE=0.12) years and the mean years of work on DOE sites was 9.3 (SE=0.08) years. All models adjusted for age, sex, race/ethnicity, baseline BMI, smoking at baseline (current, former, and never; pack-years), baseline spirometry category, and comorbidities (hypertension, diabetes, and cardiovascular disease) at baseline.

Hazard ratios for each mortality outcome by spirometry category at cohort entry are presented in Table 4 and cumulative incidence plots by outcome are provided in the Supplemental Materials (Figures S1-S4). Compared to those with normal spirometry at cohort entry, workers with obstruction, restriction, or mixed obstruction/restriction were at significantly increased risk for mortality due to all causes, cardiovascular diseases, respiratory diseases, and lung cancer. The HR for workers with RSP were 1.50 (95% CI=1.37-1.64) for all causes, 1.86 (95% CI=1.58-2.29) for cardiovascular diseases, 2.31 (95% CI=1.76-3.03) for respiratory diseases, and 1.66 (95% CI=1.21-2.28) for lung cancer. A separate model (not shown) for COPD mortality as a sub-category of all respiratory diseases found a HR of 2.78 (95% CI=1.82-4.26) among those with RSP. Workers with mixed obstruction/restriction were at very high risk for all categories of mortality, with HR over 2.00 for each cause and HR over 4 for respiratory disease and lung cancer. Kaplan-Meier all-cause mortality survival curves by spirometry category are provided in Figure 3, demonstrating similar overall survival for those with restriction or obstruction and much worse survival for those with mixed spirometry pattern.

Sensitivity Analyses

Confounding by BMI

While we controlled for BMI in the multivariate models of RSP, we conducted sensitivity analyses by restricting the models to only those with normal BMI or overweight. Results of the overall associations are provided in the Supplemental Materials (Table S3). While the reduced model had lower statistical power, the PR point estimates for remaining covariates were substantially the same as the primary BMI adjusted models. Notably, increased risk remained for parenchymal changes, pleural plaque, and diffuse pleural thickening. A similar model limiting by BMI was developed for risk by trade group and resulting risk estimates by trade group are provided in the Supplemental Materials (Figure S7). The PR estimates and trends by trade were comparable to the main analyses, suggesting adequate control for confounding by BMI in the main analyses.

Coexistence of Parenchymal and Pleural Changes

Some workers (n=161) with pleural changes also had parenchymal changes with a profusion score ≥ 1/0 (Table 1). While our models adjusted for parenchymal profusion score, residual confounding by presence of parenchymal changes could impact relative risk estimates for pleural plaque and diffuse pleural thickening. To address this issue, we performed sensitivity analyses wherein workers with parenchymal changes with profusion score ≥ 0/1 were omitted. These results are provided in the Supplemental Materials (Table S4). Omitting workers with parenchymal changes altered the PR point estimates for pleural plaque and diffuse pleural thickening relatively little, supporting results of the primary analyses based on larger numbers and greater statistical power.

Choice of Reference Category for Risk by Trade

RSP relative risk estimates by construction trade group were based on an internal referent population of workers. However, as noted previously, the prevalence of RSP in our internal referent population of workers in administrative, scientific, or security jobs was high (21.5%) compared to published data from NHANES, suggesting that the risk of RSP among construction workers was underestimated in our main analyses. We conducted sensitivity analyses wherein we limited the reference population to a much smaller group of 208 workers (33 RSP cases) in administrative/support occupations, likely our least occupationally exposed group. The resulting relative risks of RSP by construction trade are provided in the Supplemental Materials (Figure S8), demonstrating higher risks by trade compared to our main analyses, although the PRs have wider confidence intervals. Overall, these sensitivity analyses support the conclusion that RSP among construction trade workers was underestimated in our primary analyses.

Secondary Analyses Using GLI 2012 Prediction Equations

The overall prevalence of RSP was 18.3% using the GLI 2012 prediction equations compared to 27.9% in the primary analyses based on NHANES III predictions. Detailed results using GLI 2012 predictions are provided in the Supplemental Materials. Table S1 provides results of the multivariate log-binomial model showing associations with RSP compared to normal spirometry. While the overall prevalence of RSP was lower using GLI 2012, the associations of RSP with BMI, smoking, parenchymal and pleural chest x-ray changes, and comorbidities (hypertension, diabetes, and cardiovascular disease) were comparable to the main analyses using NHANES III predictions. However, using GLI 2012 predictions, RSP PRs were not significantly different by gender or race/ethnicity. Relative risk estimates for construction trades using GLI 2012 predictions were slightly higher for most trades compared to the main analyses using NHANES III predictions (Figure S1).

