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## 1.0 Executive Summary

**Background:** Occupational exposure to respirable coal mine dust can cause a broad spectrum of respiratory diseases, encompassed by the term coal mine dust lung disease (CMDLD).[2] Prevalence rates of coal workers' pneumoconiosis (CWP) and progressive massive fibrosis (PMF) have risen to levels not seen since the 1970s among both active and former miners in the United States (U.S.).[1,2] Our understanding of this resurgence has relied almost exclusively on chest imaging evidence measured at one point in time. This very likely underestimates the true burden of disease given that significant morbidity from lung function impairment may be found absent radiographic abnormalities. Lung function impairment has not been extensively explored in this population, and as noted above there is a paucity of information on cardiovascular disease (CVD). CMDLDs confer significantly increased risk for mortality in affected workers as well.[3–7] Earlier reports based on death certificates coded for pneumoconiosis showed that deaths from this disease in the U.S. decreased from 1968 through 2006, and cited more stringent dust regulations and declining coal mine employment as major reasons for this trend.[8,9] Follow-up of one of these studies found that years of potential life lost per decedent had increased between 1999 and 2016, suggesting increased disease severity in recent decades.[10] These studies were not based exclusively on populations of coal miners and did not address other nonmalignant respiratory diseases (NMRD) such as chronic obstructive pulmonary disease (COPD). Recent increases in CWP prevalence and its most severe form, PMF,[2,11,12] may have led to reversal in this mortality trend. Even less is known about risk of CVD and other causes of mortality in miners despite the presence of stressors such as noise, vibration, shift work, prolonged work hours/overtime, and diesel exhaust, all of which have been associated with adverse health outcomes with the potential for increased mortality.[13,14]

**Methods:** We used data from four primary sources for this work, including the National Institute for Occupational Safety and Health's (NIOSH) Coal Workers' Health Surveillance Program (CWHSP); the U.S. Department of Labor's (DOL) Federal Black Lung Program (FBLP); the National Death Index (NDI); and detailed clinic data from one black lung medical provider in West Virginia. We linked all of these data sets to better characterize miners' health over their lifetime from the time they were actively working (CWHSP), to post-coal mining career (FLBP), to death (NDI). We characterized the radiographic and physiologic progression of disease for those miners with at least two International Labour Office (ILO) classifications of chest radiographs (CXRs) and lung function tests across either the FBLP or CWHSP data sets. We described the relationship between radiographic severity of disease and findings from multiple tests including spirometry, diffusion capacity, arterial blood gas tests, and cardiopulmonary exercise tests (CPET) to better understand lung function impairment in U.S. coal miners, even in the absence of radiographic disease. Finally, we performed an all-cause mortality analysis of the linked data to examine predictors of death from non-malignant respiratory and cardiovascular disease. The major explanatory and confounding variables we proposed to explore included mining tenure, measures of lung function, radiographic severity of pneumoconiosis, geographical region, and smoking status.

**Results:** Our findings on radiographic progression demonstrate that CWP can develop and/or progress rapidly to PMF absent further coal mine dust exposure. We found that 42% of miners who had no evidence of CWP at their baseline CXR had developed simple CWP and 3% had developed PMF by the time of their FBLP claim. Likelihood of progression to PMF was most

significantly associated with increasing small opacity profusion on earlier CXR, controlling for region and coal mine employment tenure. In our examination of progression of lung function decline, we found that having mined in Central Appalachia was associated with worsening mean forced expiratory volume in one second ($FEV_1$) percent predicted (pp) compared to miners from the rest of the U.S., controlling for age, years between tests, and coal mine employment tenure. After controlling for the confounding effect of smoking, we found that the time between spirometry tests was the strongest predictor of progression, suggesting that former miners should receive frequent lung function testing to monitor and/or intervene to impede the loss of further lung function.

In our analyses of the expanded physiologic test data from one West Virginia black lung clinic, we demonstrate that these additional physiologic tests, including diffusion capacity, arterial blood gas, and CPETs are critical for understanding the true burden of disease and impairment in this population of workers. Moderate to severe diffusion impairment was frequently observed in this large population of former coal miners, even among those with normal $FEV_1$.

The findings from our mortality study, the largest and most comprehensive to date, demonstrate that U.S. coal miners experience excess mortality from respiratory diseases including pneumoconiosis, chronic lower respiratory diseases, and lung cancer, compared to total U.S. and Central Appalachian populations. Of great concern, these associations are highest in the most recent birth cohort, consistent with current reports of increasing prevalence of CMDLD and PMF.

**Conclusions:** This body of work has been the most comprehensive attempt to date to characterize the full spectrum of CMDLD among U.S. coal miners and elucidate longitudinal trends in their health as a result of their occupational exposures. Our findings regarding progression of radiographic severity and lung function decline underscore the importance of continued medical surveillance of miners even after leaving the workforce. Notably, the absence of radiographic pneumoconiosis after dust exposure has ceased does not preclude development of PMF at a later time. We found that measures from additional physiologic tests such as diffusion capacity permits detection of an additional population of former coal miners with pulmonary impairment associated with coal mine dust exposure beyond that identified using CXRs and spirometry alone. Our findings highlight the increased relative contribution of obstructive lung disease to CMDLD mortality and underscores the importance of coal mine dust exposure as an important cause of occupational obstructive lung disease.

**2.0 Contents**

## 3.0 Problem Statement and Objective

**Background Information:**

Occupational exposure to respirable coal mine dust can cause a broad spectrum of respiratory diseases, encompassed by the term coal mine dust lung disease (CMDLD).[2] These lung diseases, which include the pneumoconioses, continue to occur in spite of reportedly reduced dust levels in many coal mines.[15] It is now widely recognized that prevalence rates of coal workers' pneumoconiosis (CWP) and its most severe form, progressive massive fibrosis (PMF), have risen to levels not seen since the 1970s in the U.S. This trend has been observed among active coal miners participating in the Coal Workers' Health Surveillance Program (CWHSP),[1,16,17] as well as among former miners applying for Federal Black Lung Program (FBLP) benefits.[2] The Central Appalachian states of Kentucky, Virginia, and West Virginia have seen the steepest increases in rates of this debilitating disease.[1,2,16,18–20]

While this alarming increase in severe disease has been well-documented, there have been fewer studies of the rate of disease progression, both radiographically and physiologically, over the lifetime of the miner. Historically CWP has been characterized as slowly progressive,[21] but recent reports have documented the increase in cases of rapidly progressive pneumoconiosis (RPP), usually defined as an increase in small opacity profusion of more than one International Labour Office (ILO) subcategory on chest radiograph (CXR) over five years, and/or the development of PMF after 1985.[19,22] Recent CWHSP data from active working miners who developed PMF showed that the mean time from a normal CXR to PMF was approximately 21 years, with some progressing to PMF in less than ten years.[23] Our analysis of progression among former miners in the FBLP indicated that progression to PMF can occur in as little as two years after evidence of simple CWP.[24] The progression of disease, measured radiographically or physiologically over the lifetime of the miner, can help us understand the exposures that led to this severe form of illness and as a result, how best to intervene and institute preventive measures.

Previous work on the resurgence of CMDLD has relied almost exclusively on radiographic evidence of disease ("classic pneumoconiosis" such as coal workers' pneumoconiosis and silicosis), with less attention paid to COPD and lung function impairment associated with coal mine dust exposure. These other manifestations of CMDLD are the most substantial contributors to the burden of respiratory impairment in this population.[6,7] This impairment is related to the cumulative exposure to coal mine dust. Lung function impairment, as measured by resting pulmonary function tests (PFTs), cardiopulmonary exercise testing (CPET), and resting and exercise arterial blood gases (ABGs), has not been extensively explored in this population. CPET has been demonstrated to be a more sensitive test to detect impairment caused by occupational exposure to coal mine dust than either resting pulmonary function testing or chest imaging such as chest radiography.[25] This is especially apparent in those with breathlessness who only have minimal radiographic findings of pneumoconiosis.[26] While early studies described the utility of CPET in this population, there has been no recent assessment of impairment among coal miners as measured by CPET.

Dr. Donald Rasmussen was a prominent pulmonary physician in Beckley, West Virginia who examined over 50,000 U.S. coal miners during his remarkable career. He developed exercise

protocols to identify respiratory impairment in coal miners that preceded or occurred in the absence of typical radiographic features of CWP or other classic pneumoconioses. His pioneering work was instrumental in the creation of regulations to protect miners' health in the U.S.[27–29] His later data has not been analyzed or published and likely represents the largest repository of physiologic testing in coal miners spanning decades.[30,31]

Accurate data on mortality in this population is limited, as mortality estimates rely on death certificates coded for CWP rather than on data from well-described cohorts. We previously completed an initial mortality study of over 34,771 coal miners who participated in both the FBLP and CWHSP programs. Proportional mortality from non-malignant respiratory disease (NMRD), specifically the pneumoconioses, increased across birth cohorts, with the highest proportions observed in miners born after 1940. This increase is most pronounced among younger miners and may reflect increased mortality from PMF, which previous studies have shown is occurring more frequently and in younger U.S. coal miners.[32] A concerning finding from this analysis was that a substantial proportion (41%) of miners with PMF, as determined through the federal benefits process, did not have pneumoconiosis listed as a contributing cause of death on their death certificate, further underscoring the limitations of studies relying solely on accurate coding of death certificates.

