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Occupational Risk Factors in Chronic Obstructive Pulmonary Disease

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ABSTRACT

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Introduction: Chronic obstructive pulmonary disease (COPD) causes increased disability and mortality in the U.S. population. Approximately 15% of cases of COPD can be attributed to occupational exposure. There are gaps in the knowledge of the relationships between occupational exposure and COPD and further investigation can provide information helpful in improving COPD preventive strategies in the workplace. The objective of this project was to assess COPD prevalence in population based studies and characterize the relationship between COPD and occupational exposure.

Methods/Results: Three separate U.S. population-based cross-sectional studies of COPD were conducted. In the first study, a COPD job exposure matrix (JEM) was created to characterize exposure of working adults to vapors-gas, dust, and fumes (VGDF). Next the JEM was applied to investigate the association between occupational exposure and COPD using data from a large population-based study where good quality spirometry and questionnaire data on chronic bronchitis, wheeze, and severity and duration of exposure to VGDF were collected. In the second study, COPD prevalence was estimated for the older U.S. population (40–79 years of age) over two periods, years 1988–1994 and years 2007–2010. The results show that COPD prevalence is declining. However, COPD still remains a significant problem. In the third study, prevalence estimates of COPD for the U.S. working population by major occupational groups were estimated. Higher odds of COPD were found among certain occupation groups.

Conclusions: The findings from this study provide perspective on contemporary trends in COPD prevalence and confirm that COPD remains a substantial problem in the U.S. population and more specifically in the working population. Exposure to VGDF continues to be associated with COPD as does smoking. This research expands the evidence on the association of COPD with VGDF exposure and certain occupation groups highlighting current trends in the U.S. occupations at risk for COPD. Understanding these evolving trends in COPD prevalence helps to develop strategies and interventions to further reduce exposure to VGDF and tobacco smoking to reduce the burden of COPD.

DEDICATION

I dedicate this dissertation in the memory of my beloved wife Bobbi who dedicated her life to me and our children. Our 27 years together seemed so brief. I love you and deeply miss you.

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Introduction

Chapter 1

1.1 Introduction

Chronic obstructive pulmonary disease (COPD) is a disease with broad public health implications. COPD is estimated to cause about 3 million deaths globally per year (1). A more complete understanding of the risk factors associated with COPD and populations afflicted by the disease will help to guide and improve intervention strategies to prevent COPD. Tobacco smoking is strongly associated with COPD and the estimated population attributable risk due to tobacco smoking is approximately 80% (2). In addition, inhalation of aerosolized particles, gases, and/or vapors in the workplace is also known to be associated with increased risk of COPD. A strategic priority goal of the National Institute for Occupational Safety and Health (NIOSH) is to conduct research and provide guidelines to prevent and reduce COPD at workplace (3). This study contributed to the understanding of the role of occupation and smoking as risk factors for COPD in the U.S. population.

There are several important definitions developed by the American Thoracic Society (4) for the diagnosis and understanding of COPD and are quoted in this paragraph. COPD is a preventable and treatable disease state characterized by airflow obstruction that is not fully reversible. Airflow obstruction is usually progressive and is associated with an abnormal inflammatory response of the lungs to noxious particles or gases, primarily caused by cigarette smoking. There are two underlying pathological conditions, which may be present in COPD: first, chronic bronchitis which is clinically defined as a chronic productive cough for 3 months in each of 2 successive years in a patient in whom other causes of productive cough have been excluded; second, emphysema which is pathologically defined as the presence of permanent enlargement of the airspaces distal to the terminal bronchioles accompanied by destruction of their walls, and without obvious fibrosis.

Research of COPD in this project focused on several health outcomes that define COPD. In two of our studies COPD was defined by abnormally low level of lung function or airflow obstruction determined by using spirometric measurements. The results from individual spirometry tests were compared to reference lung function values of healthy never smokers of similar age, gender, race, and height. If the observed lung function value fell below the lower limit of normal (LLN), a person would be classified as having airflow obstruction. LLN approximates the one-sided 95% confidence limit for the expected value, where 5% of healthy persons who have never smoked would be identified as abnormal (4). In addition, COPD was identified through questionnaires by asking the participant about healthcare provider diagnosed chronic bronchitis or emphysema.

The focus of the current study was to investigate the prevalence of the various COPD outcomes in several cross-sectional studies and estimate their association with occupational risk factors such as vapors-gas, dust or fumes (VGDF), or the association with occupational categories. An additional focus of our study was to develop and test a job exposure matrix for COPD outcomes based on reported job and industry where a study participant worked. The results of this study are intended to provide information to guide NIOSH to address its strategic priority goal to improve intervention strategies to prevent development of COPD associated with workplace exposures. In addition, the information will help NIOSH stakeholders and the broader international occupational health community to develop intervention strategies based on our publications in peer reviewed journals.

1.1.1 Prevalence and Costs of COPD

Chronic obstructive pulmonary disease (COPD) is a leading cause of morbidity and mortality globally according to the World Health Organization (WHO). COPD causes approximately 3 million deaths annually, and this number is projected to increase for years (1).

In the U.S., an estimated 15.0 million people had physician diagnosed COPD in 2010 and 12.0 million had undiagnosed COPD. COPD ranks third in causes of mortality resulting in approximately 100,000 deaths annually (5–7). The National Heart, Lung, and Blood Institute estimated the total annual cost of COPD for 2010 as $49.9 billion (8). The COPD associated disability also reduces the probability of being employed by 8.6% (7).

COPD is a chronic disease which usually develops and is more prevalent among older adults (9, 10). Therefore for the three studies, data for adults starting at either age 40 or 45 were analyzed.

1.1.2 Occupational Risk Factors and Their Contribution to COPD

The American Thoracic Society stated that approximately 15% of COPD cases in the general population of the developed countries are attributable to occupational risk factors (11, 12). A more recent study of the general U.S. population estimated the overall fraction of COPD attributable to work exposure as 19% overall and 31% among never smokers (13). To prevent work-related COPD, occupational risk factors should be identified, including types of industries, occupations, and specific types of exposures that increase the risk of COPD in the working population.

Epidemiological studies help to improve our knowledge of occupational risk factors and the literature reflects studies identifying various workplace risk factors associated with COPD. Hedrick (14) concluded that certain occupations are likely to increase the risk of COPD and that there are probably interactions between smoking and exposures that make the effect worse. Blanc and Toren (15) from their review of the literature concluded that there is a causal association between work-related exposure and COPD. They summarized occupational risks (exposure) of the 14 studies from 2000 through 2006 with endpoints of either COPD or chronic bronchitis evaluated through questionnaire or spirometry. Significant associations were found with exposures to dust, fumes, mineral dust, dusty trades, biological dust, and among laborers and by occupation.

The role of biological agents in questionnaire ascertained chronic bronchitis and spirometry ascertained COPD among farmers was investigated by Eduard et al. (16). Exposures were measured on the Norwegian farms and the odds of either chronic bronchitis or COPD were significantly higher with increased concentrations of total dust, organic dust, spores, inorganic dust and silica.

Exposure to dust in coal and hard-rock miners is associated with increased severity of emphysema (11). Hnizdo found a combined effect of smoking and dust exposure on COPD among gold miners (17). Blanc, Menezes et al. (18) found an association between dusty trades and COPD for males and females throughout the world. Trupin et al. (19) reported that people with a COPD or chronic bronchitis diagnosis were two times more likely to report a past work exposure to gases, dusts, vapors, or fumes. Bergdahl et al. (20) found an increased risk of construction worker mortality from COPD from any airborne exposure or to inorganic dust and the hazard ratio doubled among never smokers.

Blanc et al. (21) created an overall COPD job exposure matrix (JEM) and applied it to their Kaiser case-control study. They found significantly higher odds of COPD with high exposure to VGDF as assessed by the JEM.

1.2 Gap in the Literature

Although much is known about the risk factor of smoking and its relationship with COPD (4, 22), less is known about the occupational risk factors including VGDF. The creation of a job exposure matrix specific for COPD helped to improve our understanding of the association between COPD and VGDF exposure and also current trends in COPD by occupation and exposure as work conditions evolve in the U.S. Population-based studies can collect information about exposure through either self-reported exposure in a questionnaire or by providing information about the industry and occupation where participants worked. Because there are usually no direct measurements of occupational exposure in population-based studies, JEMs have been developed to assign a level of potential exposure to study participants, based on their reported occupation. The JEM is designed to assign an exposure score reflecting the potential agents and level of potential exposure for each occupational category defined by a standardized three digit occupational code. The occupational information from studies can then be coded into the standardized occupational codes and matched with the COPD JEM to help in our understanding of the COPD risk in relation to the VGDF exposure (21, 23). Another method of assessment of the risk of COPD in relation to the VGDF exposure is to compare the odds of COPD in each occupational group with a reference group. Both this method and the JEM method were employed in this project to help to fill the literature gap. Our project is linked with the Healthy People 2020 Respiratory Diseases, Chronic Obstruction Pulmonary Disease objectives RD-10 (to reduce deaths) and RD-11 (to reduce hospitalizations) from COPD among adults (24).

1.3 Purpose of the Current Research

Because the potential occupational risk factors for COPD are varied, it is important to investigate their effect using various industry or population-based studies. Our long-range goal is to understand the risk factors for COPD to provide information for COPD prevention. The objective of this study is to identify and characterize the risk factors for COPD. The central hypothesis is that COPD is associated with occupational risk factors including exposure to VGDF and with smoking. The hypothesis has been formulated by a review of the literature (18, 21, 25–31) and an investigation of COPD associations in another study population (32, 33). The rationale for the proposed study is to identify the risk factors for COPD. It will also build on past research efforts to update and refine previous research findings and knowledge regarding risk factors for COPD. This will provide a more clears contemporary understanding of risk factors to help aid prevention.

Gaps in the knowledge of COPD risk factors and the contribution of occupational exposure to COPD are explored through three specific aims. The three aims are investigated through the three studies presented in Chapters 2, 3, and 4 using secondary data analysis of quantitative data obtained from population-based cross-sectional studies. The first aim (Chapter 2) was to create and test a JEM for COPD using data from the Multi-Ethnic Study of Atherosclerosis (MESA) lung study. The JEM was created by an industrial hygienist and a consensus was reached by three industrial hygienists to reflect the typical agents and severity of exposures in each occupation to ascertain occupational exposure scores. The exposure scores included an overall VGDF score and more specific exposure scores for dust, organic dust, mineral dust, gas-vapors, and fumes. The second aim (Chapter 2) was to determine if occupational exposure to VGDF is a risk factor for COPD. The associations between occupational exposures and COPD were determined using either the JEM or self-reported VGDF exposure ascertained by questionnaire in this MESA cohort. COPD was determined by spirometry (pulmonary function test) or by self-report of healthcare provider diagnosis of chronic bronchitis.

The third aim was to determine the prevalence and trend of COPD using two national studies of the U.S. population. The first study (Chapter 3) used data from a national study of the U.S. population (National Health and Nutrition Examination Surveys (NHANES)) which incorporated spirometry defined airflow obstruction to compare COPD prevalence between two sampling periods 1988–1994 and 2007–2010. We estimated prevalence of COPD for the 40–79 year old population. The second study (Chapter 4) used data from a national study of the U.S. population (National Health Interview Survey (NHIS)) which incorporated self-reported doctor-diagnosed chronic bronchitis or emphysema defined COPD for years 2004–2011. We estimated prevalence and prevalence odds ratios (POR) for COPD for major occupational groups among the 40–70 year old working population.

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Chapter 2

Occupational Risk Factors for COPD Phenotypes in the Multi-Ethnic Study of Atherosclerosis (MESA) Lung Study

2.1 Introduction

Chronic obstructive pulmonary disease (COPD) is characterized by airflow limitation that is not fully reversible, is usually progressive and associated with inflammatory response to noxious particles and gasses (1). COPD is one of the leading causes of morbidity and mortality worldwide. According to the World Health Organization, COPD affects approximately 65 million people worldwide and is responsible for approximately 3 million deaths annually. This prevalence and associated mortality is projected to increase, and by 2030 COPD is expected to be the third leading cause of death (2, 3). In the U.S. in 2009, there were 137 082 deaths from chronic lower respiratory disease (primarily COPD), the third leading cause of mortality (4, 5).

The American Thoracic Society (ATS) estimated that approximately 15% of COPD in the general population is attributable to occupational sources (6). The estimated cost of occupational COPD in the U.S. in 1996 was approximately $5 billion (7). The estimated fraction of COPD attributable to work exposure in the U.S. population is 19% overall and 31% among never smokers (8). Several recent population-based studies show associations between COPD and occupational risk factors, which include vapor-gas, dust, and fume (VGDF) exposure (9–15). Few of these studies, however, have included a large number of U.S. minority groups that may be at increased risk (16).

The aim of this study is to further identify and characterize occupational risk factors for COPD in an older, multiethnic U.S. sample using a newly developed job exposure matrix (JEM) and questionnaire ascertained exposure. Specifically, we aim to evaluate whether occupational exposure to VGDF as ascertained by a questionnaire and JEM are risk factors for airflow limitation, chronic bronchitis and wheeze.

2.2 Methods

2.2.1 Study Population

The Multi-Ethnic Study of Atherosclerosis (MESA) recruited a population-based sample of participants 45-84 years old that were free of clinical cardiovascular disease in 2000-2002 from six predominantly large urban U.S. communities located in California, Illinois, Maryland, Minnesota, New York, and North Carolina. The participation rate was 60% among those screened and deemed eligible (17). The four race/ethnicity groups in this analysis were White, Black, Chinese, and Hispanic.

The MESA Lung Study enrolled MESA participants that were sampled from those that underwent baseline measurements of endothelial function, consented to genetic analyses, and underwent an examination during the MESA Lung Study recruitment period between 2004 and 2006 (Figure 2.1) (18).

2.2.2 Occupational Exposure Assessment

We used two methods of occupational exposure assessment: (1) responses to questions on exposure to VGDF; and (2) JEM for the assessment of COPD risk constructed by NIOSH industrial hygienists. The JEM made use of the self-reported current occupation and industry if employed or the occupation where last employed if retired (ascertained using questions, see Appendix for pertinent excerpts from the questionnaires). The reported industry and occupation were coded by trained staff from the National Institute for Occupational Safety and Health (NIOSH) into U.S. Census 2000 occupation and industry coding.

2.2.3 Construction of the NIOSH JEM

To construct a generalizable JEM, we used the University of California San Francisco (UCSF) JEM Census occupational codes and added the additional MESA Census occupational codes not available in the UCSF JEM (9). An industrial hygienist then constructed the NIOSH JEM by assigning an exposure score (1, 2, or 3) representing the likelihood of the presence and severity of the VGDF exposure (low, medium, and high) for each Census occupation code based on expert opinion. In addition, the method of exposure coding applied in the Weinmann et al. (14) study was adopted for assigning the exposure scores in this study (19). The hygienist similarly created separate scores representing the likelihood and severity of exposure to vapor-gas, fumes, dust, and subcategories of dust (mineral; organic). Two certified industrial hygienists then reviewed and discussed the preliminary JEM scores and assigned a final consensus score. Environmental tobacco smoke was considered in the overall VGDF score for occupations with likely exposure (e.g., bartenders and waitresses), although a separate exposure score was not assigned.

2.2.4 Spirometry, Airflow Limitation, and Respiratory Symptoms and Diseases

Spirometry tests were conducted in 2004–2006 in accordance with the ATS/European Respiratory Society (ERS) guidelines (20) and all participants attempted at least three acceptable maneuvers. Tests were conducted using a dry-rolling-seal spirometer and software that performed automated quality checks as maneuvers were performed (Occupational Marketing, Inc., Houston, TX). All spirometry exams were reviewed by one investigator and each test was graded for quality; participants with no acceptable curves were excluded (21). All participants that completed an acceptable spirometry test and had industry and occupation data (n=3686) were included in this study.

Airflow limitation was defined as the ratio of forced expiratory volume in one second to forced vital capacity (FEV_1/ FVC) below the lower limit of normal (LLN) and $FEV_1 < LLN$ (22). NHANES-based reference equations (23) were used to estimate the LLN values, however, for Asian-Americans, a correction factor of 0.88 was applied to calculate the LLN for FEV_1 (21). The Hankinson reference equations including the correction factors for Asian-Americans have been previously validated using MESA data (21).

The other health outcomes investigated were symptoms of chronic bronchitis, wheeze, and self-reported physician-diagnosed “chronic obstructive pulmonary disease or COPD...or emphysema.” Chronic bronchitis (Medical Research Council) was defined as 3 or more months of chronic productive cough per year in 2 or more years (Appendix). Wheeze was defined by the question, “In the last 12 months, have you had wheezing or whistling in your chest?”

The National Heart, Lung, and Blood Institute (NHLBI) funded the MESA study and the ancillary MESA Lung Study; the JEM coding was funded by the National Institute for Occupational Safety and Health (NIOSH). The MESA study protocol was approved by the Institutional Review Board in each field center and the NHLBI; the current analysis was approved by the Institutional Review Board of NIOSH. Written informed consent was obtained from each participant.