Kaplan-Meier survival curves by GLI-2012 spirometry categories are shown in Figure S2, demonstrating patterns very comparable to the main analyses. Finally, mortality hazards ratios for all-causes, cardiovascular disease, respiratory disease, and lung cancer by GLI 2012 spirometry category are provided in Table S2. HR for all outcomes except cardiovascular disease were higher using GLI 2012 predictions. However, HRs for cardiovascular disease among those with restriction (HR=1.81, 95% CI=1.53-2.15) or mixed spirometry (1.98, 95% CI=1.51-2.60) were highly elevated and statistically significant using GLI 2012 predictions.

Analyses Using Data from Only Initial Examinations

Main cross-sectional analyses were based on each worker's most current BTMed examination (53% initial and 47% follow-up). Sensitivity analyses were performed using each worker's initial examination and the same statistical models for associations with RSP and risks by trade group as the main analyses. Results are provided in the Supplemental Materials (Table S5 and Figure S9). All analyses using only initial exams were comparable to the main analyses, further supporting robustness of study findings.

DISCUSSION

The objectives of this study were to determine if RSP is associated with occupation and mortality. We found that RSP was significantly associated with most construction trades, even after adjustment for other known risk factors for restrictive lung disease, such as obesity, smoking, hypertension, diabetes, and cardiovascular disease. Furthermore, we found that spirometric restriction on baseline assessment is associated with a significantly higher risk for mortality due to all causes, cardiovascular diseases, respiratory diseases, and lung cancer.

Overall Results

The overall prevalence of RSP in this largely construction worker population was very high (27.9%). Prevalence of RSP by age category compared to NHANES estimates for the U.S. population are provided in Table 5.[9] Compared to either 1988-1994 or 2007-2010 NHANES data, the prevalence of RSP in this population was much higher. Notably, the prevalence of RSP in our reference group for risk estimates by construction trade group was much higher than NHANES.

RSP risk factors and associations identified in multivariate analyses of prevalence were largely consistent with results from published population-based analyses and included smoking, BMI (underweight and obese), and comorbidities (hypertension, diabetes, and cardiovascular disease).[12,15] We observed reduced crude RSP prevalence among females and a slightly reduced PR for females compared to males in the adjusted model. Risk of RSP among females compared to males has varied among published studies with some studies showing a higher risk[11,12] We were unable to determine whether less occupational VGDF exposure among females accounted for this reduction in RSP risk; however, we noted that a greater proportion of females were employed in non-construction jobs (38.2%) compared to males (16.2%). Additionally, in the models for risk by construction trade, the PR for females was not significantly reduced relative to males (PR=0.96, 95% CI=0.86-1.06). Addition of trade in the models likely served as a surrogate of occupational exposures.

Trends of RSP prevalence and model-adjusted risk with increasing age also have been variable in the literature.[3,12,15] and our multivariate prevalence analyses using LLN case definitions observed a relatively modest trend of increasing risk with increasing age. Some studies have used fixed ratio criteria to define RSP, which may have over-estimated prevalence in older age categories and exaggerated the trend with age.[9,50,60] Observed associations of RSP with obesity and dyspnea are consistent with the body of published literature, as previously reviewed.

The observed associations between RSP and chest radiographic changes by ILO criteria are consistent with the published literature.[24-26,55,61,62] We observed increased RSP prevalence with increasing ILO profusion scores as well as increasing indices of pleural plaque and diffuse pleural thickening severity. The multivariate analyses provided additional support for the association between pleural and parenchymal chest x-ray changes and RSP. Sensitivity analyses suggested that RSP associations with pleural plaque and diffuse pleural thickening were not confounded by parenchymal changes observable by chest x-ray or by BMI.

While our results support increased risk of RSP among workers with parenchymal or pleural changes, only 19.3% of individuals with RSP had pleural or parenchymal chest x-ray changes consistent with ILO criteria. Compared to chest radiographs alone, other studies using CT imaging have found a much higher prevalence of interstitial and pleural changes in an occupationally exposed population of nuclear weapons workers.[63] The overall attribution of restrictive impairment to interstitial and pleural changes may be considerably higher than is evident using chest radiographs alone.

We observed significantly increased risk of RSP among construction trade workers collectively and among most specific trade groups relative to an internal group of lesser occupationally exposed workers. Estimates of relative risk by construction trade were even higher for moderate-severe RSP. The internal reference population was not free of occupational VGDF exposures and the prevalence of RSP in this group was considerably higher than NHANES estimates for the US population. This observation and the sensitivity analyses using a smaller number of likely lesser exposed individuals support the conclusion that RSP risk among construction trade workers was significantly elevated and underestimated.