Less is known about the risk of cardiovascular disease (CVD) and other causes of mortality in miners. The U.S. mining population, including coal miners, is exposed to the stress of noise, vibration, shift work, prolonged work hours/overtime, and diesel exhaust, all of which have been associated with adverse health outcomes with the potential for increased morbidity and mortality.[13,14] Though published research is sparse, one study of U.S. coal miners reported an increased risk of mortality from ischemic heart disease associated with cumulative exposure to coal dust and with coal rank.[33] Risk factors for CVD among miners are both occupational and personal, but there is limited data exploring these disease co-factors in large mining populations.

**Problem statement:**

U.S. miners are at risk for cardiopulmonary diseases resulting from occupational exposures and personal factors. Prevalence of CWP and PMF have risen to levels not seen since the 1970s among both active and former miners in the United States.[1,2] The Central Appalachian states of Kentucky, Virginia, and West Virginia have seen the largest increases in prevalence of this debilitating disease.[1,2,16,18–20] Our understanding of this resurgence has relied almost exclusively on chest imaging evidence measured at one point in time. This very likely underestimates the true burden of disease given that significant morbidity from lung function impairment may be found absent radiographic abnormalities. Lung function impairment, as measured by resting PFTs and CPET with and without measurements of ABG, has not been extensively explored in this population, and as noted above there is a paucity of information on CVD. We examined risk factors for mining-related respiratory and cardiovascular disease (CVD) using large, previously linked data sets for U.S. coal miners. We calculated prevalence estimates of specific respiratory and cardiovascular diseases among this population sample; characterized the progression of illness during employment as well as after exposures cease; and measured overall mortality and the burden of disease-specific mortality with reference to a comparable non-mining working population using a combination of radiographic and physiologic health data.

**Main hypotheses:**

Our study goal was to expand our analysis of CMDLD in three large and previously linked data sets to develop an in-depth understanding of the risk factors for cardiopulmonary diseases and mortality in U.S. miners, with the ultimate goal of developing better targeted prevention strategies. We hypothesized that using these linked data sets:

1) We could identify factors associated with lung function declines and disease progression on imaging across the lifetime of the miner,
2) We could identify both personal and occupational risk factors for mortality from cardiovascular disease;
3) And further, we could expand our understanding of the development, progression, and manifestations of CMDLD and cardiovascular disease outcomes in a region with recognized increased prevalanece of severe disease.

To achieve these outcomes, we detailed the following specific aims.

**Aim 1/Objective 1:** Further investigate the rate of lung function decline and radiographic disease progression among U.S. coal miners participating in the CWHSP and FBLP to better understand risk factors/predictors across the working and retired lifetime of the miner.

**Aim 2**: Expand our analysis of non-malignant respiratory disease and cardiovascular disease to identify health indicators most closely associated with reduced survival among this population of U.S. coal miners.

Objective 2: Identify health indicators most closely associated with reduced survival among this population of U.S. coal miners through an expanded analysis of mortality from non-malignant respiratory and cardiovascular disease.

**Aim 3**: Conduct epidemiologic analyses of comprehensive and sizeable clinical data from one clinic in West Virginia.

Objective 3: Perform a comprehensive characterization of the population of coal miners captured in the clinical database maintained by Dr. Donald Rasmussen ('Rasmussen data') between 2004 and 2015.

Objective 4: Link data from the CWHSP, FBLP, and National Death Index (NDI) to the Rasmussen data to further explore progression of disease as well as associations between coal mining tenure, CMDLD severity, lung function, smoking, and time to death through Cox proportional hazards regression models. Characterize the underlying and contributing causes of death among the thousands of coal miners seen by Dr. Rasmussen between 2004 and 2015.

## 4.0 Research Approach

**Aim 1/Objective 1:** Further investigate the rate of lung function decline and radiographic disease progression among U.S. coal miners participating in the CWHSP and FBLP to better understand risk factors/predictors across the working and retired lifetime of the miner.

**Task 1.1:** Quantify the decline in lung function, as measured by changes in forced expiratory volume in one second ($FEV_1$), forced vital capacity (FVC), and $FEV_1$/FVC ratio, for those miners with at least two valid spirometry test in either the CWHSP and/or FBLP data sets.

Miners with at least two spirometry tests across either the FBLP or CHWSP data sets were identified and included in this analysis. There were 11,780 coal miners with at least two valid spirometry tests within or between the two programs. We analyzed results from the first and last pre-bronchodilator spirometry tests from miners seen across either program. We calculated percent predicted (pp) and lower limits of normal (LLN) for forced expiratory volume in one second ($FEV_1$), forced vital capacity (FVC), and $FEV_1$/FVC ratio. We determined prevalence of patterns of spirometric abnormality (restrictive, obstructive, and mixed obstructive/restrictive). We also determined the prevalence of moderate to severe impairment ($FEV_1$<70pp). We further classified miners who worked most of their coal mining career in Kentucky, Virginia, or West Virginia as Central Appalachian miners for comparison to miners from the rest of the U.S.

Only 1,343 (11%) of these miners had a test in the CWHSP which had data on miner sex and race available. For all of the remaining miners, and based on demographic information from other large coal miner data sets, we assumed non-Hispanic White race/ethnicity and male sex in calculating race and gender-specific predicted values for $FEV_1$ and FVC.[34] Therefore, the miners in this analytic data set were overwhelmingly non-Hispanic White males. We excluded cases with less than two years between first and last tests; those with greater than 30% increase in $FEV_1$ on second test (e.g., 70pp to 100pp), or greater than 50% decrease in $FEV_1$ on second test; and those with less than five years coal mine employment, as verified by the U.S. Department of Labor (DOL) through Social Security Administration records.

We used descriptive statistics to calculate changes in lung function between tests for these miners and used linear regression to examine the association between years of coal mine employment (CME) and decline in $FEV_1$pp between spirometry tests, controlling for age at first spirometry and years between tests.

**Task 1.2:** Characterize the radiographic progression of disease for those miners with International Labour Office (ILO) classifications of CXRs in the CWHSP and FBLP data sets. Characterize the progression across profusion categories of simple CWP as well as progression to PMF.

Miners with at least two CXRs across either the FBLP or CWHSP data sets were identified and considered in this analysis. We compared the ILO classifications of the first and last CXRs of miners who had at least two CXRs across either program at least two years apart. Those miners whose disease category had increased to a higher profusion score, or who had progressed to PMF

within that time period were labeled 'progressors' while the remaining miners were labeled 'non-progressors'. PMF was defined using the standard ILO classification showing large opacities of category A (one or more large opacities > 10 mm in diameter, with a summed long axis dimension(s) of ≤ 50 mm); B (one or more large opacities having the sum of longest dimension(s) > 50 mm but not exceeding the equivalent area of the right upper lung zone); or C (one or more large opacities, with combined areas exceeding the equivalent area of the right upper zone). Small opacity profusion scores were classified on an 11-point scale corresponding to each minor category of profusion defined by the ILO guidelines (note the lowest two categories, ILO categories 0/- and 0/0 were combined).

Student's t-test was used to evaluate bivariate relationships between progression status and continuous variables such as age, coal mine employment tenure in years, small opacity profusion category, and time between CXRs. Chi-square tests were used to evaluate differences in distribution of categorical variables. Multivariable logistic regression models were used to examine the relationship between progression and age, time between CXRs, total years of CME, geographic region, and small opacity profusion category at time of first CXR.

The extremely small number of miners with evidence of pneumoconiosis and more than one x-ray in the CWHSP precluded an analysis of radiographic progression within the CWHSP data set alone.

**Aim 2:** Expand our analysis of mortality of non-malignant respiratory diseases and cardiovascular disease to identify health indicators most closely associated with reduced survival among this population of U.S. coal miners.

**Objective 2:** Identify health indicators most closely associated with reduced survival among this population of U.S. coal miners through an expanded analysis of mortality from non-malignant respiratory and cardiovascular disease.

**Task 2.1:** Perform a detailed epidemiologic analysis of the expanded mortality data, linked with the health data from the CWHSP and FBLP, to examine predictors of death from non-malignant respiratory and cardiovascular disease. The major explanatory and confounding variables we explored included mining tenure, $FEV_1$ percent predicted, radiographic severity of pneumoconiosis, geographic region, body mass index (BMI), and smoking status.

*Data Sources*
We obtained vital status and cause of death data from a combination of Social Security Administration and National Death Index (NDI) sources on former U.S. coal miners who had participated in either the CWHSP or the FBLP between 1970 and 2017. We requested mortality data on all miners from either program who were known to be deceased using Social Security Administration vital status queries performed by either DOL, which operates the FBLP, or the National Institute for Occupational Safety and Health (NIOSH), which operates the CWHSP, on their respective populations. Additional records of CWHSP miners were submitted with unknown vital status.

Mortality data from the general U.S. population from 1979 to 2017 was obtained from the National Vital Statistics System (NVSS) through a combination of publicly available and special request data files. Special request data files were necessary to obtain state of death which the NVSS has not made publicly available in their data since 2004.[35] Relevant to our study, the NVSS data include underlying cause of death, age at death, year of birth, and state of death. Cause of death was coded using the International Classification of Diseases (ICD)-9 for years 1979 to 1998, and ICD-10 for years 1999 through 2017.