2.2.5 Data Analysis

A logistic regression model was used to estimate the association between occupational risk factors and the dichotomous variable of airflow limitation. The occupational risk was evaluated using self-reported exposure and exposure established using the NIOSH JEM. The occupational exposure variables individually evaluated in the logistic model included self-reported exposures to vapor-gas, dust, fumes; severity of VGDF exposure, years of exposure to VGDF, and exposure scores assigned by the JEM. An additional variable (number of VGDF agents) was created to reflect the number of agents (i.e., vapor-gas, dust, and/or fumes) to which the person reported exposure (none, one, two, or three). The covariates adjusted for in the model were age, gender, race/ethnicity, education, body mass index (BMI), smoking status, pack-years, cigar-years, pipe-years, environmental tobacco smoke, and asthma. BMI was divided into four categories: < 25, $25 – <30$, $30 – <35$, and ≥ 35 kg/m^2 to reflect the potential effect of BMI on lung function (24). Since there were few participants with BMI<18 these were combined into the <25 category. In addition, separate models for never smokers were evaluated.

To investigate the combined effect of the occupational exposure and smoking on the various health outcomes, we created interaction variables combining smoking status (ever/never) and occupational exposure status [i.e., self-reported exposure (yes/no) or JEM (no=low, yes=medium or high) for dust, vapor-gas, and fumes, and VGDF]. The data were then analyzed using a model with three dummy variables comparing those with occupational exposure only, smoking only, and both smoking and occupational exposure to those without any of the two exposures, to determine a trend in the odds ratios. In addition, to test the interaction effect on a multiplicative scale, we included in the logistic model occupational exposure, smoking, and the interaction term (9, 10).

2.3 Results

Demographic data for age, race/ethnicity, smoking status, BMI, and education are presented in Table 2.1. There were 3667 individuals with spirometry and complete information used in this analysis out of 3686 included in the occupational sample (Figure 2.1). The study sample was 36% non-Hispanic White, 26% African-American, 22% Hispanic and 16% Chinese-American, and 44% had never smoked cigarettes. Table 2.1 shows the characteristics of the sample overall, stratified by race/ethnicity, and restricted to never smokers (45%). A large proportion had education beyond high school (66.7%) and 44.3% were employed in the management or professional occupational group while 19.3% were blue-collar workers. The prevalence of moderate airflow limitation (FEV_1/FVC < LLN and FEV_1 < LLN) was 5.7% overall, 6.7% for males, 4.7% for females, and 2.1% among never smokers.

Frequencies of occupational exposures as ascertained by a questionnaire and by the job exposure matrix are also presented in Table 2.1. For all participants, 37.9% self-reported exposure to dust, 19.4% to vapor-gas, and 24.2% to fumes, and 13.7% and 5.2% reported moderate and severe VGDF exposure, respectively. According to the JEM, the medium and high exposures totaled 12.0% for dust (5.3% for mineral dust, 7.6% for organic dust), 17.6% for vapor-gas, 4.6% for fumes, and the overall medium to high VGDF exposure was 15.1%. The proportion who were retired at the time of spirometry was 41.6%.

The adjusted odds ratios for the associations of airflow limitation with occupational exposure, in the whole cohort, show significant associations with self-reported vapor-gas exposure (Table 2.2). The dose-responses for severity of exposure and for the number of exposures reached statistical significance at the highest categories. The number of cases was, however, too small to perform meaningful analysis using race/ethnic stratification.

Among never-smokers, airflow limitation was associated with the highest severity of self-reported exposure to VGDF with the odds ratio almost seven times that of "All" participants (Table 2.2). Among never-smokers, there was also an increasing trend in the odds of airflow limitation as the number of self-reported VGDF agents (exposure to 0, 1, 2, or 3 agents) increased, $P < 0.01$, with exposure to three agents associated with five times higher odds of airflow limitation (OR 5.1, 95% CI 1.5–16.7). Additionally, never-smokers exposed to VGDF for 15 or more years had over triple the odds of airflow limitation (OR 3.3, 95% CI 1.3–8.7). Also among never-smokers, the odds of airflow limitation was more than doubled with self-reported exposure to vapor-gas (OR 2.7, 95% CI 1.1–6.7) and increased 4-fold with exposure to fumes (OR 4.2, 95% CI 1.7–9.9) in comparison to those not exposed.

For associations with exposure to dusts as ascertained by the JEM, the odds ratios for airflow limitation doubled for highest level of exposure, especially among males, and nearly tripled for organic dust exposure among females (Table 2.2). We did not find significant association between airflow limitation and the JEM VGDF score (results not shown). There was a low Spearman rank correlation (0.21, $P<0.001$) between self-report of VGDF and the JEM VGDF. Figure 2.2 shows the odds ratios for self-reported specific exposures (vapor-gas, dust, fumes) and the severity of exposure to VGDF and airflow limitation.

Odds ratios for the associations between airflow limitation and the combined effect of smoking and each of the occupational exposures are reported in Table 2.3. For all the specific exposures to vapor-gas, dust, fumes, and general VGDF exposure there was an increasing trend in the odds ratios, including for the category with both exposures present. However, none of the odds ratios for the interaction effect were statistically significant at $p<0.05$ level, rejecting the hypothesis that there is multiplicative interaction. The combined associations were similar for males and females.

Self-reported doctor-diagnosed COPD associations reached statistical significance with self-reported dust exposure among "All" participants (OR 1.7, 95% CI 1.0–2.6), vapor-gas among "All" participants (OR 2.0, 95% CI 1.2–3.3), especially among females, and self-reported years of exposure to VGDF for 1-15 and over 15 years (Table 2.4). COPD also was associated with self-reported exposure to all three VGDF agents among "All" participants (OR 2.6, 95% CI 1.4–5.0), among females (OR 6.0, 95% CI 1.9–19.2), and among never-smokers (OR 14.2, 95% CI 2.1–94.9). COPD was associated with severity of exposure, especially in the highest severity category (OR 2.8, 95% CI 1.3–6.1).

Chronic bronchitis was associated with self-reported dust, vapor-gas, fumes, severity of exposure, years of exposure and the number of VGDF agents (Table 2.5, Figure 2.2), but not with the JEM exposure scores. Likewise, wheeze was associated with self-reported dust, vapor-gas, fumes, severity of exposure, years of exposure, and the number of VGDF agents (Table 2.5, Figure 2.2), but not with the JEM exposure scores.

For chronic bronchitis, the combined effect of smoking and self-reported VGDF exposure or JEM assigned VGDF exposure was evaluated in a manner similar to airflow limitation. Similarly, for all the exposures (vapor-gas, dust, fumes, and VGDF) there was an increasing trend in the odds ratios, including for the category with both exposures present (results not shown). However, none of the odds ratios for the interaction effect were statistically significant at $p<0.05$ level, rejecting the hypothesis that there is multiplicative interaction.

2.4 Discussion

We found that airflow limitation, physician-diagnosed COPD, chronic bronchitis, and wheeze were associated with self-reported occupational exposure to vapors, gas, dust and fumes in a large, multi-ethnic study of participants 45 to 84 years of age when initially recruited during 2000–2002. Associations were particularly strong among never smokers and for the severity of exposure. This study adds to our understanding about the association of VGDF exposure with non-malignant respiratory conditions and about the two methods of ascertainment of occupational exposure: self-reported using a questionnaire and a JEM.

We found that airflow limitation was associated with JEM-assigned scores for VGDF, dust and organic dust. To compare results for self-reported dust exposure with those for JEM-assigned dust exposure (low, medium, or high), the self-reported exposure had elevated odds while with the JEM the highest assigned dust category was significant (Table 2.2). The increased risk associated with highest JEM dust exposure category was primarily in males. This result may suggest that the JEM's three levels of exposure categorization may better capture the highest exposure level while the dichotomous self-reported dust exposure cannot differentiate the exposure levels.

Using the JEM, we also investigated the association of airflow limitation with exposure to organic dust for which we did not have self-reported data, and found that for "All" participants there was an increasing trend for airflow limitation across the level of exposure (i.e., low, medium, and high) ($X^2 = 3.8$, $P = 0.05$). The association was statistically significant in females. This indicates that the JEM method may be useful also in the evaluation of occupational exposures for which self-report data are not available.

Among never-smokers (Table 2.2), associations with airflow limitation were observed for self-reported severity of VGDF exposure, the number of self-reported agents, and number of years exposed to VGDF agents. These findings are consistent with a study reported by Blanc et al. (9) where self-reported VGDF and JEM assigned VGDF exposure were found to be associated with COPD. However, in our study we did not find a significant association between airflow limitation and the JEM VGDF. The low Spearman rank correlation between self-reported VGDF and the JEM VGDF may indicate that the participants' own knowledge of their exposure was better than the JEM when the information about the longest held job was not available.

Self-reported doctor-diagnosed COPD was associated with self-reported dust, vapor-gas, number of years of exposure to VGDF, increasing severity of exposure to VGDF, and increasing number of agents (Table 2.4). Some of the odds of COPD were increased 2-fold or greater among never-smokers. This result is consistent with a study by Blanc et al. (9).

Chronic bronchitis is a major component of COPD; therefore Medical Research Council (MRC)-defined chronic bronchitis as determined by several questions was evaluated for association with occupational exposure (Appendix). Chronic bronchitis was associated with self-reported occupational exposure to dust, vapor-gas, fumes, severity of exposure to VGDF, years of exposure to VGDF, and with the increasing number of agents (none, one, two, or three) of vapor-gas, dust, and/or fumes (Table 2.5). This result reinforces the well-known association between occupational exposure and "industrial bronchitis" (15, 25-27). We also investigated the association of chronic bronchitis with the combined effect of smoking and each exposure. The results (not tabulated) were similar to those for airflow limitation.

Wheeze is a symptom often associated with airflow limitation (28, 29). In our study, wheeze within the last year was associated with occupational exposures to vapor-gas, dust, fumes, a progressive gradient of severity of exposure to VGDF, and with the increased number of the VGDF agents reported by participants. These associations were also consistent by gender and among never smokers (Table 2.5). The associations of chronic bronchitis and wheeze with occupational exposure were stronger than with airflow limitation.

This study has some limitations, which are: 1) temporality cannot be determined; 2) questionnaire data pertaining to past occupational exposure may be prone to recall bias in that respondents with disease or symptoms may have considered the presence and more severe exposure than respondents without symptoms. The use of both questionnaire self-reported exposure and JEMs should help reduce potential for misclassification bias (9, 30, 31). Since participants may not be aware that they have airflow limitation, differential misclassification would be less likely for this outcome than for reported symptoms of chronic bronchitis and wheezing. 3) For some outcomes, the highest JEM exposure category had insufficient sample size to determine a significant trend. 4) Another important limitation is that the JEM assessment was based on the most recent job. Almost 42% of the MESA-Lung participants were retired at the time of spirometry and only the most recent job prior to retirement was reported. This lack of information on the longest held job may have decreased concordance between the JEM and self-reported exposure and reduced the ability of the JEM to detect the effects of occupational exposure on disease.

The MESA study was designed prospectively to study subclinical factors for cardiovascular disease (CVD) and thus individuals with existing clinical CVD were excluded at the onset of the study (17). CVD is one of the conditions that occur with the highest COPD comorbidity (32–34). This exclusion may have introduced a survivor bias among elderly participants; yet, it is unlikely to have affected participants under 65 years. When investigating the prevalence of airflow limitation and self-report of severity, the sensitivity analysis results for the most severe category were similar for those under 65 years (n=2133) and those over 65 years (n=1375) (OR 1.8, 95% CI 0.9–3.6 vs. OR 2.2, 95% CI 0.9–5.8). Therefore, with respect to airflow limitation, survivor bias appears to be less likely in this population. However, Sin et al. reported that reduced FEV_1 is a risk for cardiovascular mortality; therefore excluding those with cardiovascular disease may also exclude individuals with reduced FEV_1 and COPD in this study resulting in reduced odds ratios for airflow limitation (32).

2.5 Conclusion

We found significant associations between the prevalence of airflow limitation and occupational exposure ascertained by both self-report and JEM. We did not find an association between COPD and the combined effect of occupational exposure and smoking on the multiplicative scale, but there was an indication of an increased risk of COPD when both exposures were present. We developed an expanded COPD JEM based on the methodology of a previously developed JEM for use in future occupational studies. Chronic bronchitis and wheeze each were associated with self-reported exposures (vapor-gas, dust, fumes, and VGDF exposure severity, years of exposure, and number of agents). Smoking cessation programs combined with the reduction of occupational exposures should be pursued to reduce the prevalence of COPD in workers.

Abbreviations

CI	confidence interval
MESA	Multi-Ethnic Study of Atherosclerosis
JEM	job exposure matrix
UCSF	University of California San Francisco
FEV_1	forced expiratory volume in one second
FEV_1/ FVC	ratio of forced expiratory volume in one second to forced vital capacity
LLN	lower limit of normal – the LLN approximates the one-sided 95% confidence limit for the expected value, where 5% of healthy persons who have never smoked would be identified as abnormal using the LLN

MRC	Medical Research Council

2.6 References

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2.7 Appendix: Pertinent Questions from Questionnaires

A trained interviewer administered a Respiratory Questionnaire to the MESA-Lung participants. Information from the MESA-Lung study in this analysis was supplemented through other MESA questionnaires where participants were asked to identify race/ethnicity using the 2000 Census questions. The respondents were then categorized into one of four racial/ethnic groups.

The script provided to the interviewers for the question was extracted from page 13 of the "MESA-Lung field Center Manual of Operations and Procedures Version 1.9 April 8, 2005. The interviewers were instructed to read every question EXACTLY as written, including the responses. For clarification, they were instructed to re-read the question and answers for the participant. If the participant had questions regarding the definitions for the three questions, they were only allowed to provide the definitions in the "Note" section. The number of times (interviews) that the note for the questions was used was not captured.

The occupational exposure was determined by the following questions:

Q.13. Have you ever been exposed at work to:
(This is "ever" exposure, and it does not have to be daily exposure)**.**

> **Vapors or gas** Answer "yes" or "no" or "don't know".
> Note: vapors are really synonymous with gas, that is the form into which liquids are naturally converted by the action of a sufficient degree of heat.
>
> **Dust** Answer "yes" or "no" or "don't know".
> Note: dust is fine particulate matter which is light enough to be to be easily raised and carried up into the air.
>
> **Fumes** Answer "yes" or "no" or "don't know".
> Note: fumes are volatile matter produced by and usually accompanying combustion (where there's smoke, there's fumes -- although the converse is not completely true).

If yes to any of the above, answer the following:
For how many years were you exposed at work to vapors, gas, dust or fumes?
Provide the number of years. ___ years

How long ago was your last exposure?
Select "current" or provide the number in months OR in years.

____ current OR ___ months OR ____years

Was the exposure "mild" or moderate" or severe'? ___ mild ___ moderate ___severe

Select one. Note that the exposure is in order of increasing level.

Wheezing was determined by the following question:

In the last 12 months, have you had wheezing or whistling in your chest?

☐Yes

☐No

Asthma was determined by the following question:

Have you ever had asthma?

☐Yes

☐No

COPD was determined by emphysema questions and the following question:

Has a doctor ever told you that you had any of the following:

Chronic obstructive pulmonary disease or COPD?

☐Yes

☐No

☐Don't know

MRC Bronchitis is based on cough and phlegm questions from the spirometry questionnaire:

> "Do you usually bring up phlegm from your chest on most days for 3 or more months during the year?"
> "For how many years have you brought up phlegm from your chest like this?"
> "Do you usually have cough on most days for 3 or more months during the year?"

If respondent has a cough on most days for 3 or more months during the year, usually brings up phlegm from chest on most days for 3 or more months during the year and did this for 2 or more years, it was considered MRC Bronchitis.

Emphysema was based on the Medical History interview administered questionnaires from Exam 1 – 4. During Exam 1, the interviewer asked, “Has a doctor ever told you that you have any of the following;

Q.1 Emphysema?”

☐Yes

☐No

☐Don’t know

During Exams 2 – 4, the interviewer asked,

Q.2 Has a doctor told you that you have developed any of the following since your last MESA visit on____: Emphysema?

☐Yes

☐No

☐Don’t know

The occupation was determined by the following four open-ended questions from the survey:

Q.9 For whom do/did you work? (name of company, business, organization or other employer) If you are not working now, please respond regarding your main occupation before you stopped working.

Q.10 What type of business or industry is/was this? (e.g., hospital, newspaper publishing, mail order house, auto repair shop, bank, etc.)

Q.11 What kind of work do/did you do or what was your job title? (e.g. registered nurse, personnel manager, auto mechanic, accountant, grinder operator, etc.)

Q.12 What are/were your most important activities or duties? (e.g. patient care, directing hiring policies, repairing automobiles, reviewing financial records, operating grinding mill, etc.)