Consistent with other published studies, we observed that workers with RSP were at significantly increased risk of all-cause mortality as well as mortality due to respiratory diseases, cardiovascular disease, and lung cancer.[7,12,15,18,20,21] Workers with mixed obstruction/restriction were at even greater mortality risk for each cause studied.

The overall prevalence of RSP in the secondary analyses using GLI 2012 prediction equations was lower (18.3%) and consistent with other comparisons of NHANES III and GLI 2012 results.[64] Using the GLI 2012 predictions, there were no significant differences in risk by gender or race/ethnicity; however, associations of RSP with BMI, smoking, chest x-ray parenchymal and pleural changes and comorbidities (hypertension, diabetes, cardiovascular disease) were comparable to the main analyses. Additionally, RSP risks by construction trade group were slightly higher using GLI predictions and associations of RSP with mortality for each cause category were comparable to results using NHANES III predictions. Thus, both the main analyses and the supplemental analyses support increased risk of RSP among construction trades as well as increased mortality risks among those with RSP.

Strengths and Limitations

Strengths of our study include a sizable population, large case numbers, chest radiographs read by ILO criteria to define interstitial lung disease and pleural changes, smoking histories, and good respiratory symptom and medical history data. BTMed participants are entirely volunteers and it is not possible to determine whether or what kind of bias might occur. Mortality among BTMed participants has been investigated on several occasions and overall all-cause mortality has been found to be reasonably close to that expected based on general population death rates.

A possible limitation is the case definition for RSP based on pre-bronchodilator spirometry. Most research on the effects of bronchodilation on spirometry case definitions has been with obstruction and changes in FEV_1 and have demonstrated that airway obstruction prevalence based on post-bronchodilator spirometry may be 25–35% lower than found without use of bronchodilators in population-based studies.[65] This effect is stronger in younger individuals, decreases in individuals between 60 and 74 years of age,[66] and decreases in high risk populations. A recent study among individuals at high risk for COPD found that only 9% had some reversal of airways obstruction with bronchodilators, and 60% of those still had an FEV1/FVC < 70% (the definition used in that study).[67] Generally, identified risk factors and relative risk estimates have been comparable with or without post-bronchodilator spirometry.[66] While use of pre- bronchodilator spirometry could impact RSP prevalence estimates, we expect the effects on relative risk estimates and identified RSP risk factors, including risk between construction trades, in our study would be minor.

As with nearly all epidemiological studies concerning RSP, our case definition of restrictive impairment was spirometry-based, without measures of TLC. While our RSP case definition is commonly used in large population studies, true clinical restriction is diagnosed based on reduced total lung capacity (TLC).[68,69] Measurement of TLC is normally done in a pulmonary laboratory setting, which is not practical for geographically dispersed surveillance programs such as BTMed or in large population-based epidemiological studies. A study that compared restriction by spirometry (i.e. FVC < LLN) versus measurement of TLC in older individuals found spirometry to have a sensitivity of 32%, specificity of 95%, and positive predictive value of 81%.[68] Generally, restriction case definitions based on both FVC and the FEV_1/FVC ratio, such as used in the current study, have been shown to improve the sensitivity and positive predictive value of spirometry in identifying restriction.[2,70,71] In populations with a higher prevalence of restrictive impairment, such as the current study, the spirometry-based definition may serve as a reasonable proxy of true restriction, but is still subject to misclassification, which likely dampens estimates of relative risks.

Mortality analyses were based on the underlying cause of death from death certificates, which are subject to some degree of misclassification. However, the estimates of mortality risks by spirometry category were based on internal analyses using Cox regression, which should minimize potential effects of death certificate disease misclassification on relative-risk estimates

An additional limitation is our lack of an unexposed internal reference population for estimation of relative risks by construction trade group. This limitation decreased the magnitude of relative risk estimates for construction work overall as well as work within specific construction trade groups.

The overall impact of these limitations suggests that relative risk estimates for construction trade work should be considered conservative; they are generally underestimates.

CONCLUSIONS

RSP is relatively common in the general U.S. population based on NHANES data. Construction trade workers are exposed to many substances known to cause interstitial diseases as well asbestos-related pleural plaque and diffuse pleural thickening, which are associated with RSP. Construction trade workers are at significantly increased risk for RSP independent of obesity. Individuals with RSP are at increased risk for all-cause mortality as well mortality attributable to respiratory diseases, cardiovascular diseases, and lung cancer. RSP should be considered among the health effects documented among US nuclear weapons workers. More attention should be given to RSP in occupational medicine and epidemiology.