*National Death Index*
The NDI employs a probabilistic linkage procedure to identify death certificate records that are potential matches to the submitted data. We included all NDI records that were exact matches of first and last names, Social Security number (SSN), and date of birth to a death certificate file in their database. We also included records requiring one of the following: an exact 9-digit SSN match; an 8-digit SSN match and an exact date of birth match; or a 7-digit SSN match and an exact date of birth match.[36]

The NDI provides the underlying and contributing causes of death for matched records. The underlying cause of death is defined by the World Health Organization as "(a) the disease or injury which initiated the train of events leading directly to the death, or (b) the circumstances of the accident or violence which produced the fatal injury".[37] In addition to the underlying cause of death, a maximum of 20 additional conditions that contributed to the death were provided by the NDI.

*Selected Causes of Death*
We examined selected underlying and contributing causes of death including NMRD, lung cancer, and ischemic heart disease (IHD). We examined subcategories of NMRD including pneumoconioses and chronic lower respiratory disease (CLRD). NMRD was identified using ICD-9 codes 460–519 and ICD-10 codes J00-J99. We identified pneumoconioses other than asbestosis, which includes CWP, silicosis, and pneumoconiosis resulting from exposure to inorganic dusts, using ICD-9 codes 500, 502, 503, 505 and ICD-10 codes J60–J62, J64. CLRD, including COPD, chronic bronchitis, emphysema, and asthma, was identified using ICD-9 codes 490–494, and 496; and ICD-10 codes J40–J47. We defined lung cancer as ICD-9 code 162 and ICD-10 code C34. We identified IHD, including acute myocardial infarction and chronic ischemic heart disease, using ICD-9 codes 410–414 and ICD-10 codes I20–I25.

*Statistical Analysis*
We characterized proportional mortality from selected underlying causes of death, employing Chi-square tests and logistic regression to test for significant trends across birth cohort and age group. Causes of death examined were NMRD, pneumoconioses excluding asbestosis (n = 46), CLRD, lung cancer, and IHD. We examined differences in mortality trends between those with and without a determination of PMF from the FBLP adjudication process. This determination process has been described previously.[38]

We computed mortality odds ratios (MOR) to compare mortality from all NMRD, pneumoconioses, CLRD, all malignant neoplasms, lung cancers, and IHD among former U.S. coal miners and the U.S. white male population.[39,40] MORs represent the ratio of odds of death

from a specific cause in the study population to odds of death from that specific cause in a comparison population.[41,42] MORs were computed for the entire study period of 1979 – 2017 by birth cohort (birth before 1920, 1920 – 1929, 1930 – 1939, and 1940 or later), as well as by age group within birth cohorts (<65 years, 65–74 years, and 75 years and older). We also calculated MORs for a subgroup of miners, restricting analysis to miners who last worked in the Central Appalachian states of Kentucky, Virginia, and West Virginia. All analyses were restricted to those aged 45 and older at time of death, as deaths from the selected causes were so rare in younger ages that estimates of proportionate mortality or MORs were unstable.

**Task 2.2:** Examine the relationship between rate of progression of radiographic disease and rate of lung function decline to mortality through the use of Cox proportional hazards models.

Using the data set of FBLP/CWHSP miners with at least two spirometry tests across either program, we performed a survival analysis using Cox Proportional Hazards (PH) models to understand the effect of lung function decline on mortality in this subset of miners while controlling for confounders and examining other risk factors. Cox PH models estimate hazard ratios (HRs) for individual predictors of time-to-event data. In this analysis, time-to-event was calculated as the years between the last exam for each miner in the FBLP/CWHSP data set and their date of death, as provided by the NDI. Miners who did not die by the end of the study period, December 31, 2016, were considered right censored. This was calculated using the exact dates and rounded to the nearest number of years.

We created a life table to understand the survival differences between those with and without abnormal $FEV_1$ in our population. We conducted Cox PH models to calculate HRs for each major covariate associated with survival. HRs are a measure of survival at any given point in time in one group compared to another. In our analyses, we computed HRs comparing survival among those with a particular characteristic (e.g., abnormal $FEV_1$), to those without that characteristic, often called the control or referent group (e.g., normal $FEV_1$). In the context of this analysis, a HR of one indicates no difference in survival between the groups whereas a HR greater than one indicates reduced survival among those with the trait compared to those without it (reference group).

We explored the following covariates in the Cox PH models: $FEV_1$pp at the time of their last spirometry exam, age of the miner at the time of the exam, whether the miner had received an award in their Federal black lung benefits claim, total years of coal mining employment, and region of coal mine employment (Central Appalachia vs. the rest of the U.S.). Variables were retained based on model fit and the significance (p values <0.05) of model estimates. Of note, the FBLP/CWHSP data sets lack smoking histories.

**Aim 3:** Conduct epidemiologic analyses of comprehensive and sizeable clinical data from one clinic in West Virginia.

**Objective 3:** Perform a comprehensive characterization of the population of coal miners captured in Rasmussen data between 2004 and 2015.

**Task 3.1:** Complete data extraction from data source. Dr. Rasmussen's examinations of coal miners for CMDLD were documented in individual narrative files. Because these narratives

were structured, we were able to extract relevant free text information from the approximately 8,000 documents created over 11 years, including detailed occupational and smoking histories, medical histories, ILO classifications of CXRs, and diagnostic determinations of the presence of pneumoconiosis and disabling respiratory impairment.

The Rasmussen data includes detailed occupational, smoking, and medical histories that are embedded in narrative text. The information contained in these narratives is critical for epidemiologic analyses but required extraction into numeric or categorical fields suitable for analysis.

We extracted data from the free-text fields regarding smoking and occupational history; previous or co-existing medical conditions; and medications. The protocol for data cleaning included one student performing automated data extraction, flagging any observations with complex or incomplete data for manual review. A second student then manually reviewed and extracted the data from any observations that were flagged in the automated extraction process, as well as performed a quality check on the automated extractions by manually reviewing a 10-15% random sample of observations. If additional errors or patterns that yielded incorrect/incomplete data extraction arose, those were addressed, and the corrected automated process was rerun. The automated extraction code had greater than 95% sensitivity and specificity in extracting comorbidities, smoking start and end dates, smoking intensity, and coal mine employment start and end dates.

**Task 3.2:** Describe this population of coal miners based on demographic factors such as age, race, sex, and smoking; occupational history factors such as coal mine employment tenure and job titles; and clinical data including cardiovascular risk factors, CPETs, PFTs, measurement of ABG, and CXR findings.

Using the data set that was cleaned and developed in Task 3.1, we calculated percent predicted values and LLN for the pre-bronchodilator $FEV_1$, FVC, and $FEV_1$/FVC ratio, and diffusion capacity for carbon monoxide (DLCO) using the Global Lung Function Initiative (GLI) reference equations published by the European Respiratory Society[43] and endorsed by the American Thoracic Society. $FEV_1 < LLN$ was characterized as $FEV_1$ impairment. DLCO < LLN was characterized as impaired diffusion capacity. We used the classification for severity of $FEV_1$ and DLCO impairment described by Pellegrino, et al.[44] We defined patterns of spirometric abnormality as follows[45]:

1. Restrictive: FVC < LLN, and $FEV_1/FVC \geq LLN$
2. Obstructive: $FVC \geq LLN$ and $FEV_1/FVC < LLN$
3. Mixed obstructive and restrictive ("Mixed"): FVC < LLN and $FEV_1/FVC < LLN$

ILO classifications of CXRs were extracted under Task 3.1. For this initial characterization, each miner's last exam was used in the calculations. We examined the radiographic and physiologic characteristics of these miners separately and then characterized each physiologic measure by smoking status and radiographic severity of disease (ILO classification). We used t-tests to examine difference in means for continuous variables such as $FEV_1$ percent predicted values and Chi-Square tests to test for significant differences in the distribution of categorical variables.

**Task 3.3:** Describe correlations between (a) PFT findings ($FEV_1$, FVC, $FEV_1$/FVC ratio, TLC, DLCO) and radiologic severity of disease (ILO classification); (b) CPET findings, such as peak oxygen uptake and dead space fraction, Ventilatory Equivalents for $O_2$ and $CO_2$, and radiologic severity of disease; (c) ABG findings, including arterial blood pH, partial pressure of oxygen ($PO_2$), partial pressure of carbon dioxide ($PCO_2$) and alveolar-arterial oxygen gradient, and radiologic severity of disease; and (d) PFT, CPET, and ABG findings. In each of these correlation analyses, we controlled for demographic and occupational confounders such as age, smoking, mining tenure, and job title.

Using the approach described under Task 3.2, we examined the relationship between DLCO and spirometry findings ($FEV_1$pp, FVCpp, and $FEV_1$/FVCpp) as well as severity of radiographic disease (no CWP, simple CWP, and PMF). For each of these examinations, we performed a sub-analysis of these relationships among nonsmokers to remove confounding from cigarette smoking. Additionally, we summarized CPET and ABG findings by smoking status and radiographic disease category.

**Objective 4:** Link data from the CWHSP, FBLP, and NDI to the Rasmussen data to further explore progression of disease as well as associations between coal mining tenure, CMDLD severity, lung function ($FEV_1$), smoking, and time to death through Cox proportional hazards regression models. Characterize the underlying and contributing causes of death among the thousands of coal miners seen by Dr. Rasmussen between 2004 and 2015.

**Task 4.1:** Perform linkage of data from the Rasmussen data set to the linked data set of the CWHSP, FBLP, and NDI data using a combination of deterministic and probabilistic linkage methods. We previously linked the CWHSP, FBLP, and NDI as part of our work under grant #AFC316-53.