Table 2.1. Characteristics of participants in the MESA Lung Study and occupational exposure as ascertained by questionnaire and NIOSH job-exposure matrix (JEM)

Characteristic	All	Males	Females	Never-smokers
	n=3667	n=1878	n=1789	n=1605
Age, mean (SD)	61.1 (9.8)	61.4 (9.9)	60.7 (9.7)	60.5 (9.9)
Race/ethnicity, %				
White	36.1	36.2	36.0	31.9
Chinese	15.5	16.7	14.2	23.1
Black	26.4	25.2	27.6	22.7
Hispanic	22.1	22.0	22.2	22.3
Smoking status, %				
Never	45.1	34.0	56.6	100.0
Former	45.2	55.8	34.2	--
Current	9.8	10.2	9.3	--
Cigarette pack-years, mean (SD)	12.5 (22.6)	16.1 (25.5)	8.8 (18.4)	--
Pipe-years, mean (SD)	3.8 (26.1)	7.4 (36.1)	0.0 (0.6)	--
Cigar-years, mean (SD)	3.1 (23.7)	5.7 (31.8)	0.3 (8.6)	--
Height (cm), mean (SD)	166.3 (9.9)	172.9 (7.5)	159.5 (7.2)	164.3 (9.9)
Weight (kg), mean (SD)	78.7 (17.1)	83.6 (15.7)	73.4 (17.1)	75.7 (16.6)
Body mass index, %				
<25	30.2	28.5	31.9	34.5
25-<30	39.5	45.6	33.1	37.9
30-<35	20.3	20.3	20.4	18.9
≥35	10.0	5.6	14.7	8.7
Environmental Tobacco Smoke				
Do not live with adult smoker	57.8	66.7	48.5	66.6
Live <21 years with adult smoker	30.1	25.7	34.6	22.1
Live ≥21 years with adult smoker	12.1	7.6	16.9	11.3
Education, %				
Less than high school diploma	15.4	14.8	16.2	15.3
High school diploma	17.9	15.5	20.5	18.0
Some college/tech school	28.3	26.6	30.0	25.4
Bachelor's degree or higher	38.4	43.2	33.4	41.4
Occupational group, %				
Management/professional	44.3	46.9	41.6	46.0
Service	15.5	12.9	18.3	16.2
Sales and office	20.8	14.0	28.0	21.4
Blue-collar	19.3	26.2	12.2	16.4
Moderate airflow limitation, %	5.7	6.7	4.7	2.1
Asthma, self-report, %	11.6	9.1	14.2	11.3
COPD, self-report doctor diagnosed (emphysema or COPD), %	2.9	3.3	2.5	0.8
Chronic bronchitis,[†] %	8.0	8.1	7.9	5.7
Wheeze in last year, self-report, %	13.9	12.4	15.5	9.9
Dust, %	37.9	41.9	33.8	32.7
Vapor-gas, %	19.4	26.1	12.3	15.3
Fumes, %	24.2	30.5	17.7	18.4
Severity, %				
None	55.7	51.5	60.0	61.4
Mild	25.5	28.5	22.3	23.1
Moderate	13.7	14.3	13.1	11.7
Severe	5.2	5.7	4.6	3.8
No. of VGDF agents‡				
0	55.6	51.5	60.0	61.3
1	21.0	18.4	23.8	20.8
2	10.0	10.8	9.1	8.4
3	13.4	19.4	7.0	9.5
Years exposure VGDF, %				
None	56.2	51.8	60.7	62.0
≤15	21.9	22.6	21.1	19.1
>15	22.0	25.6	18.2	18.9

Dust JEM, %				
Low	88.0	83.2	93.1	90.6
Medium	9.2	11.9	6.3	7.4
High	2.8	4.9	0.6	2.1
VGDF JEM, %				
Low	85.0	78.3	91.9	87.7
Medium	9.8	14.0	5.4	8.5
High	5.3	7.7	2.7	3.8

†Medical Research Council (MRC) defined chronic bronchitis.

‡The number of VGDF agent was determined by exposure to gas/vapor, dust, and/or fumes.

Table 2.2. Adjusted Odds Ratios (OR) for the association of airflow limitation† with occupational exposures ascertained using questionnaire and NIOSH job-exposure matrix (JEM)

Exposure	All	Males	Females	Never-smokers
	n=3508; airflow limitation=196	n=1782; airflow limitation=115	n=1726; airflow limitation=81	n=1581; airflow limitation=32
	OR (95% CI)	OR (95% CI)	OR (95% CI)	OR (95% CI)
Dust	1.23 (0.88–1.72)	1.21 (0.77–1.90)	1.23 (0.74–2.06)	1.98 (0.88–4.49)
Vapor-gas	**1.55** (1.06–2.26)	1.55 (0.97–2.47)	1.36 (0.70– 2.65)	**2.71** (1.09–6.71)
Fumes	1.39 (0.97–1.99)	1.47 (0.93–2.32)	1.28 (0.71–2.33)	**4.15** (1.74–9.87)
Severity of VGDF				
None	1.0	1.0	1.0	1.0
Mild	1.18 (0.79–1.75)	1.24 (0.74–2.08)	1.09 (0.58–2.06)	1.64 (0.57–4.72)
Moderate	1.48 (0.94–2.34)	1.22 (0.65–2.31)	1.82 (0.92–3.61)	2.64 (0.85–8.20)
Severe	**2.13** (1.21–3.74)	1.57 (0.72–3.46)	**2.99** (1.29–6.93)	**14.75** (4.06–53.63)
X^2-trend, p-value	7.5, p < 0.01	1.3, p = 0.25	7.0, p < 0.01	13.9, p < 0.001
Years exposure VGDF, %				
None				
≤15	1.31 (0.88–1.94)	1.60 (0.95–2.71)	0.98 (0.51–1.86)	2.42 (0.90–6.52)
>15	1.31 (0.88–1.94)	1.10 (0.64–1.91)	1.63 (0.91–2.95)	**3.31** (1.26–8.69)
X^2-trend, p-value	2.0, p = 0.16	0.3, p = 0.60	2.3, p = 0.13	6.2, p < 0.05
No. of VGDF agents‡				
0	1.0	1.0	1.0	1.0
1	1.40 (0.93–2.11)	1.28 (0.71–2.32)	1.54 (0.87–2.73)	1.82 (0.63–5.22)
2	1.40 (0.81–2.40)	1.45 (0.71–2.98)	1.35 (0.57–3.19)	**3.64** (1.12–11.92)
3	**1.69** (1.06–2.70)	1.62 (0.91–2.88)	1.53 (0.63–3.68)	**5.07** (1.54–16.69)
X^2-trend, p-value	5.1, p < 0.05	2.9, p = 0.09	1.4, p = 0.23	8.8, p < 0.01
Dust JEM				
Low	1.0	1.0	1.0	1.0
Med	1.08 (0.60–1.94)	0.85 (0.40–1.81)	1.80 (0.69–4.74)	1.99 (0.49– 8.11)
High	**2.35** (1.10–5.04)	**2.28** (1.03–5.07)	- -	1.87 (0.16–21.66)
X^2- trend, p-value	3.3, p = 0.07	2.3, p = 0.13	1.0, p = 0.32	0.89, p = 0.34
Organic dust JEM				
Low	1.0	1.0	1.0	1.0
Medium	1.39 (0.70–2.77)	0.83 (0.31–2.20)	**2.87** (1.05–7.87)	3.04 (0.67–13.69)
High	2.31 (0.93–5.74)	2.23 (0.87–5.76)	--	--
X^2-trend, p-value	3.8, p = 0.05	1.5, p = 0.21	3.3, p = 0.07	0.4, p = 0.53

†Odds ratios for airflow limitation adjusted for age, race/ethnicity, gender, BMI, smoking status, cigarette pack-years, pipe-years, cigar-years, environmental tobacco smoke, asthma, and education.
‡The number of VGDF agent was determined by exposure to gas/vapor, dust, and/or fumes.

Table 2.3. Adjusted Odds Ratios (OR) for association of airflow limitation† with the interaction of smoking and occupational exposures from questionnaire and NIOSH job-exposure matrix (JEM)

Interaction association	All	Males	Females
	n=3511; airflow limitation=196	n=1785; airflow limitation=115	n=1726; airflow limitation=81
	OR (95% CI)	OR (95% CI)	OR (95% CI)
Smoking/dust‡			
Never/no	1.0	1.0	1.0
Never/yes	1.73 (0.84–3.56)	1.40 (0.43–4.59)	2.12 (0.84–5.34)
Ever/no	**4.57** (2.62–7.96)	**4.65** (1.91–11.28)	**5.08** (2.39–10.81)
Ever/yes	**5.47** (3.07–9.76)	**5.97** (2.42–14.68)	**5.15** (2.28–11.66)
Smoking/vapor-gas			
Never/no	1.0	1.0	1.0
Never/yes	2.14 (0.97–4.72)	2.07 (0.62–6.98)	2.33 (0.78–6.94)
Ever/no	**4.37** (2.71–7.05)	**5.03** (2.23–11.34)	**4.36** (2.33–8.15)
Ever/yes	**6.10** (3.46–10.77)	**7.43** (3.10–17.82)	**4.52** (1.83–11.15)
Smoking/fumes			
Never/no	1.0	1.0	1.0
Never/yes	**3.00** (1.44–6.27)	2.82 (0.86–9.31)	**3.58** (1.35–9.49)
Ever/no	**5.30** (3.15–8.92)	**5.99** (2.50–14.34)	**5.54** (2.77–11.08)
Ever/yes	**6.30** (3.52–11.30)	**8.00** (3.19–20.04)	**5.02** (2.09–12.08)
Smoking/any VGDF*			
Never/no	1.0	1.0	1.0
Never/yes	**2.47** (1.20–5.12)	**2.63** (0.78–8.86)	**2.59** (1.02–6.60)
Ever/no	**5.09** (2.70–9.61)	**5.92** (2.04–17.17)	**5.31** (2.28–12.33)
Ever/yes	**6.97** (3.68–13.20)	**8.21** (2.83–23.85)	**6.71** (2.86–15.78)
Smoking/ JEM-dust			
Never/no	1.0	1.0	1.0
Never/yes	1.39 (0.39–4.88)	--	3.33 (0.85–12.98)
Ever/no	**3.94** (2.57–6.03)	**4.16** (2.14–8.08)	**4.00** (2.23–7.15)
Ever/yes	**4.83** (2.61–8.96)	**5.13** (2.26–11.64)	3.77 (0.99–14.30)
Smoking/ JEM-vapor-gas			
Never/no	1.0	1.0	1.0
Never/yes	0.46 (0.11–2.03)	0.48 (0.06–3.93)	0.54 (0.07–4.40)
Ever/no	**3.44** (2.26–5.23)	**3.94** (2.01–7.73)	**3.47** (1.98–6.09)
Ever/yes	**3.15** (1.76–5.64)	**3.78** (1.69–8.46)	**1.81** (0.54–6.02)

†Odds ratios for airflow limitation adjusted for age, race/ethnicity, BMI, asthma, and education.
‡Smoking was ever (former or current) or never.

*Exposure was dichotomized into any of the agents (Vapor-gas, Dust and/or Fumes).

Table 2.4. Adjusted Odds Ratios for Self-reported Physician Diagnosis of COPD,[†] with occupational exposure from questionnaire

Characteristic	All		Males		Females		Never-smokers	
	n=3508; COPD = 98		n=1758; COPD = 55		n=1701; COPD = 42		n=1581; COPD = 12	
	OR	95% CI	OR	95% CI	OR	95% CI	OR	95% CI
Dust	**1.65**	1.04–2.63	1.63	0.87–3.07	1.81	0.88–3.72	**4.61**	1.17–18.17
Vapor-gas	**1.96**	1.18–3.27	1.36	0.72–2.58	**3.36**	1.41–8.01	2.90	0.70–12.07
Fumes	1.44	0.87–2.36	0.93	0.49–1.78	**2.92**	1.31–6.50	**6.25**	1.37–28.57
Severity of VGDF								
None	1.0		1.0		1.0		1.0	
Mild	**1.96**	1.15–3.33	1.42	0.69–2.91	**3.18**	1.39–7.26	2.14	0.44–10.32
Moderate	**1.93**	1.01–3.67	1.17	0.47–2.94	**3.58**	1.37–9.36	1.60	0.17–14.95
Severe	**2.80**	1.29–6.09	**3.05**	1.22–7.61	1.25	0.23–6.74	**15.19**	1.92–120.5
X^2-trend, p-value	8.8, p < 0.01		3.7, p = 0.05		4.1, p < 0.05		4.7, p = 0.03	
Years exposure VGDF								
None	1.0		1.0		1.0		1.0	
≤15	**2.17**	1.26–3.74	1.64	0.79– 3.40	**3.27**	1.37– 7.83	3.46	0.85– 14.07
>15	**1.84**	1.06–3.17	1.54	0.74– 3.18	2.38	1.00– 5.65	1.86	0.31– 10.97
X^2-trend, p-value	5.6, p < 0.05		1.5, p = 0.22		5.0, p < 0.05		1.3, p = 0.26	
No. of VGDF agents‡								
0	1.0		1.0		1.0		1.0	
1	**2.31**	1.34–3.96	2.04	0.96–4.32	**2.73**	1.21–6.17	1.38	0.25–7.66
2	1.31	0.59–2.90	0.95	0.33–2.75	2.11	0.61–7.32	2.90	0.28–29.98
3	**2.59**	1.35–4.98	1.68	0.75–3.79	**6.00**	1.88–19.20	**14.22**	2.13–94.88
X^2-trend, p-value	7.0, p < 0.01		0.9, p = 0.34		9.1, p < 0.01		6.5, p = 0.01	

[†]Odds ratios for self-reported physician diagnosis of COPD or emphysema adjusted for age, race/ethnicity, BMI, smoking status, cigarette pack-years, pipe-years, cigar-years, environmental tobacco smoke, asthma, and education.
‡The number of VGDF agent was determined by exposure to vapor-gas, dust, and/or fumes.

Table 2.5. Adjusted Odds Ratios for chronic bronchitis† and wheeze‡ with occupational exposure from questionnaire

Characteristic	All		Males		Females		Never smokers	
Chronic bronchitis	n=3508; chronic bronchitis = 280		n=1782; chronic bronchitis = 143		n=1726; chronic bronchitis = 137		n=1581; chronic bronchitis = 91	
	OR	95% CI	OR	95% CI	OR	95% CI	OR	95% CI
Dust	**1.95**	1.49–2.55	**2.45**	1.66–3.61	**1.60**	1.09–2.33	**1.96**	1.23–3.12
Vapor-gas	**1.54**	1.13–2.09	**1.87**	1.28–2.75	1.11	0.65–1.91	1.33	0.75–2.38
Fumes	**1.66**	1.25–2.20	**1.81**	1.24–2.65	1.46	0.95–2.26	1.39	0.82–2.38
Severity of VGDF								
None	1.0		1.0		1.0		1.0	
Mild	**1.83**	1.35–2.48	**2.14**	1.38–3.30	**1.58**	1.02–2.44	1.12	0.63–1.98
Moderate	**2.04**	1.42–2.93	**2.73**	1.65–4.53	1.48	0.87–2.54	**2.25**	1.23–4.13
Severe	1.70	1.00–2.88	1.25	0.54–2.89	**2.38**	1.17–4.84	**3.38**	1.43–7.97
X^2-trend, p-value	14.7, p < 0.001		8.1, p < 0.01		6.8, p < 0.01		10.8, p = 0.001	
Years exposure VGDF								
None	1.0		1.0		1.0		1.0	
≤15	**1.57**	1.13–2.17	**1.77**	1.11–2.82	1.36	0.86–2.16	1.23	0.69–2.19
>15	**2.23**	1.63–3.03	**2.52**	1.61–3.94	**2.05**	1.32–3.19	**1.81**	1.04–3.13
X^2-trend, p-value	22.9, p < 0.0001		16.6, p < 0.0001		10.1, p < 0.01		5.4, p < 0.05	
No. of VGDF agents*								
0	1.0		1.0		1.0		1.0	
1	**1.58**	1.14–2.20	1.38	0.81–2.35	**1.71**	1.11–2.63	1.48	0.85–2.60
2	**2.41**	1.64–3.56	**2.85**	1.67–4.87	**1.91**	1.07–3.41	1.56	0.73–3.30
3	**2.15**	1.47–3.15	**2.53**	1.57–4.08	1.57	0.79–3.14	**2.09**	1.04–4.18
X^2-trend, p-value	22.9, p < 0.0001		18.6, p < 0.001		5.1, p < 0.05		4.8, p < 0.05	
Wheeze	n=3508; wheeze = 488		n=1783; wheeze = 219		n=1726; wheeze = 269		n=1564; wheeze = 156	
	OR	95% CI	OR	(95% CI)	OR	(95% CI)	OR	(95% CI)
Dust	**1.76**	1.43–2.18	**2.13**	1.54–2.95	**1.56**	1.17–2.08	**1.83**	1.28–2.63
Vapor-gas	**1.62**	1.26–2.07	**1.65**	1.20–2.28	**1.52**	1.03–2.23	1.32	0.84–2.08
Fumes	**1.53**	1.21–1.92	**1.60**	1.16–2.21	**1.43**	1.02–2.01	**1.64**	1.09–2.47
Severity of VGDF								
None	1.0		1.0		1.0		1.0	
Mild	**1.67**	1.30–2.14	**2.0**	1.37–2.90	**1.46**	1.04–2.04	1.39	0.90–2.13
Moderate	**1.95**	1.45–2.61	**2.61**	1.69–4.03	**1.54**	1.02–2.32	**1.98**	1.20–3.27
Severe	**3.15**	2.16–4.60	**3.03**	1.75–5.26	**3.52**	2.04–6.07	**4.55**	2.35–8.81
X^2-trend, p-value	44.6, p < 0.0001		25.5, p < 0.0001		18.9, p < 0.0001		20.6, p < 0.0001	
Years exposure VGDF								
None	1.0		1.0		1.0		1.0	
≤15	**1.97**	1.54–2.53	**2.60**	1.79–3.79	**1.51**	1.07–2.13	**1.72**	1.09–2.70
>15	**1.92**	1.48–2.48	**1.93**	1.31–2.85	**2.04**	1.44–2.90	1.55	0.97–2.48
X^2-trend, p-value	28.9, p < 0.0001		12.5, p < 0.0001		16.9, p< 0.0001		8.2, p < 0.01	
No. of VGDF agents*								
0	1.0		1.0		1.0		1.0	
1	**1.84**	1.42–2.37	**2.23**	1.47–3.37	**1.62**	1.16–2.25	**1.72**	1.12–2.63
2	**1.75**	1.25–2.45	**2.09**	1.28–3.41	1.52	0.95–2.45	**1.66**	0.92–2.97
3	**2.14**	1.57–2.90	**2.41**	1.60–3.63	**1.92**	1.17–3.16	**2.11**	1.22–3.67
X^2-trend, p-value	27.2, p < 0.0001		17.3, p < 0.0001		9.5, p < 0.01		8.8, p < 0.01	

†Odds ratios for MRC defined chronic bronchitis adjusted for age, race/ethnicity, BMI, smoking status, cigarette pack-years, pipe-years, cigar-years, environmental tobacco smoke, and education.
‡Odds ratios for wheeze in last 12 months adjusted for age, race/ethnicity, BMI, smoking status, cigarette pack-years, pipe-years, cigar-years, environmental tobacco smoke, and education.
*The number of VGDF agent was determined by exposure to vapor-gas, dust, and/or fumes.