This study used both NHANES III and GLI 2012 spirometry prediction equations and found slightly lower RSP overall prevalence but higher RSP relative-risks by trade group using the GLI 2012 predictions. GLI 2012 equations are based on considerably larger numbers of participants than NHANES III, especially for non-whites, span a higher age range, and provide a set of equations where ancestral origins are unknown or uncertain. Additional studies using GLI 2012 prediction equations in occupational studies are needed.

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Table 1: Cross-Sectional Study Population Characteristics by Spirometry Category

Parameter	Normal (N=10636)	Obstruction[1] (N=1251)	Restriction[2] (N=5063)	Mixed[3] (N=1195)	P-value[5]
Mean Age (SE)	62.2 (0.12)	63.3 (0.36)	64.4 (0.16)	66.9 (0.30)	<.001
Male Sex (%)	9681 (91.0)	1118 (89.4)	4727 (93.4)	1131 (94.6)	<.001
Caucasian Race (%)	8818 (82.9)	1081 (86.4)	4375 (86.4)	1085 (90.8)	<.001
Years at a DOE Site, Mean (SE)	9.8 (0.10)	8.6 (0.28)	10.2 (0.15)	9.0 (0.30)	.025
Years in Construction Trades, Mean (SE)	22.2 (0.15)	23.0 (0.43)	22.7 (0.21)	24.2 (0.44)	.051
Spirometry Mean (SE)					
% Predicted FVC	95.0 (0.11)	95.0 (0.36)	67.8 (0.14)	61.7 (0.36)	<.001
% Predicted FEV_1	97.3 (0.12)	74.3 (0.41)	70.5 (0.17)	44.9 (0.37)	<.001
FEV_1/FVC Ratio %	77.3 (0.06)	58.7 (0.23)	78.0 (0.10)	53.6 (0.26)	<.001
Respiratory Symptom N (%)[6]					
Cough	2577 (24.2)	509 (40.7)	1692 (33.4)	685 (55.7)	<.001
Phlegm	2435 (22.9)	524 (41.9)	1551 (30.6)	681 (57.0)	<.001
Dyspnea	2727 (25.6)	563 (45.0)	2515 (49.7)	894 (74.8)	<.001
Wheeze	1714 (16.1)	444 (35.5)	1508 (29.8)	681 (57.0)	<.001
mMRC Dyspnea Score, Mean (SE)	1.0 (0.01)	1.6 (0.05)	1.8 (0.02)	2.7 (0.04)	<.001
B-Reader Category N (%)[5]					
Pleural Changes Only	954 (9.0)	145 (11.6)	686 (13.6)	207 (17.3)	<.001
Parenchymal (≥1/0) Changes Only	164 (1.5)	32 (2.6)	109 (2.2)	28 (2.3)	
Both Pleural and Parenchymal (≥1/0)	159 (1.5)	32 (2.6)	161 (3.2)	58 (4.9)	
No B-Read Results Available	95 (0.9)	8 (0.6)	43 (0.9)	11 (0.9)	
Cigarette Smoking Status N (%)					
Current Smoker	1422 (13.4)	413 (33.0)	817 (16.1)	394 (33.0)	<.001
Former Smoker	4670 (43.9)	604 (48.3)	2526 (49.9)	659 (55.2)	
Never Smoked	4544 (42.7)	234 (18.7)	1720 (34.0)	142 (11.9)	
Smoking Pack-Years, Mean (SE)	16.0 (0.22)	33.9 (0.85)	23.2 (0.40)	42.6 (0.96)	<.001
Physician Diagnosis (N) (%)					
Asthma	945 (8.9)	283 (22.6)	770 (15.2)	360 (30.1)	<.001
Chronic Bronchitis	587 (5.5)	173 (13.8)	580 (11.5)	305 (25.5)	<.001
Emphysema	258 (2.4)	214 (17.1)	353 (7.0)	423 (35.4)	<.001

Mean BMI (SE)[7]	29.6 (0.05)	27.2 (0.15)	31.5 (0.09)	28.6 (0.18)	<.001
Hypertension History N (%)	5645 (53.1)	633 (50.6)	3271 (64.6)	719 (60.2)	<.001
Diabetes History N (%)	1735 (16.3)	160 (12.8)	1529 (30.2)	255 (21.3)	<.001
Cardiovascular Disease History N (%)	3666 (34.5)	472 (37.7)	2466 (48.7)	653 (54.6)	<.001

[1] Obstruction case definition: FVC ≥ LLN and FEV_1/FVC < LLN.
[2] Restriction case definition: FVC < LLN and FEV_1/FVC ≥ LLN.
[3] Mixed case definition: FVC < LLN and FEV1/FVC < LLN
[4] Cough, phlegm, dyspnea and wheeze defined in text.
[5] p-value comparing those with restriction to those with normal spirometry..
[6] Chest x-ray B-reader results were not available for 157 workers.
[7] BMI was missing for 60 workers.