Deidentified data from the Rasmussen data include an expanded set of variables for a subset of Appalachian miners. These variables are not currently included in the FBLP and CWHSP data sets. They contain detailed occupational histories; smoking histories; medical histories including diabetes, hypertension, and hyperlipidemia; ILO classifications of chest radiographs; lung function testing at rest including spirometry, lung volume measurements and diffusion capacity; and, in most cases, complete cardiopulmonary exercise tests with metabolic parameters and arterial blood gas data for miners seen in Dr. Rasmussen's clinic between 2004 and 2015.

Probabilistic methods are required as the Rasmussen data does not contain identifiers such as social security number (SSN), date of birth, and name. We used a combination of deterministic and probabilistic linkage methods to merge the expanded clinical data with the linked FBLP/CWHSP data sets. Specifically, we tested several linkage approaches using various combinations of the following clinical variables: spirometry date, $FEV_1$ and FVC measurements, and the miner's height, weight, and age (from which we estimated year of birth). The linkage approach that we ultimately used included spirometry date, year of birth, as well as the $FEV_1$ and FVC measurements. Our approach assumed that this combination of variables was unlikely to be repeated across any two individuals in the expanded data set or

FBLP/CWHSP data set. In fact, only nine individuals in the Rasmussen data set linked to more than one record in the FBLP/CWHSP data set, and these were removed for the analyses described below.

**Task 4.2:** Measure the lung function decline among those miners from the Rasmussen data that have serial lung function tests across the CWHSP and FBLP data sets.

The FBLP does not include smoking history data for the miners in its data set. The Rasmussen data, containing examinations that comprise a subset of those performed for the FBLP, has detailed smoking histories that allowed us to examine lung function decline as it relates to coal mine employment tenure, job titles, and demographic variables while controlling for smoking.

Using the linked FBLP/CWHSP/Rasmussen data set, we identified those miners with at least two spirometry tests across these data sets and employed a very similar research approach to that described in full under Task 1.1. We analyzed results from the first and last pre-bronchodilator spirometry tests from these miners and calculated pp and LLN for $FEV_1$, FVC, and $FEV_1$/FVC ratio. We determined prevalence of patterns of spirometric abnormality (restrictive, obstructive, and mixed restrictive/obstructive). We also determined the prevalence of moderate to severe impairment ($FEV_1$<70pp). As nearly all miners seen by Dr. Rasmussen were Central Appalachian miners, we did not investigate the role of region in this analysis. In an effort to reduce the possibility of including erroneous value, we excluded those with less than two years between first and last tests; those with greater than 30% increase in $FEV_1$pp on second test (e.g., 70pp to 100pp) or greater than 50% decrease in $FEV_1$ on second test; and those with less than five years of verified coal mine employment.

We calculated descriptive statistics regarding the change in lung function between tests for these miners and used linear regression to examine the association between years of CME tenure and decline in $FEV_1$pp between spirometry tests, controlling for age at first spirometry, years between tests, radiographic disease severity, and smoking history (pack years and smoking status).

**Task 4.3:** Using the linked data set described in Task 4.1, describe the proportionate mortality from underlying and contributing causes of death among deceased miners in the Rasmussen data. Describe and compare mortality patterns among those miners with lung function impairment on PFT and/or CPET and with imaging findings of CWP or PMF.

The methods employed for this task are described in detail under Task 2.1. Using the linked FBLP/CWHSP/Rasmussen data set we were able to explore the mortality experience of those miners seen by Dr. Rasmussen in his West Virginia black lung clinic between 2004 and 2015. In brief, we examined the underlying and contributing causes of death for deceased miners in the FBLP/CWHSP/Rasmussen records provided by the NDI.

To ensure comparability between this task and the results from Task 2.1, we examined the same underlying and contributing causes of death including NMRD, lung cancer, and IHD. We characterized mortality from selected underlying causes of death, employing Chi-square tests and logistic regression to test for significant trends across birth cohort and age group. Causes of death

examined were NMRD, pneumoconioses excluding asbestosis, CLRD, lung cancer, and IHD. We examined differences in mortality trends between those with and without a determination of PMF from the FBLP adjudication process. This determination process has been described previously.[38] All analyses were restricted to those aged 45 and older at time of death.

**Task 4.4:** Examine associations between coal mining tenure; CMDLD severity; lung function impairment measured on resting and exercise studies; smoking; comorbidities such as diabetes, hypertension, and dyslipidemia; and time to death through Cox proportional hazards regression models.

Similar to the approach described under Task 2.2 and using the FBLP/CWHSP/Rasmussen linked data set described under Task 4.1, we performed a survival analysis using Cox PH models to understand the largest risk factors for mortality in this population of miners.

Cox PH models estimate HRs for individual predictors of time to event data. In this analysis time-to-event was calculated as the years between the last exam for each miner in the Rasmussen data set and the date of death, as provided by the NDI. This was calculated using the exact dates and rounded to the nearest number of years.

We explored the following covariates in the Cox PH models: $FEV_1$pp at their last spirometry exam, age of the miner at the time of the exam, whether or not the miner had won their Federal black lung benefits claim, total years of coal mining employment, smoking status (nonsmoker vs former/current smoker), smoking pack years, severity of radiographic disease at the time of their last chest radiograph on record, and self-reported hypertension diagnosis. Variables were retained based on model fit and the significance (p values $<0.05$) of model estimates.

## 5.0 Research Findings and Accomplishments

**Aim 1/Objective 1:** Investigate the rate of lung function decline and radiographic disease progression among U.S. coal miners participating in the CWHSP and FBLP to better understand risk factors/predictors across the working and retired lifetime of the miner.

*Progression of Lung Function Decline*

There were 11,780 coal miners with at least two valid spirometry tests within or between the two programs. Only 1,343 (11%) of these miners had a test in the CWHSP which had data on miner sex and race available. For all of the remaining miners, we assumed non-Hispanic White race/ethnicity and male sex in calculating race and gender-specific predicted values for $FEV_1$ and FVC.[34] Therefore, the miners in this analytic data set were overwhelmingly non-Hispanic White males (Table 1). Seventy-eight percent of these miners had worked the majority of their careers in Central Appalachia (Kentucky, Virginia, or West Virginia) and had approximately 22 years of coal mine employment on average.

An examination of each miner's first spirometry test in these data revealed that the mean $FEV_1$pp is 77.4, and 48% have an abnormal $FEV_1$ ($FEV_1 < LLN$). Among those with an abnormal $FEV_1$, 41% had moderately severe to very severe impairment ($FEV_1pp < 60$). Mean FVCpp was 82.8 in this group, and 43% of miners had abnormally low FVC values at their first spirometry test. At the time of their last available spirometry test, the proportion of

miners with abnormally low $FEV_1$ and FVC values increased to 53% and 50%, respectively. Mean $FEV_1$pp declined to 73.7 and mean FVCpp declined to 79.0 at the time of miners' last spirometry test.

**Table 1.** Characteristics of miners with at least two spirometry tests across either or both the Coal Worker's Health Surveillance Program or the Federal Black Lung Program, 2000-2016 (n=11,780).

| **Miner Characteristic** | **n** | **%** |
|---|---|---|
| Sex | | |
| Male | 11,770 | 99.9 |
| Female | 10 | 0.1 |
| Race | | |
| Non-Hispanic White | 11,704 | 99.4 |
| Non-Hispanic Black | 68 | <0.6 |
| Hispanic | 8 | <0.1 |
| Coal Mine Employment Tenure | | |
| Years Claimed (mean, std) | 25.3 | 8.9 |
| Years Verified[a] (mean, std) | 21.7 | 9.3 |
| Region | | |
| Central Appalachia | 9,237 | 78.4 |
| Rest of the U.S. | 2,543 | 21.6 |
| Mean $FEV_1$ Percent Predicted (mean, std) | | |
| At time of initial spirometry | 77.4 | 20.9 |
| At time of last spirometry | 73.7 | 22.2 |
| Abnormal $FEV_1$ ($FEV_1$ < LLN) | | |
| At time of initial spirometry | 5,678 | 48.2 |
| At time of last spirometry | 6,274 | 53.3 |
| Abnormal FVC (FVC < LLN) | | |
| At time of initial spirometry | 5,077 | 43.1 |
| At time of last spirometry | 5,942 | 50.4 |

[a] The DOL provides both the years of coal mine employment claimed by the miner and verified by social security records.

Of those with normal $FEV_1$ at the time of their first spirometry (n = 6,102), 26.1% had abnormal $FEV_1$ values at the time of their last spirometry. Among those who experienced a decline in $FEV_1$pp (n = 7,094), the mean (std) decline was 3.6 pp per year (std 4.8 pp). Linear regression demonstrated that having mined in Central Appalachia yielded significantly higher mean decline in $FEV_1$pp compared to miners from the rest of the U.S., controlling for age, years between tests, and coal mine employment tenure. We were unable to control for smoking habits in this analysis as this data was not available in either data set. There were very few miners in the FBLP data with serial spirometry tests in the CWHSP data set, as NIOSH has only been collecting spirometry data since 2005. As a result, we were unable to compare the rate of change in lung function while the miner was still working compared to after they had left the industry.