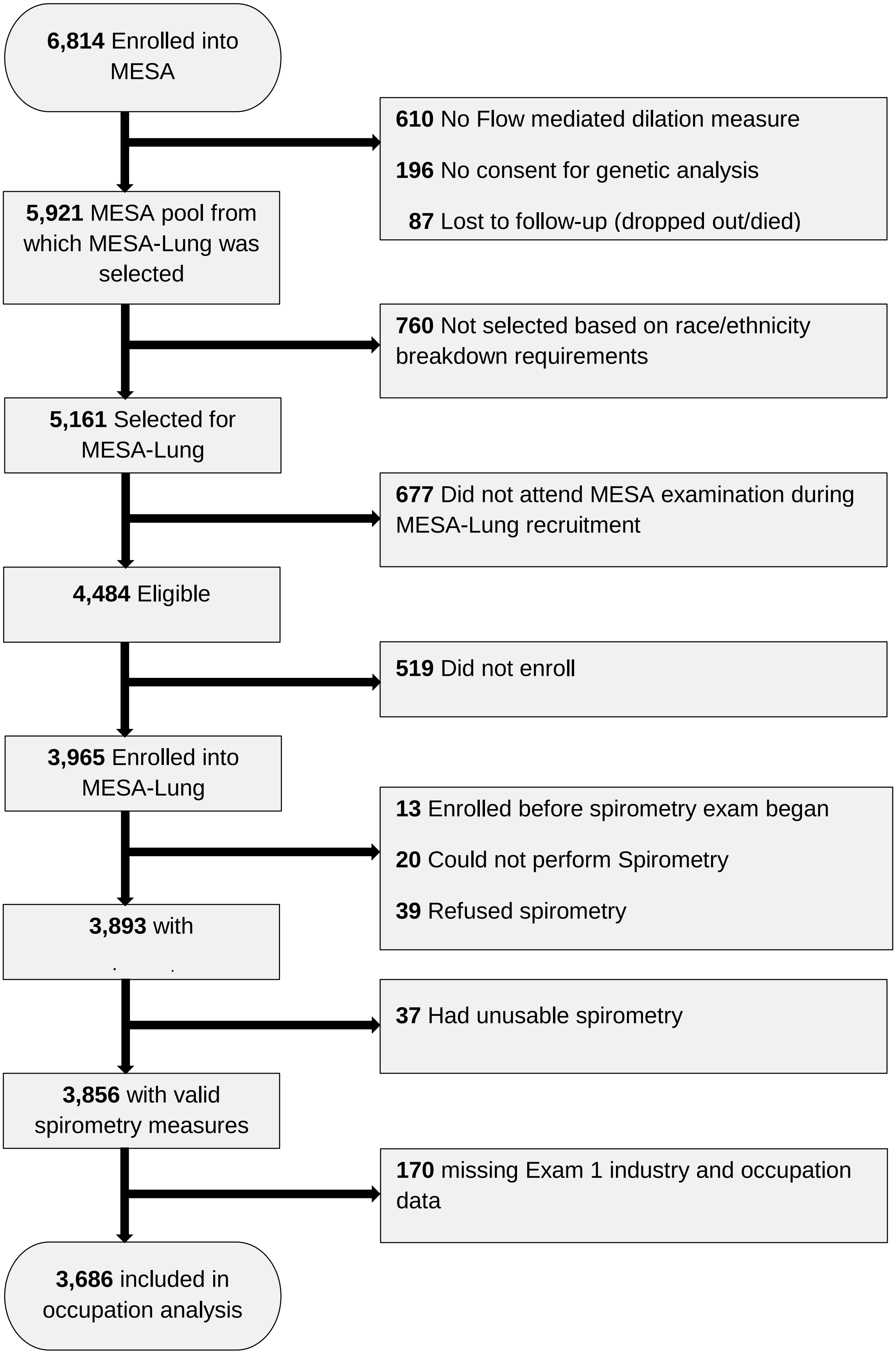

Figure 2.1. Algorithm of recruitment and exclusions for the MESA Lung Study occupational analysis.

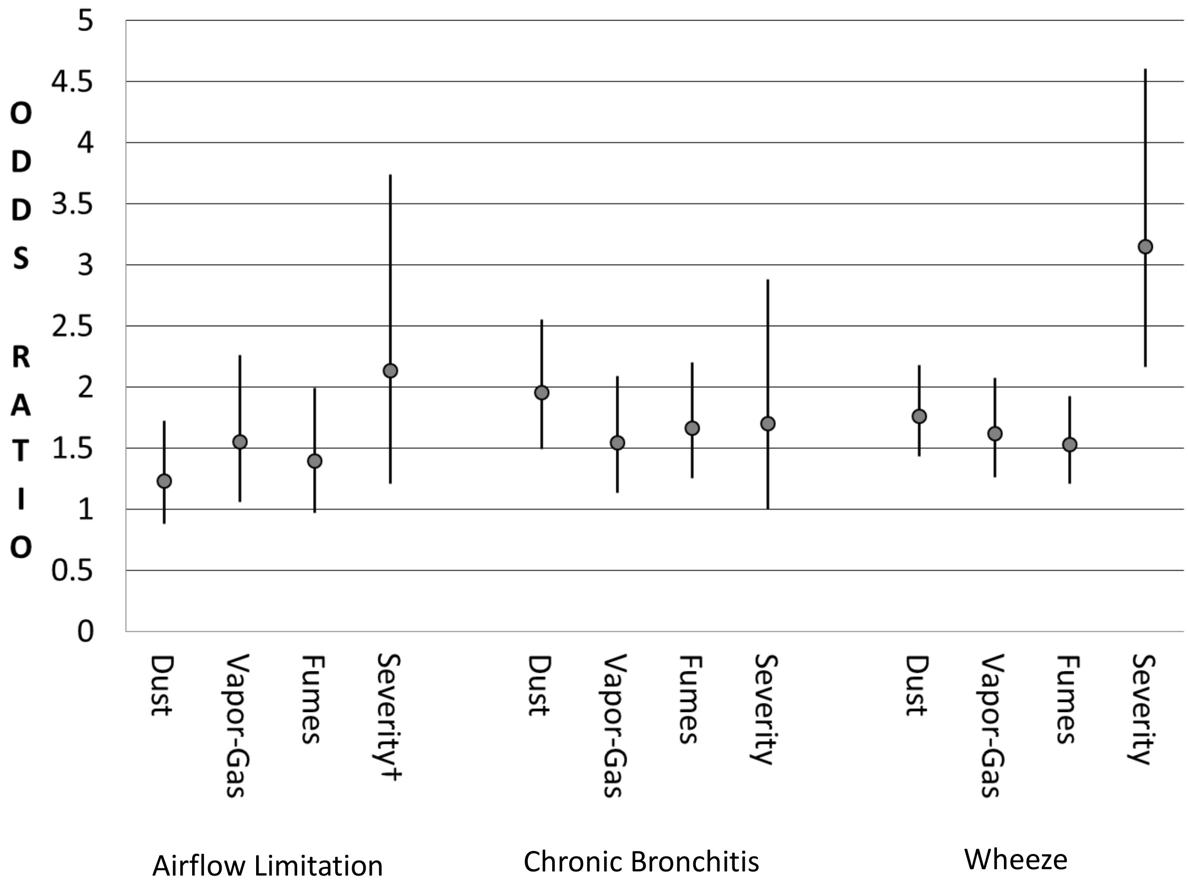

Figure 2.2. Adjusted Odds Ratios for airflow limitation, chronic bronchitis, wheeze and self-reported exposures.
†Severity is the most severe exposure to VGDF

Chapter 3

Prevalence of Airflow Obstruction in U.S. Adults Aged 40–79 Years: NHANES Data 1988–1994 and 2007–2010

3.1 Introduction

Chronic obstructive pulmonary disease (COPD) is a leading cause of morbidity and mortality worldwide (1). In the U.S., an estimated 15.0 million people had doctor-diagnosed COPD in 2010 and 12.0 million had undiagnosed COPD. COPD ranks third in causes of mortality resulting in about 100,000 deaths annually (2– 4). COPD is a costly disease; direct and indirect healthcare costs are higher among COPD patients when compared to other patients. In a case-control study, COPD patients used 50–60% more medical services (inpatient, emergency department and office visits) than controls (5). The National Heart, Lung, and Blood Institute estimated the total annual cost of COPD for 2010 to be $49.9 billion (6). COPD associated disability also reduces the probability of being employed by 8.6% (3). Despite the decreased prevalence of smoking over the last several decades (7, 8), a recent study reported that there was little change in the overall prevalence of COPD among 20–79 year olds between the periods 1988–1994 and 2007–2010 using the NHANES pre-bronchodilator (pre-BD) spirometry data based mainly on the Global Initiative for Chronic Obstructive Lung Disease (GOLD) criteria (9) to define COPD (10).

Spirometry measurements of the forced expiratory volume in the first second (FEV_1) and the FEV_1 to forced vital capacity (FVC) ratio are recommended for the diagnosis of COPD and for the study of COPD prevalence (11). The interpretation of the ratio differs, however, depending on what professional recommendations are used. The American Thoracic Society (ATS) recommends that a FEV_1/FVC ratio below the lower 5^{th} percentile (the lower limit of normal, or LLN) as determined from a representative sample of healthy non-smokers, be used to define airflow obstruction (12). The Global Initiative for Chronic Obstructive Lung Disease (GOLD) (9, 13) recommends that post-bronchodilator (post-BD) spirometry with a ratio of

FEV_1/FVC below 0.7 be used to identify COPD (14). Several studies have shown that the GOLD criteria can potentially over-diagnose COPD prevalence and over-estimate the COPD burden in older adults, especially if pre-BD spirometry is used for the determination (15–18). Since COPD is a costly disease, it is important to ensure that the estimates of the COPD prevalence and burden in the current U.S. population are consistent and reliable to assure sufficient planning and funding for prevention, treatment, and research.

The aim of our study was to evaluate changes in the prevalence of airflow obstruction among older adults (40–79 years) for two periods of the NHANES study 1988–1994 and 2007–2010. In contrast to the Ford et al. study (10), our focus is on using the ATS criteria to define airflow obstruction. Since we applied the NHANES III reference equations in the determination of the presence of airflow obstruction, we also tested how well the NHANES III (1988–1994) equations fit the 2007–2010 data for healthy non-smokers to assess reliability of the estimates. To determine the potential effect of using pre-BD spirometry on the estimation of the prevalence of COPD, rather than post-BD spirometry as recommended by GOLD, we also evaluated the change in the COPD GOLD Stage I and II status when using pre-BD and post-BD spirometry in the NHANES participants who had both tests.

3.2 Methods

The National Center for Health Statistics of the Centers for Disease Control and Prevention conducts the NHANES, which is a cross-sectional survey of the civilian, non-institutionalized U.S. population (19). Household interviews and standardized physical examinations [in mobile exam centers (MEC)] are used to collect data. The NHANES survey samples are selected through a complex, multistage, probability design. The NHANES 2007–2010 survey cycles oversampled major U.S. demographic subgroups and the study procedures are detailed in the references (20, 21). Informed consent was obtained from all participants and the National Center for Health Statistics Research Ethics Review Board approved the protocol.

This study was based on analysis of publicly available NHANES 1988–1994 and 2007–2010 spirometry data. During 1988–1994, 9616 persons aged 40–79 were interviewed, of these 8495 had both an interview and examination, and of these 7667 (79%) had valid spirometry [the spirometry test met reliability/reproducibility quality control check (spprelia=1) and there were two or more successful maneuvers (sppmaneu>1)] and height data, and were used in our study. During 2007–2010, 7296 persons aged 40–79 years were interviewed and had a MEC examination, and of these 7104 were eligible for spirometry. Of the 7104, 1281 participants were excluded from spirometry for various reasons [safety reasons (649), limited time available in the MEC (337), subject refusals (113), or other reasons (182)], and 346 had invalid spirometry tests or missing height. Of those interviewed, 5476 (75%) had valid data and were included in our study.

3.2.1 Spirometry

NHANES 2007–2010 spirometry testing was performed in accordance with recommendations of the ATS (22) using Ohio 822/827 dry-rolling seal volume spirometers with biological filters (A-M Systems PFT Filter Kit B) to minimize infection risks. These were the same spirometers that were used in the NHANES III (1988–1994) spirometry testing. The methods of spirometry measurements and the spirometry equipment were similar for both surveys except for the following: 1) The spirometry software was slightly different with a display of both the volume-time and flow-volume curves available for inspection by the technician in 2007–2010 and provided immediate feedback to improve the quality of the tests; only the flow-volume curve was displayed in 1988–1994, 2) NHANES III did not use in-line filters, 3) the minimum number of maneuvers performed per test session was three for NHANES 2007–2010 and five for NHANES 1988–1994, and 4) the 2007–2010 survey included new annual refresher training and bi-weekly, as opposed to monthly, quality control reports by the National Institute for Occupational Safety and Health (NIOSH).

In the 2007–2010 survey, participants whose test results indicated airflow obstruction (FEV_1/FVC < LLN or $FEV_1/FVC < 0.7$) were selected for post-bronchodilator (post-BD) spirometry. However, of the 1137 (20.8%) selected adults 40–79 years of age, only 577 (50.7%) had the test done. Therefore, for comparison with NHANES 1988–1994, and because of the relatively low participation in the post-BD testing, only the pre-BD spirometry was used in the determination of the COPD prevalence. Nevertheless, the participants with the pre-BD and post-BD spirometry in NHANES 2007–2010 were used to estimate the potential bias due to using pre-BD tests in the estimation of COPD prevalence when applying the GOLD criteria.

Airflow obstruction definitions. Using the ATS criteria, mild or worse airflow obstruction was defined as the ratio of FEV_1 to FVC below the lower 5^{th} percentile (i.e., LLN) (12). We modified the GOLD Stage I criteria, mild or worse airflow obstruction to define it as pre-BD $FEV_1/FVC < 0.7$ (13). Moderate or worse airflow obstruction was defined as FEV_1/FVC < LLN plus FEV_1 < 70% predicted based on the ATS criteria and as $FEV_1/FVC < 0.7$ plus FEV_1 < 80% predicted based on the GOLD criteria. Severe airflow obstruction was defined as for moderate, but using FEV_1 < 50% predicted, for both ATS and GOLD. U.S. population reference equations developed from NHANES III data were used to derive the predicted and LLN values for both periods (23). Reference values are available for non-Hispanic white, non-Hispanic black, and Mexican Americans. In this study, for the "other" race category, we applied a correction factor of 0.88 to the corresponding values for non-Hispanic whites, which has been previously published as an adjustment factor for Asian participants. For the "other Hispanic" group, we applied the predicted values for Mexican Americans.

Demographic variables of interest in this study for both time periods included gender, self-reported age, self-reported race/ethnicity including non-Hispanic (NH) white, NH black, and Mexican American, and self-reported education, self-reported smoking status, and calculated body mass index (kg/m^2). We also used the absence of self-reported respiratory symptoms of chronic bronchitis and wheezing and health care provider diagnosed respiratory disease, to identify "healthy nonsmokers", i.e., individuals who did not report any of those conditions and were nonsmokers.

3.2.2 Data analysis

The age-standardized prevalence was estimated using SAS®, version 9.2 software procedure Proc SurveyReg (SAS Institute Inc. Cary, NC) (24) which accounted for the study design (19) and NHANES MEC examination weights assigned to each individual. To make estimates between the two time periods comparable with respect to the population age distribution, estimates were age adjusted by the direct method using the year 2000 Census Bureau projections for the U.S. civilian, non-institutionalized population using the following age groups: 40-49, 50-59, 60-69 and 70-79 (20, 25). The weighted frequencies and means were derived using SAS procedures Proc SurveyFreq and Proc SurveyMeans, both procedures accounted for the study design and examination weights. To compare the prevalence estimates from NHANES 1988–1994 and 2007–2010, we used the t-test and the Bonferroni adjustment of the p-values to account for multiple comparisons within each categorical variable. To estimate the burden of COPD for the U.S. population, the average U.S. population size for years 2007–2010 was estimated using the national Current Population Survey (26) population size tables.