Table 2: Prevalence and Prevalence Ratios for Restrictive Spirometry

Parameter	Parameter Category	Restriction Prevalence N(%)[1]	Adjusted Prevalence Ratio[2] (95% CI)	P-value
Gender	Men	4727 (28.4)	1.00 (Ref)	
	Women	336 (22.6)	0.90 (0.81-0.99)	.026
Age Group (Years)	≤45	256 (20.5)	1.00 (Ref)	
	45-59	1365 (25.1)	1.13 (1.01-1.27)	.043
	60-74	2424 (30.1)	1.28 (1.14-1.43)	<.001
	≥75	1018 (29.8)	1.23 (1.09-1.39)	.001
Race/Ethnicity	Caucasian	4375 (28.5)	1.00 (Ref)	
	African American	453 (23.6)	0.83 (0.76-0.90)	<.001
	Hispanic	107 (28.2)	0.93 (0.79-1.08)	.356
	All Other	128 (26.5)	0.88 (0.76-1.00)	.070
BMI	Normal (18.5-24)	600 (19.6)	1.00 (Ref)	
	Underweight (<18.5)	42 (35.6)	1.84 (1.56-2.05)	<.001
	Overweight (25-29)	1646 (23.2)	1.01 (0.94-1.10)	.771
	Obese (≥30)	2757 (35.2)	1.37 (1.27-1.47)	<.001
Cigarette Smoking Status	Never Smoker	1720 (25.9)	1.00 (Ref)	
	Current Smoker	817 (26.8)	1.28 (1.19-1.38)	<.001
	Former Smoker	2526 (29.9)	1.07 (1.02-1.14)	.011
Cigarette Smoking Pack-			1.002 (1.001-1.003)	<.001
B-Read Parenchymal	<1/0	4750 (27.5)	1.00 (Ref)	
	1/0-1/2	193 (32.1)	0.97 (0.88-1.07)	.634
	2/1 or greater	77 (54.6)	1.22 (1.08-1.31)	<.001
Pleural Plaque Severity	0 None	4331 (27.2)	1.00 (Ref)	.
	≤6 (Median)	360 (31.6)	1.10 (1.01-1.19)	.018
	>6	329 (35.6)	1.15 (1.06-1.24)	<.001
Diffuse Pleural Thickening	0 None	4869 (27.5)	1.00 (Ref)	
	≤4 (Median)	68 (45.3)	1.29 (1.18-1.43)	<.001
	>4	83 (59.7)	1.31 (1.23-1.48)	<.001
Hypertension	None	1792 (22.8)	1.00 (Ref)	
	History	3271 (31.9)	1.10 (1.05-1.16)	<.001

Diabetes	None	3534 (24.4)	1.00 (Ref)	
	History	1529 (41.6)	1.35 (1.28-1.41)	<.001
Cardiovascular Disease	None	2597 (23.9)	1.00 (Ref)	
	History	2466 (34.0)	1.27 (1.21-1.33)	<.001

[1] Restriction case definition: FVC < LLN and FEV_1/FVC ≥ LLN.
[2] Prevalence ratio comparing those with restrictive spirometry to those with normal spirometry. Log-binomial model and likelihood ratio confidence intervals. Trend test p-values for ordered categorical variables were: <0.001 for age, 0.058 for parenchymal changes, 0.67 for pleural plaque severity, and 0.002 for diffuse pleural thickening severity.

Table 3: Prevalence and Prevalence Ratios for Restrictive Spirometry Relative to Normal Spirometry by Construction Trade Group