*Radiographic Progression of Disease*

We examined radiographic progression in the cohort of miners we previously examined for

radiographic progression to PMF.[24] Of the 3,351 former miners examined from the FBLP data set, 72% (n = 2,402) had previously participated in the CWHSP while they were working and had at least one ILO classification of a chest radiograph in these surveillance data. The majority of these miners had no record of a 'positive' x-ray (ILO classification of small opacity profusion 1/0 or greater) in the CWHSP (94%, n=2,250). Among those with multiple CXRs in the CWHSP data (n=436), 122 miners (28%) showed evidence of progression in their major ILO profusion category in their CWHSP CXRs. The vast majority of these CWHSP 'progressors' had initial ILO classifications of 0/0 or 0/1 and had subsequently been classified as 1/0, 1/1, or 1/2 on their later CXRs (83%, n = 101).

Among those miners who had participated in the CWHSP and FBLP (n=2,402), 2,250 (94%) had a negative ILO classification (small opacity profusion score of 0/-, 0/0, or 0/1) indicating no coal workers' pneumoconiosis on their last or only CWHSP CXR. Of these, 42% (n = 946) had developed simple CWP (small opacity profusion major category 1, 2, or 3). Three percent (n = 70) had findings consistent with PMF at the time of their last CXR in the FBLP database. Among those miners with chest x-rays indicating simple CWP in the CWHSP (n = 152, 6%), 23% progressed to category 2 or 3 simple CWP and 12% progressed to PMF (n = 18) by the time of their final FBLP claim. We found that likelihood of progression to PMF was most significantly associated with increasing small opacity profusion on earlier CXRs, controlling for region and coal mine employment tenure.

**Aim 2:** Expand our analysis of mortality of non-malignant respiratory diseases and cardiovascular disease to identify health indicators most closely associated with reduced survival among this population of U.S. coal miners.

**Objective 2:** Identify health indicators most closely associated with reduced survival among this population of U.S. coal miners through an expanded analysis of mortality from non-malignant respiratory and cardiovascular disease.

*Mortality Analysis of U.S. Coal Miners, 1970–2016*
There were 235,550 U.S. coal miners included in the final data set used in this mortality study. Mean age at death was 76 years (std 10.6 years), and the majority of miners were born prior to 1920 (68%). Forty-three percent of miners were considered "Central Appalachian miners." The most common underlying causes of death were IHD (25%), NMRD (20%), malignant neoplasms excluding lung cancer (13%), and lung cancer (10%). Among those with NMRD as the category of underlying cause of death (n = 47,932), the two most prevalent causes were COPD (n = 20,185, 42%) and pneumoconiosis (n = 17,207, 36%) (Table 2).

Miners with a determination of PMF (n = 2,829) were significantly younger at time of death than those without this determination (74 vs. 78 years, respectively; $p < 0.0001$). A significantly higher proportion of miners with PMF were born in the most recent birth cohorts (1930 and after; 33%) compared to miners without PMF (14%; $p < 0.0001$). Central Appalachian miners comprised the majority of PMF cases (56%).

Pneumoconiosis was listed as the underlying cause of death in 7% of the overall population but was a contributing cause of death in 19% of deaths. Surprisingly, only 38% of miners with PMF had pneumoconiosis listed as a contributing cause of death on their death certificates.

**Table 2.** Descriptive characteristics of deceased miners (n = 235,550) participating in the Coal Workers' Health Surveillance Program or applying for Federal Black Lung Program benefits between 1970 – 2017, by PMF status.[a]

| | **All Deceased Miners (n = 235,550)** | | **Miners without PMF (n=232,721)** | | **Miners with PMF (n=2,829)** | | |
|---|---|---|---|---|---|---|---|
| **Variable** | **n** | **%** | **n** | **%** | **n** | **%** | **p-value*** |
| Age at Death | | | | | | | |
| 45-65 | 33,015 | 14.0 | 32,502 | 14.0 | 513 | 18.1 | < 0.001 |
| 65-74 | 61,559 | 26.1 | 60,684 | 26.1 | 875 | 30.9 | |
| ≥75 | 140,976 | 59.9 | 139,535 | 60.0 | 1441 | 50.9 | |
| Birth Cohort | | | | | | | |
| <1920 | 158,885 | 67.5 | 157,835 | 67.8 | 1050 | 37.1 | < 0.001 |
| 1920-1929 | 42,992 | 18.3 | 42,140 | 18.1 | 852 | 30.1 | |
| 1930-1939 | 15,742 | 6.7 | 15,342 | 6.6 | 400 | 14.1 | |
| 1940+ | 17,931 | 7.6 | 17,404 | 7.5 | 527 | 18.6 | |
| Underlying Cause of Death[b] | | | | | | | |
| NMRD | 47,932 | 20.4 | 46,904 | 20.2 | 1028 | 36.3 | < 0.001 |
| CWP | 14,824 | 6.3 | 14,395 | 6.2 | 429 | 15.2 | < 0.001 |
| Pneumoconioses | 17,207 | 7.3 | 16,660 | 7.2 | 547 | 19.3 | < 0.001 |
| COPD | 20,185 | 8.6 | 19,869 | 8.5 | 316 | 11.2 | < 0.001 |
| Lung Cancer | 22,833 | 9.7 | 22,550 | 9.7 | 283 | 10.0 | 0.575 |
| IHD | 58,900 | 25.0 | 58,440 | 25.1 | 460 | 16.3 | < 0.001 |
| Contributing Causes of Death[c] | | | | | | | |
| NMRD | 113,952 | 48.4 | 112,073 | 48.2 | 1879 | 66.4 | < 0.001 |
| CWP | 38,021 | 16.1 | 37,212 | 16.0 | 809 | 28.6 | < 0.001 |
| Pneumoconioses | 44,583 | 18.9 | 43,523 | 18.7 | 1060 | 37.5 | < 0.001 |
| COPD | 61,032 | 25.9 | 60,096 | 25.8 | 936 | 33.1 | < 0.001 |
| Lung Cancer | 25,729 | 10.9 | 25,410 | 10.9 | 319 | 11.3 | 0.545 |
| IHD | 81,283 | 34.5 | 80,476 | 34.6 | 807 | 28.5 | < 0.001 |
| Region Last Worked[d] | | | | | | | |
| Central Appalachia | 101,160 | 43.0 | 99,574 | 42.8 | 1586 | 56.1 | < 0.001 |
| Rest of the U.S. | 134,390 | 57.1 | 133,147 | 57.2 | 1243 | 43.9 | |

[a] Progressive massive fibrosis (PMF) as determined through the Federal Black Lung Program benefits' claims process.
[b] Non-malignant respiratory disease (NMRD) category contains coal workers' pneumoconiosis (CWP), all pneumoconioses, emphysema, and chronic obstructive pulmonary disease (COPD) categories.
[c] Categories are not mutually exclusive. Individuals are categorized based on underlying and contributing causes of death.
[d] Central Appalachia includes the states of Kentucky, Virginia, and West Virginia.
* P-value based on results of Chi-square test of proportions between those with and without PMF.

The odds of death from NMRD across all birth cohorts of coal miners in this population were, on average, twice as high as those of the U.S. population of white males aged 45 years and older at time of death. In Central Appalachia, there was an eight-fold increase in odds of death from NMRD among miners born after 1940 ($MOR_{BC\geq1940}$ 8.25; 95% C.I. 7.67, 8.87), compared with the general Central Appalachian population (Table 3).

All birth cohorts of miners had significantly elevated odds of death from lung cancer compared with the non-mining U.S. population. In Central Appalachia, odds of lung cancer mortality were significantly elevated among the earliest and latest birth cohorts ($MOR_{BC<1920}$ 1.31; 95% C.I. 1.27, 1.35; $MOR_{BC\geq1940}$ 1.14; 95% C.I.1.07, 1.21). We found no evidence of increased odds of mortality from all malignant neoplasms in either the national or Central Appalachian analyses.

The Central Appalachian population of miners had significantly lower odds of death from IHD compared to their non-mining counterparts, with each successive birth cohort experiencing lower odds of death from this cause. Nationally, there were significant reductions in odds of IHD mortality in most strata of age and birth cohort.

**Table 3.** Mortality odds ratios (MOR) and 95% CI, by birth cohort, for selected underlying causes of death among a population of deceased US coal miners (n = 235,550) and the general US population, for deaths occurring between 1979 and 2017. Significant MORs are in bold font ($p < 0.05$).