To investigate the suitability of the NHANES III based reference equations for the 2007–2010 data, we fit the NHANES III reference equations to a group of "healthy-nonsmokers" 20–79 as defined above. For each person we calculated the predicted values for FEV_1, FVC, and the FEV_1/FVC ratio based on the person's ethnicity, age, height, and gender using the NHANES III reference equations. Next, we calculated the standardized differences between the observed and predicted values [i.e., z-score=(observed-predicted)/residual standard deviation]. The mean z-score and the lower 95% confidence limit were then plotted against categorized age, for adults 20 to 79 years of age and a t-test was used to test whether the mean z-score values differed significantly from zero.

To estimate the percentage of those with COPD defined by GOLD Stage I criteria using pre-BD spirometry and post-BD spirometry, we used the data for those participants who had post-BD spirometry and calculated the unweighted percentage with COPD for pre-BD spirometry and post-BD spirometry.

3.3 Results

Table 3.1 provides the descriptive statistics for the NHANES 1988–1994 and 2007–2010 participants aged 40–79 with valid spirometry and height, n=7667 and n=5476, respectively. The two study samples were similar with respect to mean age (57.5 vs. 57.0 years) (data not shown) and gender distribution. The 2007–2010 sample population had, however, a higher level of education, where 47.6% had at least some college education or graduated vs. 27.2% in 1988–1994. Also, the NHANES 2007–2010 sample had a higher proportion of never-smokers (49.6% vs. 42.6%) and the combined categories of ex-smokers and current smokers showed a decrease in mean pack-years of smoking (22.9 vs. 26.7). The prevalence of obesity (body mass index (BMI) of 35 kg/m^2 or greater) increased in 2007–2010 (15.4 vs. 10.0%).

Table 3.2 shows the age-standardized prevalence of mild+ airflow obstruction by ATS criteria (FEV_1/FVC < LLN) for the 40–79 year olds. The overall prevalence decreased from 16.6% (SE 0.8) during 1988–1994 to 14.5% (SE 0.7) during 2007–2010. The 2007–2010 prevalence of mild+ airflow obstruction decreased for 60–69 years old, males, and Mexican Americans also reached statistical significance.

Table 3.2 also shows the age-standardized prevalence of moderate+ airflow obstruction defined as FEV_1/FVC < LLN and FEV_1 < 70% predicted. The overall prevalence dropped from 6.4% (SE 0.5) during 1988–1994 to 4.4% (SE 0.4) during 2007–2010. Again, the 2007–2010 prevalence was lower, reaching statistical significance for age category 60–69, both genders, NH whites and Mexican Americans races, and higher education. Figure 3.1 shows the prevalence of airflow obstruction (ATS and modified GOLD) by age categories by time period.

Table 3.2 also shows the age-standardized prevalence for severe airflow obstruction based on the ATS criteria, for 40–79 year olds. The overall prevalence was 2.2% (SE 0.2) for years 1988–1994 and 1.1% (SE 0.2) for 2007–2010. Often, the prevalence for the years 2007–2010 was about half of the prevalence for 1988–1994 for the demographic factors.

Using the average U.S. population size for 40–79 years olds for years 2007–2010 of 126,199,000 and prevalence of ATS defined airflow obstruction of 14.5% for mild+, 4.4% for moderate+, and 1.1% for severe degree, we estimated the number of individuals in the U.S. with COPD. The burden of COPD is approximately 18.3 million with mild+ (95% CI 16.4–20.3), 5.6 million with moderate+ (95% CI 4.4–6.6) and 1.4 million with severe (95% CI 0.9–1.8).

Post-bronchodilator spirometry is required for the GOLD definition of COPD (9). In the NHANES 2007–2010 study of the 5476 adults 40–79 years of age with valid spirometry, 1137 (20.8%) were selected for BD follow-up because their spirometry results indicated airflow obstruction. However, only 577 (50.7%) had the bronchodilator test done; 315 were not tested because of safety reasons (such as uncontrolled blood pressure, irregular pulse on examination, taking medication for major arrhythmia or certain other medications, implanted defibrillator, or history of congenital heart disease) and 245 were not tested for other reasons (refusal, insufficient time, and others). The group excluded for safety reasons had significantly ($p<0.05$) lower mean FEV_1/FVC ratio than those who had the post-BD test. The group excluded for other than safety reasons did not differ statistically from those who had the post-BD test. Nevertheless, of those with a post-BD test and pre-BD GOLD Stage I (549), only 354 (64.4%) remained in the GOLD Stage I category after post-BD testing and 35.5% moved to normal.

To test how well the NHANES III reference values fit to the NHANES 2007–2010 sample population, we selected all “healthy” non-smokers 20–79 years of age from the NHANES 2007–2010 data (n=1980). The mean standardized differences between the observed and predicted values (z-score) were as follows: for FEV_1 0.047 (SE 0.02; t=2.1; $p<0.05$), for FVC 0.151 (SE 0.02; t=6.4; $p<0.001$), and for the FEV_1/FVC ratio -0.188 (SE 0.02; t=-8.5; $p<0.001$). The t-test values indicate that the observed mean z-scores were significantly different from zero especially for FVC and the ratio. Figures 3.2-3.4 show the distribution of the z-scores, the mean z-scores and their lower 95^{th} percentile, by age categories. The mean z-scores were close to zero for FEV_1 for most age categories, but consistently above zero for FVC. The higher z-score values for FVC reflect higher observed FVC values for the NHANES 2007–2010 sample than was predicted based on the NHANES III based reference equations. The higher observed FVC values then result in the lower mean FEV_1/FVC values for NHANES 2007–2010, in comparison to the predicted values derived from the NHANES III reference equations and thus a negative z-score. The mean z-scores [(Observed-Predicted)/Relative Standard Deviation] are negative for most of the age categories since predicted FEV_1/FVC values based on the NHANES III data are higher than the observed mean FEV_1/FVC values. Consequently, because the distribution of the observed FEV_1/FVC values is shifted towards zero with respect to the predicted and LLN values, the LLN values derived from the NHANES III equations identified more than 5% as being abnormal. Of the healthy non-smokers from the NHANES 2007–2010 sample, on average 7.4% were identified as having $FEV_1/FVC < LLN$.

3.4 Discussion

We analyzed NHANES spirometry data from time periods 1988–1994 and 2007–2010 to evaluate changes in the prevalence of airflow obstruction, a main feature of chronic obstructive pulmonary disease, among older adults (age 40–79). Our results show that the ATS-defined prevalence of airflow obstruction declined significantly from 16.6 to 14.5% ($p < 0.05$) for mild+ airflow obstruction categories as well as for the moderate+ airflow obstruction (6.4 vs. 4.4%, $p < 0.01$) categories. There was a statistically significant decline in the prevalence of airflow obstruction in the age category 60–69 from 20.2 to 15.4% ($p < 0.01$). In addition, the decline in the prevalence of severe airflow obstruction was significant for current smokers. Reasons for the decline in the estimated prevalence of airflow obstruction may include decrease in the prevalence of smoking in the U.S. population, and reductions in occupational exposures and air pollution.

Although our study shows decline in the prevalence of airflow obstruction, lower respiratory disease (primarily COPD) remains the third leading cause of death in the U.S. (27). The high mortality rate from COPD may be explained by higher life expectancy and decreased mortality from cardiovascular disease (27–30). Results from a recent Behavioral Risk Factors Surveillance Survey (BRFSS) showed that the prevalence of self-reported doctor diagnosed COPD increased systematically with age from 6.6% for the 45–54 year olds to 12.1% for the 65–

74 year old U.S. adults for the year 2011 (4). The BRFSS prevalence of doctor-diagnosed COPD of 12.1% for 65–74 year olds is lower than the prevalence of ATS defined mild+ airflow obstruction of 14.4% for the 60–69 and 17.2% for the 70–79 age ranges observed in our study. This difference may reflect different diagnostic methods other than spirometry results, i.e. symptoms of chronic bronchitis or shortness of breath in the doctor-diagnosed COPD, medical diagnosis of COPD without pulmonary function testing (31), or differences in the survey methods. Nevertheless, the observed declining trend in the prevalence of airflow obstruction based on spirometry measurements, as observed in our study, is likely to be reflected in declining morbidity and mortality from COPD in the future if the trend in the decreasing exposure to particulates continues (32, 33).

However, a previous study by Ford et al. reported no significant differences between NHANES III and NHANES 2007–2010 sample populations in the prevalence of COPD (overall prevalence 14.6% vs. 13.5%, p>0.05) (10) for ages 20–79 years using GOLD Stage I and II criteria and pre-BD spirometry. Ford et al. estimated the prevalence of airflow obstruction at 29.4% in the 60–79 years age group. Ford et al. did not apply any reliability/reproducibility criteria to the NHANES III data while our NHANES III analysis was limited to those with reliable spirometry exams and at least 2 maneuvers, which may explain some of the differences with our study. Our results also show that the differences in the prevalence of GOLD Stage I and Stage II for the two time periods are not statistically significant, for most age categories (Figure 3.1). Using the GOLD criteria, Ford et al. estimates that in the larger U.S. population 20–79 age group, 28.9 million have mild or more severe airflow obstruction based on GOLD Stage I, 12.9 million have moderate and more severe obstruction based on GOLD Stage II and 1.5 million have severe airflow obstruction based on GOLD Stage III. Our estimate of the burden of COPD based on the prevalence of ATS-defined airflow obstruction, the main feature of COPD, for the U.S. population 40–79 age group is approximately 18.3 (95% CI 16.4–20.3) million for mild+ airflow obstruction, 5.6 (95% CI 4.4–6.6) million for moderate+ airflow obstruction, and 1.4 (95% CI 0.9–1.8) million for severe airflow obstruction. Our estimate for the 40–79 age group based on pre-BD criteria was approximately 25.2 (95% CI 22.3–27.8) million for GOLD Stage I (mild+), 11.4 (95% CI 9.7–12.9) million for GOLD Stage II (moderate+), and 1.4 (95% CI 0.9–1.9) million for GOLD stage III (severe). There are large differences between the modified GOLD and ATS-based estimates for mild+ obstruction (25.2 vs. 18.3 million ≈ 6.9 million) and for moderate+ obstruction (11.4 vs. 5.6 million ≈ 5.8 million).

Many publications have reported that the usage of fixed FEV_1/FVC ratio criterion of 0.7, especially when using pre-BD spirometry, leads to over estimation of the COPD prevalence in older adults (15–18, 34, 35). The PLATINO study indicates that applying GOLD Stage I criteria to pre-BD spirometry, rather than post-BD spirometry as required by GOLD recommendations, may overestimate the COPD prevalence by approximately 35% (36). However, Tashkin et al. (37) reported substantial acute bronchodilator reversibility in patients with early COPD who had no other features of asthma suggesting that BD reversibility may not be a completely reliable way of distinguishing asthma and COPD.

We have determined using the z-score analysis that usage of the NHANES III equations may potentially lead to a slight overestimation of the prevalence of airflow obstruction in the 2007–2010 data. Although the reference equations fit well to the FEV_1 data, FEV_1 z-scores were around zero, z-scores for FVC (i.e., for both the predicted and LLN values were systematically above zero and above -1.645, respectively, for most age categories) and the mean z-score was significantly higher than zero. As expected, the resulting z-score values for the ratio of

FEV_1/FVC were lower than zero for the predicted value and below -1.645 for the LLN values, and the mean z-score was significantly lower than zero. This may be due to better spirometry quality in the 2007–2010 testing period. Consequently, more "healthy never smokers" from 2007–2010 population sample were classified with airflow obstruction using the NHANES III LLN criteria for the FEV1/FVC ratio (7.4%) rather than the expected 5%, potentially leading to overestimation of the prevalence of airflow obstruction (Figure 3.5). This, in turn, likely underestimates the true difference between the NHANES III and current NHANES estimates.

Limitations of the study include the exclusion of those participants who were unable to perform spirometry including those on continuous daytime oxygen therapy in 2007–2010 (101 of 40–79 year olds). To investigate the potential effect of their exclusion on the estimated prevalence, we added 44 of those that reported doctor-diagnosed emphysema and were excluded from spirometry because they were on continuous daytime oxygen therapy into the airflow obstruction group and recalculated the age-adjusted prevalence. Using ATS criteria, for 2007–2010 and adding those additional cases, the overall prevalence of airflow obstruction increased from 14.5 to 15.0%. The decline in prevalence between the two periods was no longer statistically significant ($p=0.075$). Among the 60–69 year olds, inclusion of the emphysema cases increased the prevalence from 15.4% to 16.0% for 2007–2010 and the decline from NHANES III remained statistically significant ($p<0.05$). Generally, because of stringent spirometry review of the flow-volume curves, it is unlikely that participants with airflow obstruction would be excluded from these two studies due to invalid spirometry.

3.5 Conclusion

In conclusion, the prevalence of ATS-defined airflow obstruction decreased significantly from 1988–1994 (16.6%) to 2007–2010 (14.5%), $p<0.05$ in the U.S. while prevalence rates are increasing worldwide. We estimated, based on the prevalence of ATS-defined airflow obstruction, a main determinant of COPD, that approximately 18.3 million adults aged 40–79 have mild+ airflow obstruction, 5.6 million have moderate+ airflow obstruction, and 1.4 million have severe airflow obstruction in the current U.S. population.

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Table 3.1. Descriptive statistics for NHANES 1988-1994 and NHANES 2007-2010 data (Unadjusted percentage of selected characteristics of adults age 40-79 who had valid spirometry)

NHANES	Demographic data					
	NHANES 1988-1994			NHANES 2007-2010		
	Sample n	**Population N (thousand)***	**Frequency Percent†**	**Sample‡ n**	**Population N (thousand)***	**Frequency Percent†**
Overall	7,667	89,151		5,476	126,199	
Age						
40-49	2,408	33,187	31.4	1,654	43,667	30.2
50-59	1,719	21,999	22.4	1,472	39,984	26.9
60-69	2,042	20,100	26.6	1,428	26,573	26.1
70-79	1,498	13,864	19.5	922	15,975	16.8
Gender						
Males	3,675	41,913	47.9	2,724	62,708	49.7
Females	3,992	47,237	52.1	2,752	65,634	50.3
Race						
NH White	3,601	71,943	47.0	2,704	92,301	49.4
NH Black	1,972	8,608	25.7	1,046	13,399	19.1
Mexican American	1,800	3,162	23.5	923	7,813	16.9
Other Hispanic	--		--	591		10.8
Other	294		3.8	212		3.9
Education						
<High school grad	3,333		43.7	1,569		28.7
High school	2,218		29.1	1,293		23.6
Some college	1,035		13.6	1,435		26.2
College graduate	1,036		13.6	1,173		21.4
Body mass index						
<30	5,332		69.4	3,474		64.2
≥30 – <35	1,551		20.1	1,106		20.4
≥35	774		10.0	834		15.4
Smoking status						
Never smoker	3,268		42.6	2,714		49.6
Ex-smoker	2,511		32.8	1,643		30.0
Current smoker	1,888		24.6	1,117		20.4
Pack-years (n, mean, (SE))						
Ex-smoker + current smoker	4,280		26.7 (0.4)	2,659		22.9 (0.5)
Current smoker	1,821		23.7 (0.5)	1,100		25.9 (0.8)

* Current Population Survey
† Age-weighted and age-standardized weighted prevalence
‡ Sample excludes those with missing values for height

Table 3.2. Age-standardized prevalence of ATS defined mild+ ($FEV_1/FVC<LLN$); moderate+ ($FEV_1/FVC<LLN$ and $FEV_1<70\%$); and severe airflow obstruction ($FEV_1/FVC<LLN$ and $FEV_1<50\%$) among U.S. adults aged 40-79 years, by periods 1988-1994 and 2007-2010