Trade Group[1]	Number of Workers	All Restriction[2]		Moderate-Severe Restriction[3]	
		Prevalence N (%)	Prevalence Ratio (95% CI)[4]	Prevalence N (%)	Prevalence Ratio (95% CI)[4]
Administrative, Scientific or Security Workers (Reference)	822	177 (21.5)	1.00 (Ref)	69 (10.9)	1.00 (Ref)
All Construction Trades	14887	4217 (28.3)	**1.32 (1.17-1.51)**	1864 (17.9)	**1.59 (1.29-2.01)**
Asbestos Worker/Insulator	479	169 (35.3)	**1.61 (1.37-1.88)**	79 (25.6)	**2.17 (1.69-2.77)**
Boilermaker	325	103 (31.7)	**1.47 (1.20-1.77)**	45 (19.6)	**1.87 (1.34-2.57)**
Carpenter	1111	310 (27.9)	**1.33 (1.15-1.56)**	141 (18.6)	**1.67 (1.30-2.18)**
Cement or Brick Mason/Plasterer	288	74 (25.7)	**1.39 (1.10-1.72)**	42 (22.0)	**1.95 (1.38-2.71)**
Electrician	2766	785 (28.4)	**1.28 (1.12-1.47)**	307 (15.6)	**1.40 (1.11-1.79)**
Ironworker	845	210 (24.9)	1.17 (0.99-1.39)	92 (15.2)	**1.36 (1.03-1.80)**
Laborer	2341	630 (26.9)	**1.34 (1.17-1.55)**	307 (18.3)	**1.72 (1.37-2.19)**
Machinist	155	33 (21.3)	1.05 (0.75-1.41)	17 (14.7)	1.36 (0.82-2.12)
Millwright/Mechanic	355	94 (26.5)	1.19 (0.97-1.45)	44 (17.7)	**1.40 (1.00-1.94)**
Operating Engineer	1012	291 (28.8)	**1.33 (1.14-1.55)**	125 (18.0)	**1.60 (1.24-2.09)**
Other Construction-Related NEC[5]	269	85 (31.6)	**1.31 (1.06-1.60)**	38 (19.1)	**1.54 (1.08-2.15)**
Painter	490	116 (23.7)	1.19 (0.98-1.44)	42 (12.5)	1.22 (0.86-1.71)
Plumber, Steamfitter, Pipefitter	2846	826 (29.0)	**1.34 (1.17-1.54)**	370 (18.4)	**1.66 (1.32-2.11)**
Roofer	173	39 (22.5)	1.24 (0.92-1.63)	18 (16.1)	1.61 (0.98-2.50)
Sheet Metal Worker	824	252 (30.6)	**1.39 (1.19-1.62)**	109 (19.2)	**1.66 (1.28-2.19)**
Teamster	608	200 (32.9)	**1.40 (1.19-1.65)**	88 (21.8)	**1.64 (1.25-2.17)**

[1] Individual trade shown for those with 100 or more participants and 10 or more RSP cases.
[2] Restriction case definition: FVC < LLN and FEV_1/FVC ≥ LLN.
[3] Moderate to severe restriction case definition: FVC < LLN, FEV_1/FVC ≥ LLN, and FEV_1 < 70% predicted
[4] Log-binomial models adjusted for age, sex, race/ethnicity, BMI category, and smoking (status and pack-years), and comorbidities (hypertension, diabetes, and cardiovascular disease). Significant prevalence odds-ratios (p<0.05) are **bolded**.
[5] Includes other construction-related trades with too few participants for detailed analyses.

Table 4: Mortality Hazard Ratios by Spirometry Category at Cohort Entry[1]

Spirometry Category at Cohort Entry[2]	Number at Risk	All-Causes		Cardiovascular Disease[2]		Respiratory Disease[3]		Lung Cancer[3]	
		Events	HR (95%	Events	HR (95%	Events	HR (95%	Events	HR (95%
Normal	9458	1116	1.00	298	1.00	97	1.00	83	1.0
Restriction	3974	880	1.50	304	1.86	122	2.31 (1.76-	77	1.66 (1.21-
Obstruction	1077	217	1.47	55	1.42	43	2.93 (2.03-	30	1.93 (1.26-
Mixed	936	381	2.36	87	2.05	112	6.79 (5.07-	78	4.34 (3.12-