| | Birth Cohort | | | |
|---|---|---|---|---|
| **Underlying Cause of Death[a]** | **<1920** | **1920 - 1929** | **1930 - 1939** | **≥ 1940** |
| ***Deaths in all states*** | *n = 158,885* | *n = 42,992* | *n = 15,742* | *n = 17,931* |
| Nonmalignant Respiratory Disease | **2.09 (2.07, 2.12)** | **2.17 (2.12, 2.23)** | **2.01 (1.93, 2.10)** | **1.80 (1.73, 1.89)** |
| Chronic Lower Respiratory Disease | **1.61 (1.58, 1.64)** | **1.53 (1.48, 1.58)** | **1.46 (1.38, 1.54)** | **1.40 (1.32, 1.49)** |
| Malignant Neoplasms | **0.95 (0.94, 0.96)** | 0.99 (0.97, 1.01) | **0.95 (0.92, 0.98)** | 1.00 (0.97, 1.03) |
| Lung Cancer | **1.32 (1.30, 1.34)** | **1.47 (1.43, 1.52)** | **1.44 (1.38, 1.51)** | **1.32 (1.26, 1.38)** |
| Ischemic Heart Disease | **0.89 (0.88, 0.90)** | 0.98 (0.96, 1.00) | 0.99 (0.96, 1.03) | 0.99 (0.96, 1.02) |
| ***Deaths in Central Appalachia[b]*** | *n = 55,132* | *n = 23,729* | *n = 10,345* | *n = 11,954* |
| Nonmalignant Respiratory Disease | **2.08 (2.04, 2.13)** | **3.04 (2.94, 3.15)** | **4.19 (3.97, 4.43)** | **8.25 (7.67, 8.87)** |
| Chronic Lower Respiratory Disease | **1.78 (1.73, 1.84)** | **1.70 (1.62, 1.78)** | **2.18 (2.03, 2.34)** | **3.17 (2.90, 3.46)** |
| Malignant Neoplasms | 0.98 (0.96, 1.00) | **0.80 (0.77, 0.82)** | **0.80 (0.76, 0.83)** | 0.97 (0.92, 1.01) |
| Lung Cancer | **1.31 (1.27, 1.35)** | 1.04 (1.00, 1.08) | 1.03 (0.98, 1.09) | **1.14 (1.07, 1.21)** |
| Ischemic Heart Disease | **0.93 (0.91, 0.95)** | **0.91 (0.88, 0.93)** | **0.81 (0.78, 0.85)** | **0.72 (0.69, 0.76)** |

[a] Underlying cause of death is defined as the most proximate cause of death for an individual.
[b] Central Appalachia includes the states of Kentucky, Virginia, and West Virginia.

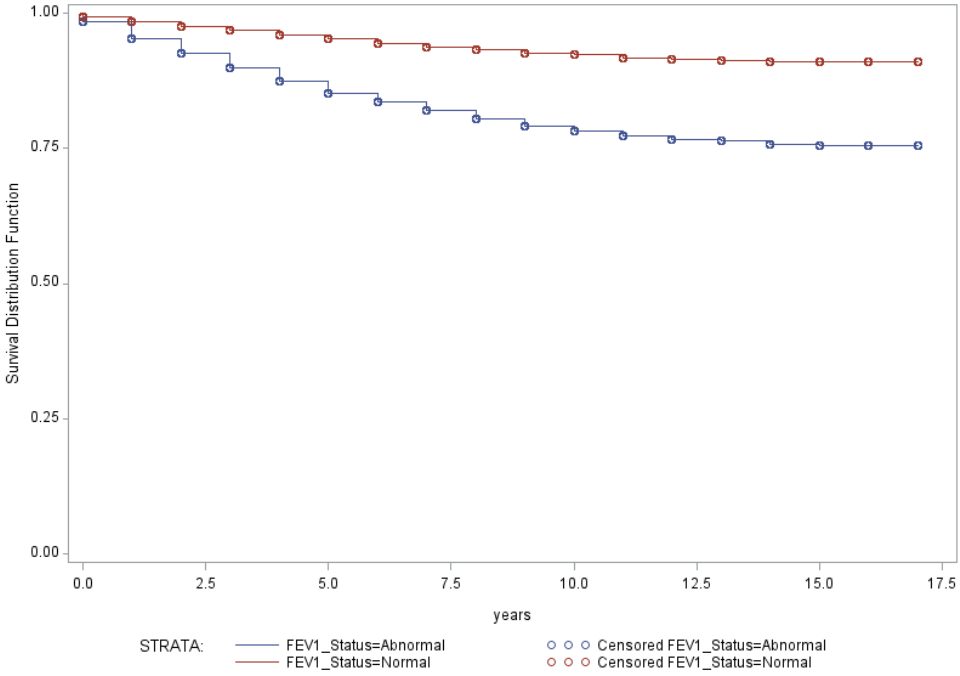
*Loss of Lung Function and Mortality*

We identified 38,102 miners with valid spirometry results between 2000 and 2016 across either the FBLP and/or CWHSP programs. Ten percent (n = 3,817) of these miners had died by December 31, 2016, the end of the follow-up period for this analysis.

In Cox PH modeling among those with at least five years of verified CME, we found that $FEV_1$pp, age, mining region, and whether the miner had been awarded their claim for federal black lung benefits were significant predictors of probability of death among this population. Higher $FEV_1$ was significantly associated with increased survival (HR 0.97, 95% CI 0.97, 0.97). Interestingly, having mined in Central Appalachia for most of one's career was an additional independent predictor of decreased survival (HR 1.24, 95% CI 1.15, 1.33). One of the strongest predictors of increased mortality rate was winning one's federal black lung benefits claim (HR 3.42, 95% CI 3.18, 3.68), which likely reflects the severe disease in miners awarded claims. When $FEV_1$ < LLN (abnormal $FEV_1$) is used in these models as a binary variable in place of $FEV_1$pp, we see that miners with an abnormal $FEV_1$ had nearly three times the mortality rate of those with a normal $FEV_1$ (HR 2.72, 95% CI 2.53, 2.93). Those with abnormal $FEV_1$ had lower

probability of survival at nearly every time point compared to miners with a normal $FEV_1$ value (Figure 1).

**Figure 1.** Difference in survival probabilities between miners with normal (red) and abnormal (blue) $FEV_1$ values, as defined as $FEV_1$ < lower limit of normal.




**Aim 3:** Conduct epidemiologic analyses of comprehensive and sizeable clinical data from one clinic in West Virginia.

**Objective 3:** Perform a comprehensive characterization of the population of coal miners captured in the clinical database maintained by Dr. Donald Rasmussen ('Rasmussen data') between 2004 and 2015.

*Data Extraction*
Using a combination of automated extraction and manual review, we extracted cigarette smoking status (current, former, never); smoking frequency (number of packs per day); age started, stopped, and total years of smoking; pack years; and other tobacco product use. The automated data extraction process was able to correctly classify 5,749 (84%) of the observations in the Rasmussen data. The remaining 1,125 observations have been manually reviewed and the relevant data points have been manually extracted. A quality check on the automated smoking data has been completed (n = 600 observations).

From the occupational history free-text narratives, we have extracted the start and end years of CME, total years of CME, and job titles held by each miner throughout their career. These job titles have been extracted from the narrative and matched to underground and surface coal mining jobs originally described by Lainhart et al.[46] Of the original 6,847 observations, only

654 (9.5%) were flagged for manual review due to complex work patterns. Job codes were identified for all observations.

From the history of present illness free-text narratives, we extracted information on 34 conditions, with particular emphasis on identifying those with hypertension and other cardiovascular conditions. From the medical history narrative, we extracted additional data on comorbidities.

*Rasmussen Data: Population*
6,776 unique coal miners were identified in the Rasmussen data set. They were overwhelmingly male (>99.5%) and non-Hispanic white (>98%). The mean age was 63 years with a mean CME of 27 years (n = 6,201; median 27). Miners had many job titles and duties throughout their careers. The most commonly held job duties included hand loading/general mining (61%); a job in mine development (53%); roof bolting (48%); shuttle car operations (47%); timbermen (43%); continuous mining machine operator (35%); and loading machine operator (29%). The majority of these miners had smoked at some point during their lives (66% ever-smokers). Thirty-one percent were never-smokers and 2.5% had unquantifiable smoking histories based on the available data. Among ever-smokers, the mean pack-years was 26.7 (median 23.8). This detailed smoking information is a major strength of this data set as it is lacking in all other sources available to investigators.

These miners had a high prevalence of cardiopulmonary comorbidities. The most common were systemic hypertension (59%), COPD (21%), and/or having had a myocardial infarction (17%) or coronary artery bypass graft (12%). These comorbid conditions were self-reported and were extracted from the free-text field of "history of present illness" in each miner's medical record.

*Clinical Findings*
There were 5,426 ILO classifications of CXRs in the analytic data set. Approximately half (52%) were classified as normal (major ILO category 0) indicating no parenchymal abnormalities consistent with pneumoconiosis. Simple CWP was classified in 2,255 miners (42%), and PMF was classified in 354 miners (6.5%; Table 4).

There were 3,933 unique miners with spirometry results in the Rasmussen data set. Our initial analyses were performed on findings from the last exam of these 3,933 miners. Mean $FEV_1$pp was 80% (std 20.4; Table 5), and 41% of these miners had an abnormal $FEV_1$ ($FEV_1$ < LLN). Mean $FEV_1$, FVC, and $FEV_1$/FVC percent predicted were significantly lower in ever smokers compared to never smokers ($p < .001$ for each comparison of means). Of miners with an abnormal spirometric pattern, airflow obstruction, defined as having an obstructive or mixed obstructive/restrictive spirometric abnormality, was found in 48% of never smokers and 75% of ever smokers.

**Table 4**. International Labour Office (ILO) classification of chest x-rays from coal miners seen by Dr. Rasmussen between 2004 and 2015 (n = 5,426).

| ILO classification of pneumoconiosis | Major ILO category | n | % |
|---|---|---|---|
| No pneumoconiosis | 0 | 2,817 | 51.9 |
| Simple CWP | 1 | 2,103 | 38.8 |
| | 2/3 | 152 | 2.8 |
| PMF | A | 212 | 3.9 |
| | B | 113 | 2.1 |
| | C | 29 | 0.5 |
| **Total** | | **5,426** | |

There were 3,882 miners with an ILO classification of a CXR and a spirometry test, 33% of whom were never smokers. We found that the proportion of miners with airflow obstruction increased significantly across increasing categories of radiographic CWP (absent, simple, and progressive massive fibrosis; Table 6; p <.001), among all miners and among never smokers only as well. Forty-five percent of all miners with PMF and 27% of never smoking miners with PMF had airflow obstruction. Mean $FEV_1$ percent predicted declined significantly across increasing categories of CWP among all miners and also among never smokers. In linear regression models, we found that mean $FEV_1$ was significantly lower among those with PMF compared to those without radiographic disease (-8.4, 95%CI -10.9, -5.9) after controlling for cigarette pack years. After controlling for pack years, simple CWP was not significantly associated with $FEV_1$.