NHANES	Mild+ airflow obstruction			Moderate+ airflow obstruction			Severe airflow obstruction		
	1988-94	2007-10	T-test of Difference	1988-94	2007-10	T-test of Difference	1988-94	2007-10	T-test of Difference
	P† (SE)	**P† (SE)**	**p-value**	**P† (SE)**	**P† (SE)**	**p-value**	**P† (SE)**	**P† (SE)**	**p-value**
Overall	16.6 (0.8)	14.5 (0.7)	*	6.4 (0.5)	4.4 (0.4)	**	2.2 (0.2)	1.1 (0.2)	***
Age									
40-49	12.8 (1.0)	12.7 (0.9)		3.0 (0.6)	2.3 (0.6)		1.0 (0.3)	0.3 (0.2)	
50-59	16.6 (1.2)	15.2 (1.7)		6.2 (0.7)	4.5 (0.6)		2.0 (0.3)	1.1 (0.3)	
60-69	20.2 (1.2)	15.4 (1.3)	**	10.0 (1.0)	5.8 (0.7)	**	4.1 (0.6)	1.7 (0.6)	**
70-79	22.1 (1.6)	17.2 (1.5)		11.0 (1.2)	7.8 (1.0)		3.6 (0.8)	2.3 (0.5)	
Gender									
Males	19.0 (1.1)	15.4 (0.9)	**	6.8 (0.5)	4.5 (0.5)	**	2.4 (0.3)	1.1 (0.3)	**
Females	14.6 (0.9)	13.8 (1.0)		6.1 (0.6)	4.2 (0.4)	**	2.2 (0.3)	1.0 (0.2)	**
Race									
NH White	17.3 (0.8)	15.9 (0.8)		6.7 (0.5)	4.7 (0.5)	**	2.5 (0.3)	1.0 (0.2)	***
NH Black	15.9 (1.0)	13.6 (1.2)		5.8 (0.7)	4.7 (0.7)		1.5 (0.3)	1.8 (0.5)	
Mexican American	12.7 (0.8)	8.4 (0.8)	***	3.7 (0.6)	1.7 (0.3)	*	0.8 (0.2)	0.6 (0.3)	
Education									
<High school grad	18.3 (1.4)	15.3 (1.3)		7.7 (0.8)	6.6 (1.1)		2.9 (0.5)	2.0 (0.5)	
High school grad	17.2 (1.1)	17.6 (1.6)		7.7 (0.8)	5.9 (0.6)		2.2 (0.4)	1.6 (0.4)	
Some college	16.6 (1.3)	15.0 (1.1)		6.3 (0.8)	3.7 (0.6)	**	3.1 (0.7)	0.9 (0.3)	**
College graduate	12.9 (1.5)	10.9 (1.3)		2.7 (0.6)	2.3 (0.5)		0.6 (0.3)	0.1 (0.1)	
Smoking status									
Never smoker	8.0 (0.8)	8.2 (0.8)		1.9 (0.4)	1.1 (0.2)		0.7 (0.2)	0.3 (0.1)	
Ex-smoker	16.2 (1.0)	14.5 (1.3)		6.0 (0.7)	4.5 (0.7)		1.8 (0.3)	1.1 (0.3)	
Current smoker	31.8 (1.3)	34.4 (1.8)		14.9 (1.0)	14.9 (1.3)		5.8 (0.7)	3.4 (0.7)	*

†Age-specific and age-standardized weighted prevalence
*$p < 0.05$; **$p < 0.01$; ***$p < 0.001$; after Bonferroni adjustment

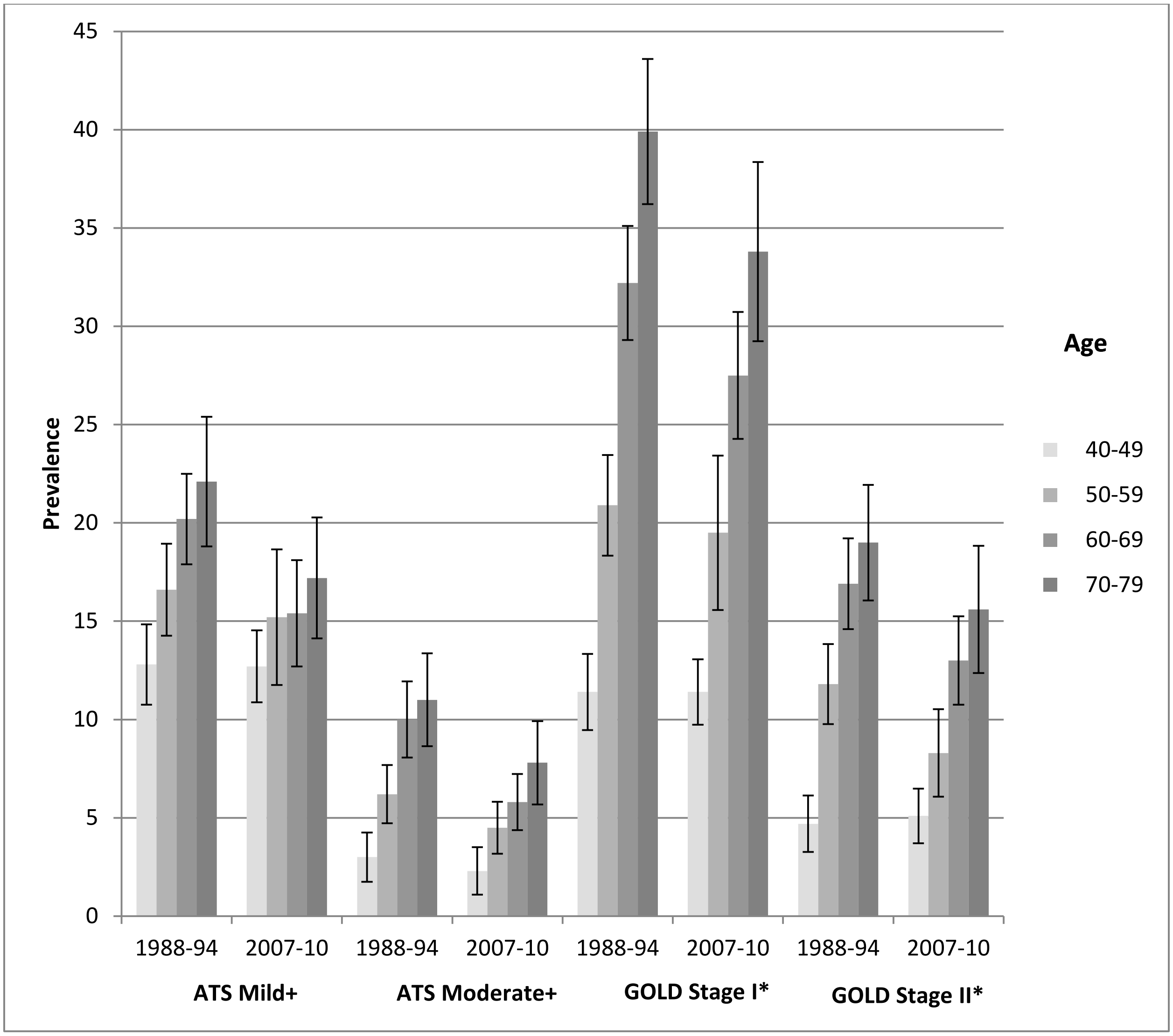

Figure 3.1. Prevalence of airflow obstruction by severity, by age category, by time period. ATS Mild+: any airflow obstruction; ATS Moderate+: Moderate and severe airflow obstruction. *Modified GOLD criteria

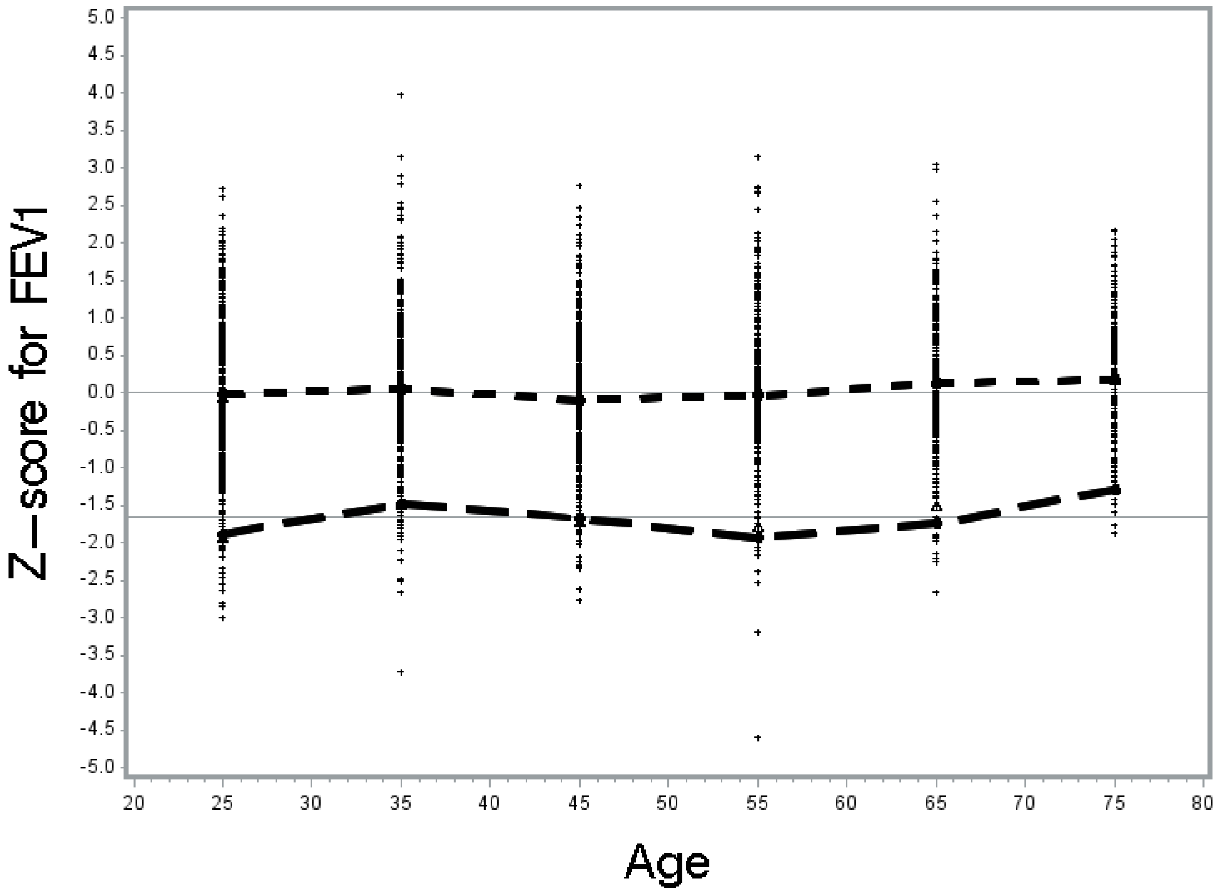

Figure 3.2. Z-score for FEV1 by age; -1.645 line is the lower limit of normal – 5th percentile; Short dashed line connects the mean z-score for each age category in relation to zero; Long dashed line connects the mean LLN for each age category

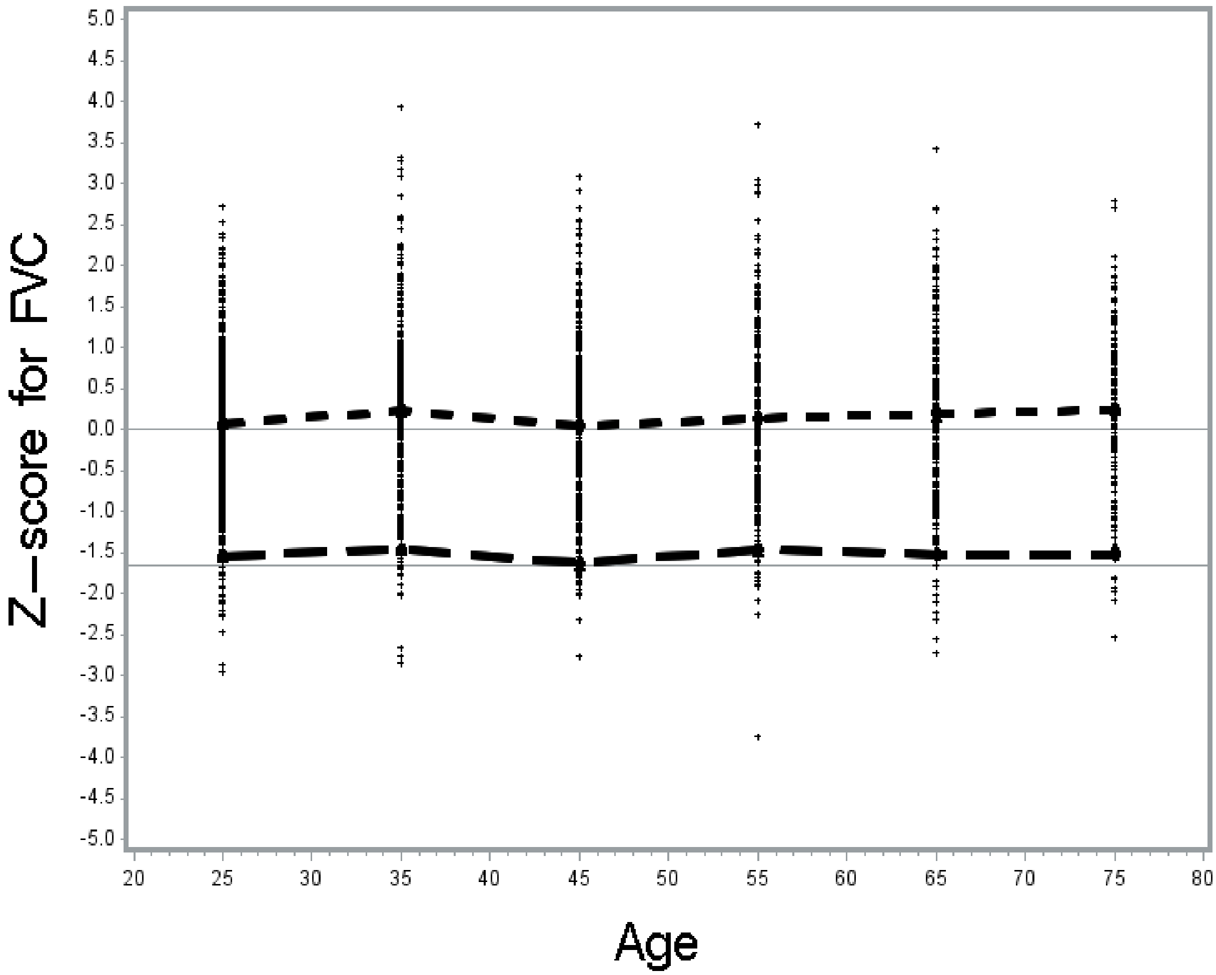

Figure 3.3. Z-score for FVC by age; -1.645 line is the lower limit of normal – 5th percentile; Short dashed line connects the mean z-score for each age category in relation to zero; Long dashed line connects the mean LLN for each age category

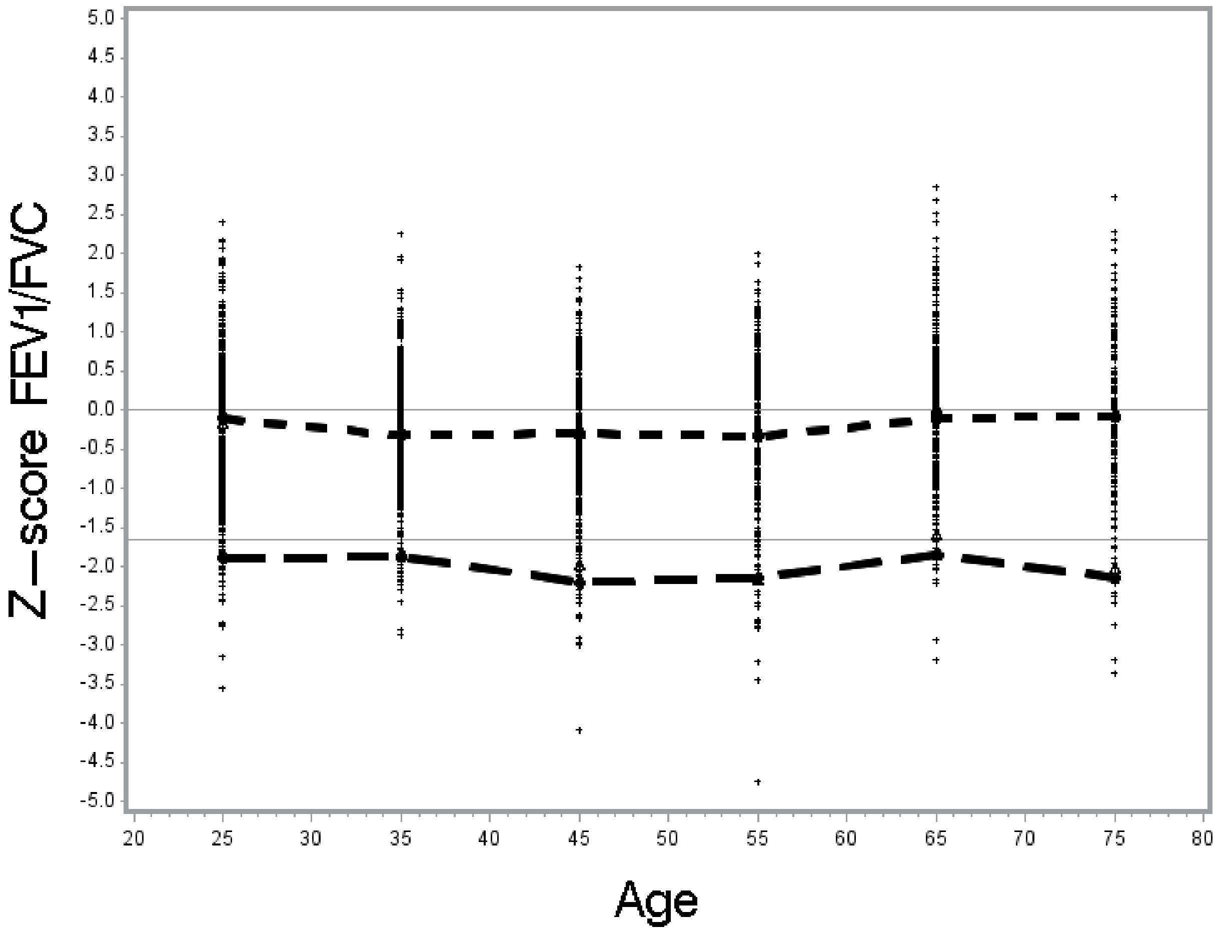

Figure 3.4. Z-score for ratio by age; -1.645 line is the lower limit of normal – 5th percentile; Short dashed line connects the mean z-score for each age category in relation to zero; Long dashed line connects the mean LLN for each age category

Chapter 4

Prevalence of Chronic Obstructive Pulmonary Disease among U.S. Working Adults Aged 40–70 Years: National Health Interview Survey Data 2004–2001

4.1 Introduction

Chronic obstructive pulmonary disease (COPD) is a primary cause of morbidity and mortality globally (1). In the U.S., COPD ranks third in causes of mortality with 100,000 deaths annually. An estimated 15.0 million people had healthcare provider diagnosed COPD in 2010, and an estimated 12.0 million potential cases were undiagnosed (2–4). The estimated total annual cost of COPD for 2010 was $49.9 billion (5). The probability of being employed is reduced by 8.6% with COPD associated disability (4).