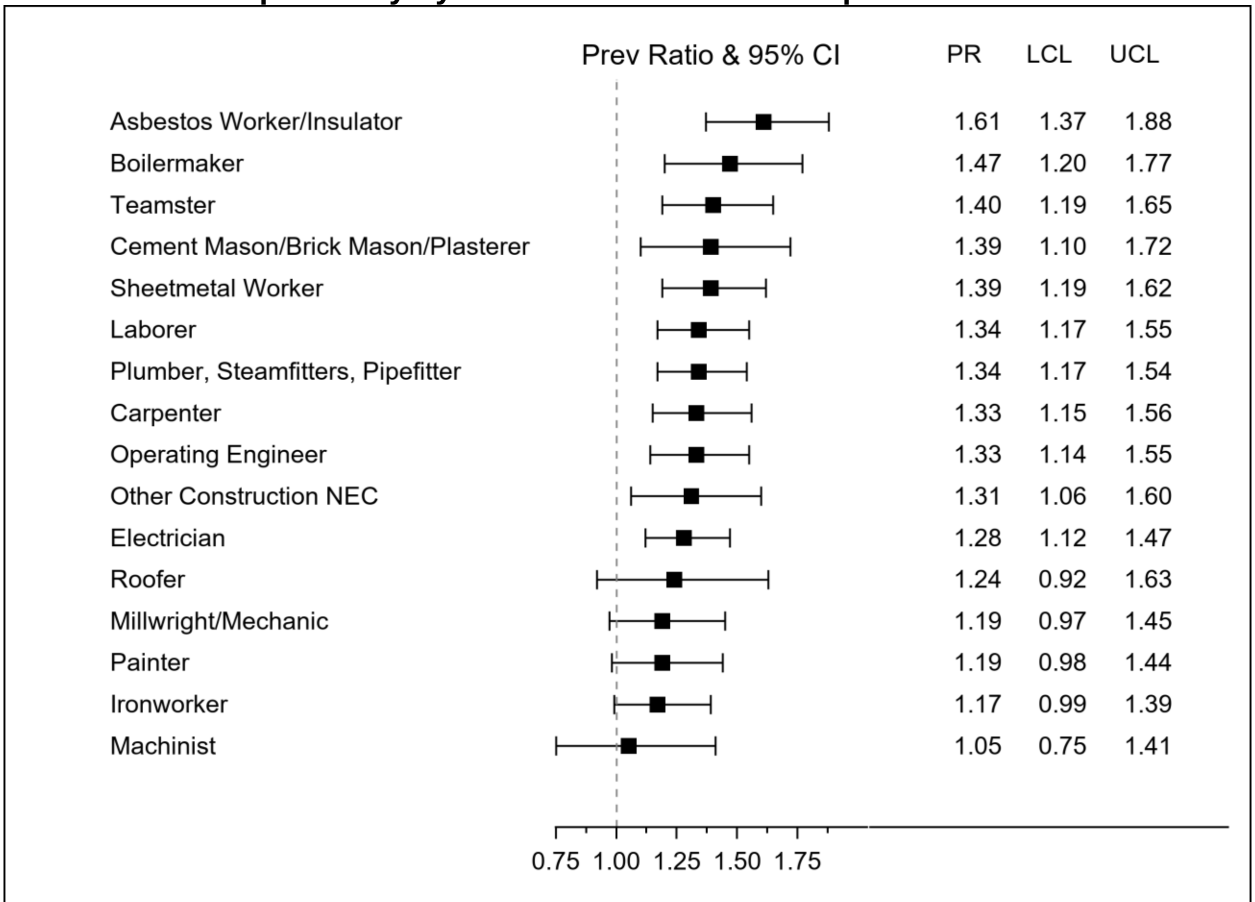
[1] Cox models adjusted for age, sex, race/ethnicity, baseline BMI, smoking at baseline (current, former, and never; pack-years), baseline spirometry category, and comorbidities (hypertension, diabetes, and cardiovascular disease) at baseline.
[2] Restriction case definition: FVC < LLN and FEV_1/FVC ≥ LLN
Obstruction case definition: FVC ≥ LLN and FEV_1/FVC < LLN
Mixed case definition: FVC < LLN and FEV_1/FVC < LLN
[3] Cause-specific competing models were used for cardiovascular diseases, respiratory diseases, and lung cancer.

Table 5: Restriction Prevalence by Age Category Compared to NHANES

Age Category (years)	US NHANES Prevalence[1,2]		Current Study Prevalence (%)[1]	
	1988-1994	2007-2010	Administrative, Scientific or Security Workers (N=822)	Construction Trade Workers (N=14887)
20-29	5.2	3.5	--[3]	--[3]
30-39	5.2	4.2	--[3]	18.8
40-49	5.7	4.9	19.2	23.5
50-59	11.6	7.0	23.3	25.7
60-69	11.2	9.0	20.9	30.1
70-69	7.9	6.9	23.7	32.0
80+	--[4]	--[4]	18.0	29.7