**Table 5**. Spirometric findings, including pattern and severity of spirometric abnormality, in coal miners seen by Dr. Rasmussen between 2004 and 2015 by smoking status (n = 3,933).

| Spirometry Finding | Overall | Never smokers | Ever smokers | *P* value[d] |
|---|---|---|---|---|
| n, % | 3,933 | 1,283 (32.6) | 2,650 (67.4) | |
| Abnormal spirometric pattern[a] | 1,603 (40.8) | 333 (26.0) | 1,270 (47.9) | <.001 |
| Restrictive pattern only (n, %) | 495 (12.6) | 172 (13.4) | 323 (12.2) | 0.281 |
| Obstructive pattern only (n, %) | 835 (21.2) | 126 (9.8) | 709 (26.8) | <.001 |
| Mixed obstructive and restrictive pattern (n, %) | 273 (6.9) | 35 (2.7) | 238 (9.0) | <.001 |
| Airflow obstruction (obstructive or mixed pattern) (n, %) | 1,108 (28.2) | 161 (12.6) | 947 (35.7) | <.001 |
| Spirometry indices | | | | |
| $FEV_1$ percent predicted (mean %, SD) | 80.4 (20.4) | 87.1 (17.8) | 77.1 (20.8) | <.001 |
| FVC percent predicted (mean %, SD) | 90.3 (17.1) | 91.7 (16.6) | 89.6 (17.3) | <.001 |
| $FEV_1$/FVC ratio (mean, SD) | 88.6 (15.2) | 94.7 (10.4) | 85.6 (16.3) | <.001 |
| $FEV_1$ impairment | | | | |
| $FEV_1$ < LLN (n, %)[b] | 1,395 (35.5) | 291 (22.7) | 1,104 (41.7) | <.001 |
| Severity of $FEV_1$ impairment[c] | | | | |
| Mild | 295 (21.1) | 96 (33.0) | 199 (18.0) | <.001 |
| Moderate | 476 (34.1) | 106 (36.4) | 370 (33.5) | |
| Moderately severe | 295 (21.1) | 47 (16.2) | 248 (22.5) | |
| Severe | 236 (16.9) | 36 (12.4) | 200 (18.1) | |
| Very severe | 93 (6.7) | 6 (2.1) | 87 (7.9) | |

$FEV_1$, Forced expiratory volume in one second; FVC, Forced vital capacity; LLN, Lower limit of normal

[a] Pattern of impairment defined as: restrictive (FVC<LLN; $FEV_1$/FVC≥LLN); obstructive ($FEV_1$/FVC<LLN; FVC≥LLN); mixed obstructive and restrictive (FVC<LLN; $FEV_1$/FVC<LLN)

[b] Forced expiratory volume in one second ($FEV_1$) considered abnormal if $FEV_1$ < lower limit of normal (LLN)
[c] Severity of $FEV_1$ impairment based on Pellegrino, et al. (2005)
[d] P values derived from t-tests for continuous variables and Chi-square tests for proportions of categorical variables

**Table 6.** Spirometric findings, including pattern and severity of spirometric abnormality, by radiographic category of coal workers' pneumoconiosis (CWP; absent, simple CWP, or progressive massive fibrosis [PMF]) among a subset of former coal miners with both a chest x-ray and spirometry test (n = 3,882).

| **Spirometry Findings in All Miners** | **No CWP (n = 2,231)** | **Simple CWP (n = 1,392)** | **PMF (n = 259)** | ***P* value** |
|---|---|---|---|---|
| Abnormal spirometric pattern | | | | |
| Restrictive pattern only, n (%) | 258 (11.6) | 191 (13.7) | 38 (14.7) | 0.092 |
| Obstructive pattern only, n (%) | 421 (18.9) | 308 (22.1) | 91 (35.1) | <.001 |
| Mixed obstructive and restrictive pattern, n (%) | 138 (6.2) | 102 (7.3) | 26 (10.0) | 0.046 |
| Airflow obstruction (obstructive or mixed pattern), n (%) | 559 (25.1) | 410 (29.4) | 117 (45.1) | <.001 |
| Spirometry indices | | | | |
| $FEV_1$ percent predicted, mean % (SD) | 81.8 (20.5) | 79.6 (20.2) | 73.8 (19.3) | <.001 |
| FVC percent predicted, mean % (SD) | 91.0 (16.9) | 89.7 (17.3) | 88.3 (17.8) | 0.01 |
| $FEV_1$/FVC ratio, mean (SD) | 89.4 (15.0) | 88.4 (15.2) | 83.6 (15.8) | <.001 |
| $FEV_1$ impairment | | | | |
| $FEV_1$ < LLN, n (%) | 722 (32.4) | 515 (37.0) | 131 (50.6) | <.001 |
| Moderate to severe FEV1 impairment, n (%) | 308 (13.8) | 237 (17.0) | 63 (24.3) | <.001 |
| **Spirometry Findings in Never Smoking Miners** | **(n = 824)** | **(n = 352)** | **(n = 94)** | ***P* value** |
| Abnormal spirometric pattern | | | | |
| Restrictive pattern only, n (%) | 107 (13.0) | 49 (13.9) | 14 (14.9) | 0.825 |
| Obstructive pattern only, n (%) | 69 (8.4) | 31 (8.8) | 23 (24.5) | <.001 |
| Mixed obstructive and restrictive pattern, n (%) | 20 (2.4) | 11 (3.1) | 2 (2.1) | 0.755 |
| Airflow obstruction (obstructive or mixed pattern), n (%) | 89 (10.8) | 42 (11.9) | 25 (26.6) | <.001 |
| Spirometry indices | | | | |
| $FEV_1$ percent predicted, mean % (SD) | 88.5 (17.5) | 86.3 (18.3) | 80.6 (16.3) | <.001 |
| FVC percent predicted, mean % (SD) | 92.4 (16.6) | 90.7 (16.8) | 90.3 (15.7) | 0.17 |
| $FEV_1$/FVC ratio, mean (SD) | 95.5 (9.4) | 94.8 (11.3) | 89.2 (12.0) | <.001 |
| $FEV_1$ impairment | | | | |
| $FEV_1$ < LLN, n (%) | 170 (20.6) | 77 (21.9) | 36 (38.3) | <.001 |
| Moderate to severe $FEV_1$ impairment, n (%) | 47 (5.7) | 28 (8.0) | 10 (10.6) | 0.10 |

$FEV_1$, Forced expiratory volume in one second; FVC, Forced vital capacity; LLN, Lower limit of normal

There were 3,228 miners with a diffusion capacity test available, 33% of which were never smokers (Table 7). Mean DLCO percent predicted was significantly lower in ever smokers (mean DLCO percent predicted 88) compared to never smokers (mean DLCO percent predicted 99; p <.001). The proportion of ever smokers with DLCO impairment was significantly higher than never smokers (p <.001). Ever smokers had higher likelihood of moderate to severe diffusion impairment.

Mean DLCO percent predicted values decreased significantly across increasing severity of radiographic CWP, both among all miners and among never smokers as well (Table 8). Similarly, the proportion of miners with impaired diffusion capacity increased significantly with increasing radiographic disease. Nineteen percent of never smokers with simple CWP and 30%

of never smokers with PMF had DLCO values below the lower limit of normal. In linear regression models, simple CWP and PMF were both significantly associated with lower DLCO values (Simple CWP -8.9, 95%CI -10.3, -7.4, p-value < 0.0001; PMF -18.1, 95%CI -20.8, -15.4, p-value < 0.0001) after controlling for cigarette pack years. These findings underscore the importance of measuring DLCO in coal miners with pneumoconiosis to better identify the presence and extent of impairment, which may not be reflected in spirometric measures alone.