COPD is a chronic disease usually more prevalent among older adults (6, 7). Balmes et al. (8) concluded that 15% of COPD is attributable to occupational exposure. Furthermore according to Bang et al. (9) certain occupation groups have higher prevalence of COPD, especially among services occupations. Therefore for the current study we analyzed data for working adults aged 40–70 years by occupation. This study is based on the most recently available National Health Interview Survey (NHIS) data (2004–2011) for COPD by occupation, representing a large sample of U.S. working adults. The aim of our study was to 1) estimate the prevalence of COPD among older working adults in the United States by major occupational groups, and 2) provide prevalence odds ratios (PORs) of COPD by major occupational groups.

4.2 Methods

The NHIS is an annual cross-sectional survey of the non-institutionalized U.S. population conducted by the National Center for Health Statistics of the Centers for Disease Control and Prevention (10). The NHIS survey samples are selected through a complex, multistage, probability design and the data are collected through personal interviews of participants aged ≥18 years. Informed consent was obtained from all participants and the National Center for Health Statistics Research Ethics Review Board approved the protocol. For our study, we

included years 2004–2011. Eight years of data were combined to improve the precision and reliability of the estimates. The survey response rate for the NHIS adults sampled ranged from 72.5% in 2004 to 66.3% in 2011. Questionnaires, documentation, and datasets are publicly available at
ftp://ftp.cdc.gov/pub/Health_Statistics/NCHS/Dataset_Documentation/NHIS/2011/srvydesc.pdf`

During years 2004-2011, of the 141 million estimated U.S. working adults 18 years and older, an estimated 73.8 million were 40–70 years of age. Currently working adults were defined as those who were employed during the week prior to their interview. We defined COPD based on a positive response to one or both questions:

Have you EVER been told by a doctor or other health professional that you had ...Emphysema?
DURING THE PAST 12 MONTHS, have you been told by a doctor or other health professional that you had ...Chronic bronchitis?

Demographic data were collected during the interview including self-reported age, gender, smoking status, and race; race was categorized as White, Black, and other. Information on each participant's current employment by industry and occupation was gathered and recoded by the National Center for Health Statistics (NCHS) for confidentiality reasons. Our study included the recoded 23 major occupation groups, which were based on Census Occupation Codes as reported by Standard Occupation Classification (SOC) codes (10). Participants with unknown and missing information for COPD were excluded from analysis. The occupation codes prior to 2004 are not directly comparable to the more recent data because of the changes in coding in 2004. Therefore, we analyzed 2004–2011 NHIS data (11).

4.2.1 Data Analysis

We estimated COPD prevalence for individuals aged 40–70 years for 2004–2011, by demographic characteristics, smoking status, and current occupation. SAS® 9.3 (SAS Institute Inc., Cary, NC) (12) software was used to analyze data and calculate estimated frequencies, standard errors, and prevalence rates with 95% confidence intervals (CIs). We used a logistic regression model to estimate prevalence odds ratios (PORs) by occupation. We chose management occupations as a reference group because we perceived that they have low likelihood of occupational exposure to agents that could contribute to COPD and because they were previously reported to have minimal risk of COPD (9). The overall models were adjusted for smoking status (current, former, never), age, gender, race, and pack-years of cigarette smoking (available for current smokers only). Models were also stratified by smoking status and never smoker estimates were presented.

4.3 Results

4.3.1 Overall COPD Prevalence and Prevalence by Occupational Categories

The overall COPD prevalence estimates, by gender, by race, and by education level are provided in Table 4.1. The estimated overall COPD prevalence for working adults aged 40-70 years was 4.18% (95% CI 4.01–4.34). Prevalence of COPD was higher among females (5.40%, 95% CI 5.12–5.67) and Whites (4.40%, 95% CI 4.22–4.59).

Among major occupational groups, the estimated prevalence of COPD was highest in healthcare support (7.11%, 95% CI 5.64–8.57), especially among females (7.70%, 95% CI 6.08–9.33) and Whites (8.42%, 95% CI 6.43–10.41) (Table 4.2). Food preparation and serving related occupations (6.46%, 95% CI 5.12–7.80) had the next highest COPD prevalence overall, again primarily among females (8.41%, 95% CI 6.52–10.31) and Whites (7.31%, 95% CI 5.59–9.03).

COPD prevalence among personal care and service (5.28%, 95% CI 4.14–6.42) is also of interest with higher odds in females (5.67%, 95% CI 4.39–6.94), Whites (5.67%, 95% CI 4.25–7.09) and Blacks (5.62%, 95% CI 3.06–8.18).

4.3.2 COPD Prevalence Odds Ratios by Occupational Categories as Compared with Management Occupations

Occupations that had significantly elevated associations with COPD included healthcare support (POR = 1.64, 95% CI 1.25–2.14); food preparation and serving (POR = 1.57, 95% CI 1.20–2.06); installation, maintenance, and repair (POR = 1.52, 95% CI 1.16–1.98); protective service (POR = 1.5, 95% CI 1.07–2.11); building and grounds cleaning and maintenance support (POR = 1.4, 95% CI 1.08–1.81); and office and administrative support (POR = 1.25, 95% CI 1.04–1.51).

Among never smokers, occupations associated with COPD included food preparation and serving (POR = 2.34, 95% CI 1.52–3.60); protective service (POR = 2.11, 95% CI 1.27–3.49); office and administrative support (POR = 1.51, 95% CI 1.11–2.07); and education, training, and library (POR = 1.44, 95% CI 1.05–1.98).

Occupations with significant PORs differed by gender. Females had elevated PORs among workers in protective services (POR = 2.12, 95% CI 1.31–3.42); food preparation and serving (POR = 1.72, 95% CI 1.25–2.37); healthcare support (POR = 1.70, 95% CI 1.24–2.33); and office and administrative support (POR = 1.34, 95% CI 1.06–1.70). In contrast, the only significant PORs for males were among education, training, and library (POR = 1.79, 95% CI 1.17–2.75); building and grounds cleaning and maintenance (POR = 1.68, 95% CI 1.17–2.42); and installation, maintenance, and repair (POR = 1.41, 95% CI 1.04–1.93).

Results from the race-specific analyses identified Whites as the subgroup with higher risk of COPD (Table 4.3). There were significantly elevated associations of occupation with COPD among workers in health care support (POR = 1.80, 95% CI 1.33–2.44); food preparation and serving (POR = 1.61, 95% CI 1.20–2.18); protective service (POR = 1.57, 95% CI 1.08–2.30); installation, maintenance, and repair (POR = 1.53, 95% CI 1.14–2.03); building and grounds cleaning and maintenance support (POR = 1.41, 95% CI 1.07–1.85); transportation and material moving (POR = 1.36, 95% CI 1.01–1.84); construction and extraction (POR = 1.35, 95% CI 1.00–1.81); office and administrative support (POR = 1.31, 95% CI 1.07–1.60) and education training and library (POR = 1.28, 95% CI 1.01–1.62).

4.4 Discussion

During 2004–2011, the overall prevalence of self-reported doctor-diagnosed COPD among working adults aged 40–70 years was 4.18% and increased with age from 3.75% for 40–54 to 5.13% for 55–70 years old. COPD prevalence was higher among females, Whites, and current smokers which was consistent with previous findings (9). Results from a study using Behavioral Risk Factor Surveillance System (BRFSS) data showed that the prevalence of self-reported doctor-diagnosed COPD (or chronic bronchitis or emphysema) among all U.S. adults increased with age from 6.6% for adults age 45–54 to 12.1% for those age 65–74 for the year 2011 (2). However, overall prevalence of COPD in our study among working adults was lower than the BRFSS estimates that would include non-working individuals with COPD associated disability.

The COPD prevalence estimates vary by occupation. As compared with overall working adults, workers in services occupations including healthcare support, food preparation and serving, and personal care and service occupations had higher COPD prevalence in our study and that of Bang et al. (9). Various factors have been associated with COPD and smoking is one of the most important risk factors (2, 13, 14). Smoking prevalence estimates among the above listed service occupations were 20% or higher and exceeded the Healthy People 2020 goal of ≤ 12% (13, 15). The prevalence of COPD for current smokers in comparison to never smokers was 5.7 times higher for personal care and service, 3.7 times higher for the healthcare support occupation, and 2.5 times for protective service. Generally, smoking and occupational exposures have been shown to have an interactive effect on an additive scale on COPD (14).

It has been estimated that 15% of COPD is attributable to occupational exposure (8). Vapors, gas, dust and fume exposures have been shown to be associated with COPD among workers in various occupations and industries (9, 16–20). Exposure to organic dust and other sensitizing agents in agricultural and food workers can lead to respiratory conditions including COPD (21). Among construction workers, exposure to inorganic dust may lead to higher COPD morbidity and mortality (22). Yet COPD prevalence among construction and agriculture was not as high as the overall working population, probably because of the selected age groups and the fact that the mean age in construction was 39 years for the overall working population (mean age not included in tables) and results were based on the current job in an older population where study participants likely had prior jobs that are not reflected in the analysis. Chronic exposure to coal and silica dust increases risk of COPD in miners (8, 23).

COPD prevalence estimates also varied by gender. Overall, females had higher prevalence than males which is consistent with findings reported by Ford et al. (24). Various factors have been associated with COPD among women, some of which are smoking, environmental tobacco smoke, biological differences, occupational exposure, or a combination of all these factors (25, 26). In our study, females employed in protective service; food preparation and serving; production; and transportation and material moving had COPD prevalence estimates that were two to four times higher than males. This is consistent with a previous study by Bang et al. (9) and a review publication by Varkey (27).

As compared to management occupations, the odds of having COPD were significantly higher among all workers in healthcare support; protective service; food preparation and serving related; building and grounds cleaning and maintenance; and installation, maintenance, and repair even after adjustment. This is also consistent with studies by Bang et al. (9) and Hnizdo et al. (28).

This study has some limitations. Disease classification and subsequent prevalence rates were based on self-reports of health care professional diagnosed emphysema and/or chronic bronchitis. Although spirometry may have been used in the COPD diagnosis, spirometry information was not collected in the NHIS study. Self-report of COPD is prone to recall bias. Chronic bronchitis may be confused with acute bronchitis and this may have resulted in misclassification (29). Additionally, some of the gender-related differences we found where females had higher prevalence of COPD may be due to higher likelihood of females visiting a doctor. In our analysis, we adjusted for smoking status (current, former smoker, never smoker) and for pack-years of cigarette smoking among current smokers. However, the data did not contain information to allow us to adjust for pack-years among former smokers. In addition, the cross-sectional study design has limitations for determining causality; the current job may not be the one that contributed to COPD, and may be affected by the presence of disease and the management reference group may be populated with individuals who had previous, higher exposure jobs.

Information detailing occupational history on the type of jobs held was not collected and was limited to employment in the week prior to the interview, considering latency, the job with causal exposure may not be reflected in the analysis. However Gomez-Marin et al. (30) concluded that for many occupational subgroups, the current occupation may represent the longest-held job. No information on occupational exposures was collected. We restricted our study to those aged 40–70 years to estimate COPD in the older age groups when the onset of COPD is more likely to occur. The cutoff of 70 years was used with the assumption that workers could have changed to a job with less exposure.

4.5 Conclusion

The present study conducted from 2004–2011 represents the most recently available data on COPD prevalence in the U.S. working population and among specific occupational categories. Prevalence estimates varied by occupation suggesting that workplace exposures in addition to different smoking habits may contribute to the COPD risk. Preventive measures such as reduction of occupational exposure (14) and interventions to reduce smoking may reduce the prevalence of COPD (31). Healthcare providers should continue screening and surveillance for work-related COPD and epidemiologic studies are needed to monitor changes in COPD prevalence among workers in at risk occupations and industries.

4.6 References

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Table 4.1. Estimated number of U.S. working adults (40–70 years) and prevalence of self-reported physician diagnosed COPD by selected characteristics, 2004–2011

Characteristic	**N†**	**COPD P***	**95% CI**
Age			
40 - 54	50,825	3.75	3.54–3.95
55 - 70	22,974	5.13	4.76–5.49
Gender			
Male	38,739	3.07	2.85–3.28
Female	35,060	5.40	5.12–5.67
Race			
White	61,952	4.40	4.22–4.59
Black	7,762	3.41	2.98–3.83
Other	4,086	2.15	1.65–2.66
Smoking status	73,799		
Current	14,220	7.47	6.96–7.97
Former	17,933	4.92	4.50–5.33
Never	41,024	2.74	2.54–2.94
Unknown/missing	622	-	-
Total	73,799	4.18	4.01–4.34

†Annual average estimates are per 1,000 population
P* Prevalence Estimates
- Prevalence estimates not calculated for missing or unknown values

Table 4.2. Estimated prevalence of COPD, by occupation, gender, and race — U.S. working adults 40–70 years, 2004–2011

Occupation	Overall			Males			Females			Whites			Blacks		
	N†	COPD P*	95% CI	N†	COPD P*	95 % CI	N†	COPD P*	95 % CI	N†	COPD P*	95 % CI	N†	COPD P*	95 % CI
Management	8,440	3.22	2.75–3.68	5,465	2.64	2.08–3.19	2,975	4.29	3.45–5.13	7,548	3.22	2.74–3.71	489	4.43	2.15–6.71
Business and financial operations	3,358	3.58	2.82–4.35	1,575	1.83	0.95–2.71	1,782	5.13	3.92–6.34	2,837	3.61	2.77–4.45	308	4.38	1.98–6.77
Computer and mathematical	1,742	2.61	1.68–3.54	1,215	2.51	1.39–3.63	527	2.84	1.29–4.38	1,460	2.68	1.64–3.73	130	-	-
Architecture and engineering	1,546	1.88	1.05–2.72	1,368	1.50	0.72–2.28	178	-	-	1,355	1.98	1.04–2.91	51	-	-
Life, physical, and social science	730	3.03	1.59–4.47	407	-	-	323	4.78	2.26–7.31	632	3.18	1.57–4.80	32	-	-
Community and social services	1,294	3.97	2.87–5.06	533	3.52	1.45–5.58	761	4.28	2.89–5.67	999	4.11	2.83–5.39	235	-	-
Legal	958	3.65	2.34–4.96	510	-	-	448	4.73	2.62–6.84	866	3.62	2.21–5.02	62	-	-
Education, training, and library	4,887	4.50	3.79–5.22	1,175	4.14	2.71–5.57	3,712	4.62	3.78–5.46	4,302	4.66	3.86–5.45	436	3.96	2.11–5.81
Arts, design, entertainment, sports, and media	1,282	3.95	2.59–5.31	648	3.71	1.83–5.59	634	4.19	2.23–6.15	1,160	3.54	2.18–4.90	67	-	-
Healthcare practitioners and technical	4,067	3.82	3.10–4.54	1,056	2.82	1.59–4.06	3,011	4.17	3.32–5.02	3,334	4.11	3.29–4.94	423	3.46	1.37–5.54
Healthcare support	1,442	7.11	5.64–8.57	170	-	-	1,272	7.70	6.08–9.33	994	8.42	6.43–10.41	367	4.47	2.65–6.29
Protective service	1,345	4.45	3.18–5.71	1,056	3.18	1.91–4.46	289	9.05	5.63–12.48	1,047	4.86	3.29–6.43	249	3.06	1.48–4.63
Food preparation and serving related	2,221	6.46	5.12–7.80	718	2.39	1.23–3.54	1,502	8.41	6.52–10.31	1,652	7.31	5.59–9.03	370	4.56	2.50–6.62
Building and grounds cleaning and maintenance	3,069	4.86	4.01–5.72	1,699	4.32	3.15–5.50	1,369	5.53	4.10–6.97	2,424	5.23	4.23–6.24	488	3.43	1.95–4.91
Personal care and service	2,088	5.28	4.14–6.42	368	-	-	1,719	5.67	4.39–6.94	1,590	5.67	4.25–7.09	311	5.62	3.06–8.18
Sales and related	6,916	3.93	3.37–4.50	3,694	2.98	2.21–3.75	3,222	5.02	4.20–5.84	6,076	4.26	3.62–4.90	442	-	-
Office and administrative support	9,690	5.32	4.76–5.89	2,131	2.96	1.99–3.93	7,559	5.99	5.32–6.65	8,160	5.66	5.01–6.31	1,093	4.16	2.87–5.46
Farming, fishing, and forestry	428	3.43	1.51–5.34	320	-	-	108	-	-	369	3.44	1.37–5.52	28	-	-
Construction and extraction	3,822	3.91	3.08–4.73	3,701	3.81	2.97–4.64	121	-	-	3,394	4.20	3.29–5.12	315	-	-
Installation, maintenance, and repair	2,830	4.31	3.42–5.20	2,714	3.98	3.09–4.87	116	-	-	2,457	4.46	3.45–5.48	240	-	-
Production	5,032	4.01	3.40–4.62	3,421	3.00	2.31–3.70	1,611	6.15	4.82–7.48	4,112	4.41	3.67–5.15	591	3.07	1.76–4.39
Transportation and material moving	4,306	4.41	3.54–5.28	3,501	3.75	2.91–4.59	805	7.25	4.37–10.13	3,439	4.88	3.80–5.97	685	1.78	0.82–2.73
Military	85	-	-	51	-	-	35	-	-	60	-	-	16	-	-
Refused, not ascertained, don't know	2,222	1.79	2.91–4.59	1,242	1.01	0.43–1.59	980	2.78	1.68–3.88	1,686	1.81	1.12–2.49	334	-	-
Total	73,799	4.18	4.01–4.34	38,739	3.07	2.85–3.28	35,060	5.40	5.12–5.67	61,952	4.40	4.22–4.59	7,762	3.406	2.98–3.83