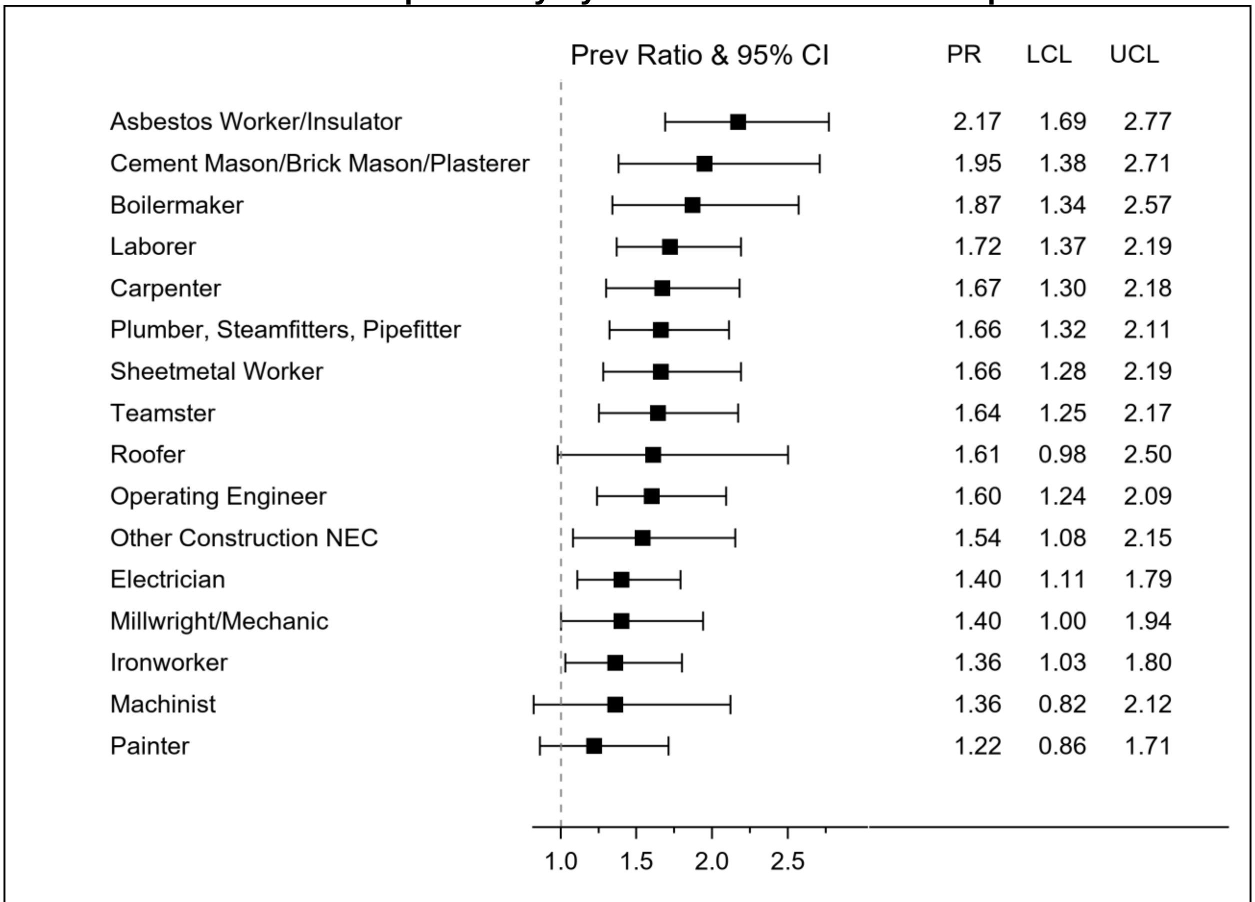
[1] Restriction case definition: FVC < LLN and FEV_1/FVC ≥ LLN
[2] Adapted from Kurth and Hnizdo, 2015
[3] Too few cases (n<5) for prevalence estimates.
[4] Kurth and Hnizdo study population included those 20-79 years of age.

Figure 1: Prevalence Ratios for Restrictive Spirometry Relative to Normal Spirometry by Construction Trade Group[1, 2]



[1] Log-binomial regression model adjusted for age, sex, race/ethnicity, BMI category, smoking (status and pack-years), and comorbidities (hypertension, diabetes, and cardiovascular disease). Reference category = workers in administrative, scientific, or security jobs.
[2] Restriction case definition: FVC < LLN and FEV_1/FVC ≥ LLN

Figure 2: Prevalence Ratios for Moderate to Severe Restrictive Spirometry Relative to Normal Spirometry by Construction Trade Group[1, 2]



[1] Log-binomial regression model adjusted for age, sex, race/ethnicity, BMI category, smoking (status and pack-years), and comorbidities (hypertension, diabetes, and cardiovascular disease). Reference category = workers in administrative, scientific, or security jobs.
[2] Moderate to severe restriction case definition: FVC < LLN, FEV_1/FVC ≥ LLN, and FEV_1 < 70% predicted.

Figure 3: All- Cause Mortality Kaplan-Meier Survival Curves by Spirometry Category