†Estimated annual average per 1,000 working population
- Relative standard errors greater than 30% are not reported
P* Prevalence estimates

Table 4.3. Adjusted COPD prevalence odds ratios POR by occupation for specific groups — U.S. working adults 40–70 years, 2004–2011

Occupation	Overall		Never Smokers		Males		Females		Whites	
	POR	**95% CI**	**POR**	**95% CI**	**POR**	**95% CI**	**POR**	**95% CI**	**POR**	**95% CI**
Management	1.00		1.00		1.00		1.00		1.00	
Business and financial operations	1.01	0.77–1.33	1.25	0.83–1.89	0.72	0.42–1.22	1.21	0.87–1.67	1.00	0.74–1.34
Computer and mathematical	0.95	0.63–1.44	0.95	0.57–1.59	1.11	0.67–1.84	0.73	0.39–1.35	0.96	0.61–1.50
Architecture and engineering	0.70	0.43–1.14	-	-	0.57	0.32–1.02	-	-	0.72	0.43–1.21
Life, physical, and social science	0.91	0.54–1.53	-	-	-	-	1.16	0.63–2.11	0.93	0.53–1.64
Community and social services	1.15	0.82–1.59	1.35	0.79–2.30	1.59	0.83–3.06	1.02	0.69–1.51	1.15	0.80–1.66
Legal	1.13	0.76–1.66	1.10	0.60–2.01	-	-	1.13	0.69–1.86	1.12	0.73–1.71
Education, training, and library	1.23	0.98–1.54	**1.44**	**1.05–1.98**	**1.79**	**1.17–2.75**	1.18	0.89–1.56	1.28	1.01–1.62
Arts, design, entertainment, sports, and media	1.13	0.77–1.66	1.11	0.59–2.07	1.46	0.82–2.58	0.97	0.57–1.65	1.01	0.66–1.54
Healthcare practitioners and technical	1.02	0.79–1.32	1.34	0.92–1.96	1.27	0.76–2.11	1.03	0.76–1.39	1.07	0.82–1.41
Healthcare support	**1.64**	**1.25–2.14**	1.57	0.98–2.49	-	-	**1.70**	**1.24–2.33**	**1.80**	**1.33–2.44**
Protective service	**1.50**	**1.07–2.11**	**2.11**	**1.27–3.49**	1.21	0.76–1.93	**2.12**	**1.31–3.42**	**1.57**	**1.08–2.30**
Food preparation and serving related	**1.57**	**1.20–2.06**	**2.34**	**1.52–3.60**	1.08	0.62–1.87	**1.72**	**1.25–2.37**	**1.61**	**1.20–2.18**
Building and grounds cleaning and maintenance	**1.40**	**1.08–1.81**	1.55	0.99–2.43	**1.68**	**1.17–2.42**	1.19	0.82–1.72	**1.41**	**1.07–1.85**
Personal care and service	1.25	0.94–1.66	0.96	0.61–1.52	1.41	0.57–3.49	1.26	0.91–1.73	1.24	0.90–1.70
Sales and related	1.05	0.84–1.33	1.41	0.97–2.04	1.07	0.74–1.55	1.06	0.80–1.40	1.13	0.89–1.44
Office and administrative support	**1.25**	**1.04–1.51**	**1.51**	**1.11–2.07**	1.08	0.72–1.62	**1.34**	**1.06–1.70**	**1.31**	**1.07–1.60**
Farming, fishing, and forestry	1.17	0.64–2.13	-	-	-	-	-	-	1.09	0.58–2.08
Construction and extraction	1.29	0.97–1.71	-	-	1.29	0.93–1.79	-	-	**1.35**	**1.00–1.81**
Installation, maintenance, and repair	**1.52**	**1.16–1.98**	1.34	0.74–2.43	**1.41**	**1.04–1.93**	-	-	**1.53**	**1.14–2.03**
Production	1.17	0.94–1.46	1.21	0.84–1.74	1.05	0.77–1.42	1.32	0.96–1.81	1.22	0.97–1.55
Transportation and material moving	1.30	0.99–1.71	1.53	0.90–2.62	1.26	0.90–1.77	1.48	0.90–2.42	**1.36**	**1.01–1.84**

\- Refused, not ascertained, don't know
Military was excluded from analysis because of relative standard errors > 30%
Overall adjusted for age, gender, race, smoking status, and pack-years
Never Smokers adjusted for age, gender, and race
Gender adjusted for age, race, smoking status, and pack-years
Whites adjusted for age, gender, smoking status, and pack-years

Chapter 5

Summary of the Research

Chapter 5

5.1 Summary

Chronic obstructive pulmonary disease (COPD) is a preventable disease that causes excess morbidity and mortality in older populations (1). A primary risk factor is tobacco smoking, but occupational exposure to VGDF also contributes to the burden of the disease. The goal of this study was to gain additional understanding about occupational risk factors for COPD by using data from three population-based cross-sectional studies. The three studies were used to explore different aspects of the relationship between COPD and occupational exposure, and each study provides additional insight into the understanding of COPD and contributed to the overall goal of the study. The three studies are detailed in Chapters 2–4. Chapter 2 incorporates the objectives of both Aim 1 and Aim 2. Aim 1 involves developing a generalizable job exposure matrix (JEM) for COPD. Aim 2 involves applying the JEM to a population based study, in this case the Multi-Ethnic Study of Atherosclerosis (MESA) lung study, to establish an association between COPD and occupational exposure. Aim 3 of the study (Chapters 3 and 4) was addressed through estimating prevalence of COPD in the U.S. population and its major occupational groups. Chapter 3 reports on the prevalence of airflow obstruction based on spirometry and compared the prevalence for two sampling periods 1988–1994 and 2007–2010 of the National Health and Nutrition Examination Surveys (NHANES). Chapter 4 reports on the prevalence of COPD for major occupational groups based on self-report of doctor-diagnosed chronic bronchitis or emphysema for years 2004–2011 using the National Health Interview Survey (NHIS) data.

In the MESA study (Chapter 2), an expanded JEM for COPD was created based upon the methodology used by Blanc et al. (2) for an overall general VGDF exposure classification for detailed occupational groups. The JEM provided an assessment of VGDF exposure for overall dust exposure, and subcategories of mineral dust and organic dust, vapor-gas, and fumes, in terms of the potential level of exposure (low, medium and high) as assigned by industrial hygiene experts. The JEM was then applied to estimate an association between potential occupation exposure levels and various COPD outcomes. Adjusted odds ratios were significantly increased for the association of airflow limitation with the high level of overall dust exposure, especially among males, and organic dust exposure for females. Adjusted odds ratios were also significantly increased for the association of airflow limitation with self-report of severe VGDF exposure, vapor-gas exposure, and exposure all three VGDF agents (vapor-gas, dust, and fumes). Self-report of physician diagnosis of COPD was associated with self-report of dust, vapor-gas, severity of VGDF exposure, years of VGDF exposure, and number of VGDF agents. Self-report of Medical Research Council defined chronic bronchitis (3) was associated with the self-reported VGDF exposures listed above for COPD and additionally with exposure to dust and fumes (see Tables 2.2, 2.4, 2.5, Chapter 2).

In general, the significant associations of COPD, chronic bronchitis, and wheeze with occupational exposure were stronger among never smokers. The association of airflow limitation with the interaction of smoking and occupational exposures was investigated. Never smokers with no occupational exposure were used as the reference group. There was an increasing trend in odds ratios including the last category of ever smokers with occupational exposure (a similar trend was found by Blanc et al. (2)). Our study adds to the knowledge and understanding of the association of COPD with VGDF exposure ascertained both through a COPD JEM and VGDF exposure questions (Tables 2.2 – 2.5, Chapter 2).

Study 2 (Chapter 3) provided the prevalence of COPD in the U.S population as determined by spirometry defined airflow obstruction and compared the study periods in NHANES 1988–1994 to NHANES 2007–2010. Overall, the prevalence of airflow obstruction declined from 1988–1994 to 2007–2010. The prevalence of airflow obstruction significantly declined from 16.6% in 1988–1994 to 14.5% in 2007–2010. Moderate or worse airflow obstruction declined from 6.4% in 1988–1994 to 4.4% 2007–2010.

Study 3 (Chapter 4) was based on the NHIS data for years 2004–2011. Overall estimated prevalence of self-reported COPD (bronchitis and emphysema) was 4.18% and the estimated COPD prevalence for major occupational groups ranged from 7.11% for healthcare support to 1.88% for architecture and engineering. The occupation groups greater than the national average were healthcare support (7.11%); food preparation and serving (6.46%); office and administrative support (5.32%); personal care and service (5.28%); building and grounds cleaning and maintenance (4.86%); education, training, and library (4.5%); protective service (4.45%); transportation and material moving (4.41%); and installation, maintenance, and repair (4.31%). Females and Whites had the highest COPD prevalence.

Study 3 also estimated prevalence odds ratios (POR) for major occupational groups using management as a reference group. The adjusted PORs that reached statistical significance were healthcare support (POR=1.64, 95% CI 1.25–2.14), food preparation and serving (POR=1.57, 95% CI 1.20–2.06), installation, maintenance, and repair (POR=1.52, 95% CI 1.16–1.98), protective service (POR=1.50, 95% CI 1.07–2.11), building and grounds cleaning and maintenance (POR=1.40, 95% CI 1.08–1.81), and office and administrative support (POR=1.25, 95% CI 1.04–2.51). These results are consistent with results found by Bang et al. (4) when evaluating NHIS 1997–2004 data.

Service occupations with higher COPD prevalence also had higher smoking prevalence, which is a major risk factor for COPD. The prevalence of COPD among current smokers in service occupations (protective service; healthcare support; and personal care and service) was 2.5 – 5.7 times greater than that of never smokers. CDC authors reported prevalence of current cigarette smoking as 16.4% among protective service workers, 23.7% among healthcare support workers, and 19.7% among personal care and service workers (5).

Never smokers were also investigated for COPD prevalence because stratification by smoking status would eliminate smoking as a confounder. Among never smokers, significant PORs for COPD were highest in food preparation and serving related occupations (POR = 2.34) followed by protective service (POR 1.5), office and administrative support occupations (POR = 1.51), and education, training and library occupations (POR = 1.44). Odds of COPD were significantly elevated for most of these occupational groups where VGDF exposure risks are often present.

5.2 Significance

The goal and focus of this study was to investigate the prevalence of COPD outcomes in several cross-sectional studies and estimate their association with occupational risk factors such as vapors-gas, dust or fumes (VGDF), or the association with occupational categories. Included in the goal was to develop and test a job exposure matrix for COPD outcomes. COPD was assessed using good quality spirometry as an objective measure. Important COPD outcome associations were found with VGDF exposures. Exposure to noxious respirable agents in combination with smoking can result in COPD occurrence with unusual severity and/or frequency (6). An important confirmation that smoking and exposure to VGDF had increased odds of COPD compared to never smokers not exposed was found in this study.

5.3 Strengths and Limitations

A major strength of this study is that we used three large study populations. Additionally, the MESA study was designed to heavily sample minority groups, and NHANES and NHIS were both large U.S. population based cross-sectional samples. NHIS had a large working population. MESA contained 3-digit occupation codes (coded by NIOSH) and provided detailed information about employment (and allowing the application of the COPD JEM). NHANES and MESA both had spirometry on a large number of individuals so that we could determine those with airflow obstruction. NHIS had occupational coding (although only at the 2-digit level) to allow comparison of occupational groups and to make prevalence estimates. A JEM for COPD was created and applied to the MESA study. The JEM, along with self-report of occupational exposure to VGDF helped us better understand occupational exposure.

A limitation of the MESA data was the lack of information about the longest held job and the COPD JEM could only be applied to the last job the worker held. The non-availability of NHANES 3-digit occupational codes to apply the COPD JEM was another limitation. However, NIOSH is working with NHANES National Center for Health Statistics scientists to provide the codes. NHIS and NHANES are both publically available only in 2-digit occupational codes which limit the ability to assess COPD risk through application of a COPD JEM. The generalizable JEM will be made publicly available and also in the future will be applied to the three-digit occupational codes for NHANES studies developed by NIOSH.

Self-report of health care provider diagnosed COPD based on emphysema or chronic bronchitis was available through NHIS. There was no spirometry performed as a part of NHIS which may have provided a more objective measure. However, spirometry may have been part of the COPD diagnosis. In the survey, acute bronchitis may have been misclassified as chronic bronchitis (7). COPD self-report may also be susceptible to recall bias.

5.4 Future Research

Future research should involve refining the COPD job exposure matrix and improving our 3-digit JEM (participants also have an occupational history) and investigating the feasibility of using a 2-digit COPD JEM. Also we plan to apply the COPD JEM to NHANES 3-digit occupational data that was coded by NIOSH and make the JEM available to the public. Our proposed study for the application of our JEM to the MESA CT scans providing the percentage with emphysema for over 6400 participants has been approved by the MESA committee.

5.5 Conclusion

The prevalence COPD is increasing globally and it has broad public health impacts. Our results indicate that the prevalence of COPD in the U.S. is declining; however it still remains the third leading cause of mortality. The odds of COPD are significantly higher among those exposed to VGDF.

In the first study, significant associations were found between the prevalence of airflow limitation and occupational exposure determined by self-reported exposure and JEM assigned scores. There was an indication of an increased risk of COPD when both smoking and VGDF exposures were present. We developed an expanded COPD JEM for use in future studies. Chronic bronchitis and wheeze each were associated with self-reported exposures (vapor-gas, dust, fumes, and VGDF exposure severity, years of exposure, and number of agents).

In the second study, the prevalence of ATS-defined airflow obstruction decreased significantly from 1988–1994 to 2007–2010. The study provided estimates of approximately 18.3 million adults aged 40–79 with mild+ airflow obstruction, 5.6 million with moderate+ airflow obstruction, and 1.4 million with severe airflow obstruction in the current U.S. population.

The third study conducted from 2004–2011 presents COPD prevalence in the U.S. working population and among specific occupational categories. Prevalence estimates varied by occupation suggesting that workplace exposures in addition to different smoking habits may contribute to the COPD risk. The occupations with the highest PORs included healthcare support; food preparation and serving; installation, maintenance, and repair; protective service; and building and grounds cleaning and maintenance all of which have potentially significant exposures to VGDF.

The three studies described in this project were population based studies which help provide direction for worker health surveillance. Lewis and Fishwick (8) provided an in-depth review of health surveillance for occupational respiratory disease. With respect to COPD, the objectives of health surveillance include quantification of the exposure health risk, identification of groups at risk for COPD, collection of COPD epidemiological data, and early detection of COPD so that the worker could be removed from the exposure or the exposure could be controlled. Fishwick et al. (9) investigated the causation of COPD by workplace exposures. It is important to determine how much of COPD is caused by workplace exposure on the working population level and the individual level for disease prevention and obtaining workers' compensation. COPD experts and occupational lung disease experts provided occupational contribution ratings for COPD cases with varying combinations of smoking exposures and occupational exposure from employment history based on hypothetical cases of COPD. The clinical raters from their occupational attribution of COPD causation made recommendations about a change of work or continuation of work in the same job. Guidotti (10) discussed the workers' compensation challenges and the new requirements in California to adopt evidence-based criteria for impairment assessment and treatment through apportionment by cause. The results of our research can better inform the health care provider about COPD in the population and the VGDF exposures to better assess the occupation contribution to COPD.

Preventive measures such as reduction of occupational exposure (2) through engineering controls, administrative controls, and an adequate respiratory protection program and interventions to reduce smoking such as smoking cessation programs may reduce the prevalence of COPD (11). COPD screening and surveillance by healthcare providers of workers exposed to VGDF should be provided to increase the awareness among workers and epidemiologic studies are needed to track changes in the COPD prevalence among workers in at risk occupations and inform workers and employers in high risk occupations to increase awareness and target preventions. Based on the results of our study and literature review some recommendations for future actions with regard to workers' COPD prevention include more resources for prevention; increasing worker participation in prevention, surveillance, and VGDF exposure reduction programs; equipping health care professionals' with additional skills in determining VGDF occupational exposure hazards and COPD diagnosis (10).

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