**Table 7**. Diffusion capacity findings, including severity of DLCO impairment, in coal miners seen by Dr. Rasmussen between 2004 and 2015 by smoking status (n = 3,228).

| Diffusion Capacity Finding | Overall | Never smokers | Ever smokers |
|---|---|---|---|
| n, % | 3,228 | 1,058 (32.8) | 2,170 (67.2) |
| DLCO pp (mean %, SD) | 91.3 (21.1) | 99.0 (19.0) | 87.9 (21.1) |
| DLCO Impairment (DLCO < LLN) | 677 (21.0) | 119 (11.2) | 558 (25.7) |
| Severity of DLCO impairment[a] | | | |
| Mild (DLCO pp >60% and <LLN) | 414 (61.2) | 86 (72.3) | 328 (58.8) |
| Moderate (DLCO pp 40-60%) | 219 (32.3) | 26 (21.8) | 193 (34.6) |
| Severe (DLCO pp <40%) | 44 (6.5) | 7 (5.9) | 37 (6.6) |

$FEV_1$, Forced expiratory volume in one second; FVC, Forced vital capacity; LLN, Lower limit of normal; DLCO, Diffusing capacity of the lungs for carbon monoxide; pp, percent predicted
[a]Severity of DLCO impairment described by Pellegrino, et al.[44]

**Table 8.** Diffusion capacity findings, including severity of DLCO impairment, by radiographic category of CWP (absent, simple coal workers' pneumoconiosis (CWP), or progressive massive fibrosis (PMF)) among a subset of former coal miners with both a chest x-ray and diffusion capacity test (n = 3,186).

| **Diffusion Capacity Findings in All Miners** | **No CWP (n = 1,811)** | **Simple CWP (n = 1,152)** | **PMF (n = 223)** | ***P* value** |
|---|---|---|---|---|
| DLCO pp (mean %, SD) | 96.5 (19.7) | 86.3 (21.5) | 78.9 (17.1) | <.001 |
| DLCO Impairment (DLCO < LLN) (n (%) | 237 (13.1) | 333 (28.9) | 95 (42.6) | <.001 |
| Severity[a] of DLCO impairment n (%) | | | | |
| Mild (DLCO pp >60% and <LLN) | 158 (66.7) | 188 (56.5) | 63 (66.3) | |
| Moderate (DLCO pp 40-60%) | 64 (27.0) | 121 (36.3) | 27 (28.4) | <.001 |
| Severe (DLCO pp <40%) | 15 (6.3) | 24 (7.2) | 5 (5.3) | |
| **Diffusion Capacity Findings in Never Smoking Miners** | **(n = 664)** | **(n = 300)** | **(n = 83)** | ***P* value** |
| DLCO pp (mean %, SD) | 103.5 (17.3) | 93.5 (19.8) | 84.4 (14.9) | <.001 |
| DLCO Impairment (DLCO < LLN) n (%) | 33 (5.0) | 57 (19.0) | 25 (30.1) | <.001 |
| Severity[a] of DLCO impairment n (%) | | | | |
| Mild (DLCO pp >60% and <LLN) | 25 (75.8) | 40 (70.2) | 19 (76.0) | |
| Moderate (DLCO pp 40-60%) | 5 (15.2) | 13 (22.8) | 6 (24.0) | <.001 |
| Severe (DLCO pp <40%) | 3 (9.1) | 4 (7.0) | 0 (0.0) | |

$FEV_1$, Forced expiratory volume in one second; FVC, Forced vital capacity; LLN, Lower limit of normal; DLCO, Diffusing capacity of the lungs for carbon monoxide; pp, percent predicted
[a]Severity of DLCO impairment described by Pellegrino, et al.[44]

There were 2,504 miners with both spirometry and CPETs. Miners with abnormal lung function ($FEV_1$ <LLN) had significantly higher dead space fraction values than those with normal $FEV_1$, indicating damage to the pulmonary gas exchanging units in those miners with abnormal $FEV_1$ values (Table 9). We did not observe the same difference in dead space fraction among never-smoking miners.

There were 2,501 miners with both spirometry and ABG tests. The alveolar-arterial gradient (A-a gradient) for oxygen at baseline and peak is higher, consistent with impairment in gas exchange, in miners with abnormally low $FEV_1$ (Table 11) and those with evidence of radiographic CWP (Table 12). However, these data also suggest that even non-smoking miners with normal $FEV_1$ or those without evidence of radiographic CWP may also have an abnormally elevated A-a gradient. We will continue to investigate this further in the coming months.

**Table 9**. Cardiopulmonary exercise testing (CPET) findings by spirometric abnormality (abnormal $FEV_1pp$ = $FEV_1$<LLN) among a subset of former coal miners with both a spirometry test and CPET (n = 2,504).

| **CPET Findings in All Miners** | **Normal $FEV_1pp$ (n = 1,896)** | | **$FEV_1pp$ < LLN (n = 608)** | | |
|---|---|---|---|---|---|
| **Variable** | **Mean** | **Std Dev** | **Mean** | **Std Dev** | ***P* value** |
| VE*/VO2 (Base) | 36.84 | 8.26 | 37.65 | 9.30 | 0.0707 |
| VE*/VO2 (Peak) | 32.00 | 6.96 | 32.52 | 6.63 | 0.1572 |
| VE*/VCO2 (Base) | 44.74 | 9.02 | 45.68 | 11.25 | 0.0785 |
| VE*/VCO2 (Peak) | 34.15 | 6.41 | 34.69 | 6.75 | 0.1196 |
| Dead space fraction (Base) | 0.37 | 0.08 | 0.39 | 0.09 | <.0001 |
| Dead space fraction (Peak) | 0.25 | 0.08 | 0.28 | 0.08 | <.0001 |
| **CPET Findings in Never Smoking Miners** | **Normal $FEV_1pp$ (n = 762)** | | **$FEV_1pp$ < LLN (n = 159)** | | |
| **Variable** | **Mean** | **Std Dev** | **Mean** | **Std Dev** | ***P* value** |
| VE*/VO2 (Base) | 35.44 | 7.51 | 34.64 | 7.93 | 0.2111 |
| VE*/VO2 (Peak) | 30.77 | 6.67 | 30.55 | 6.54 | 0.6728 |
| VE*/VCO2 (Base) | 43.19 | 7.94 | 42.02 | 9.12 | 0.1207 |
| VE*/VCO2 (Peak) | 32.95 | 6.04 | 32.48 | 6.71 | 0.3224 |
| Dead space fraction (Base) | 0.35 | 0.08 | 0.35 | 0.08 | 0.9708 |
| Dead space fraction (Peak) | 0.23 | 0.07 | 0.23 | 0.08 | 0.8592 |

VE/VO2, Ventilatory equivalent for oxygen; VE/VCO2, Ventilatory equivalent for carbon dioxide; $FEV_1$, Forced expiratory volume in one second; LLN, Lower limit of normal

*p value based on t-tests.

**Table 10.** Cardiopulmonary exercise testing findings by radiographic category of CWP (absent, simple coal workers' pneumoconiosis (CWP), or progressive massive fibrosis (PMF)) among a subset of former coal miners with both a chest x-ray and CPET (n = 2,478).

| **CPET Findings in All Miners** | **No CWP (n = 1,432)** | | **Simple CWP (n = 866)** | | **PMF (n = 180)** | | |
|---|---|---|---|---|---|---|---|
| **Variable** | **Mean** | **Std Dev** | **Mean** | **Std Dev** | **Mean** | **Std Dev** | ***P* value*** |
| VE[a]/VO2 (Base) | 36.05[a,b] | 7.49 | 38.27[a] | 9.63 | 38.72[b] | 7.90 | <.0001 |
| VE/VO2 (Peak) | 31.29[a,b] | 6.43 | 33.06[a] | 7.45 | 33.95[b] | 6.48 | <.0001 |
| VE/VCO2 (Base) | 43.44[a,b] | 8.28 | 46.87[a] | 10.96 | 47.75[b] | 9.64 | <.0001 |
| VE/VCO2 (Peak) | 33.22[a,b] | 5.92 | 35.51[a] | 6.90 | 36.39[b] | 7.26 | <.0001 |
| Dead space fraction (Base) | 0.36[a,b] | 0.08 | 0.38[a] | 0.09 | 0.39[b] | 0.08 | <.0001 |
| Dead space fraction (Peak) | 0.25[a,b] | 0.08 | 0.27[a] | 0.08 | 0.28[b] | 0.07 | <.0001 |
| **CPET Findings in Never Smoking Miners** | **No CWP (n = 589)** | | **Simple CWP (n = 254)** | | **PMF (n = 73)** | | |
| **Variable** | **Mean** | **Std Dev** | **Mean** | **Std Dev** | **Mean** | **Std Dev** | ***P* value*** |
| VE[a]/VO2 (Base) | 34.59[a,b] | 6.95 | 36.45[a] | 8.96 | 36.99[b] | 6.84 | 0.0006 |
| VE/VO2 (Peak) | 30.02[a,b] | 5.86 | 31.61[a] | 7.94 | 33.07[b] | 6.69 | <.0001 |
| VE/VCO2 (Base) | 41.89[a,b] | 7.49 | 44.63[a] | 9.11 | 45.90[b] | 8.36 | <.0001 |
| VE/VCO2 (Peak) | 31.90[a,b] | 5.32 | 34.12[a] | 6.86 | 35.79[b] | 7.66 | <.0001 |
| Dead space fraction (Base) | 0.34[a] | 0.08 | 0.36 | 0.08 | 0.37[a] | 0.08 | 0.0048 |
| Dead space fraction (Peak) | 0.22[a,b] | 0.07 | 0.24[a,c] | 0.07 | 0.27[b,c] | 0.07 | <.0001 |

VE/VO2, Ventilatory equivalent for oxygen; VE/VCO2, Ventilatory equivalent for carbon dioxide;
*p value based on ANOVA with a post-hoc Tukey's test; Matching superscripts indicate those values that are statistically different from one another.

**Table 11**. Arterial blood gas (ABG) testing findings by spirometric abnormality (abnormal $FEV_1pp = FEV_1<LLN$) among a subset of former coal miners with both a spirometry test and ABG (n = 2,501).

| **ABG Findings in All Miners** | **Normal $FEV_1pp$ (n = 1,894)** | | **$FEV_1pp$ < LLN (n = 607)** | | |
|---|---|---|---|---|---|
| **Variable** | **Mean** | **Std Dev** | **Mean** | **Std Dev** | ***P* value*** |
| pH at Base | 7.42 | 0.03 | 7.42 | 0.03 | 0.0609 |
| pH at Peak | 7.40 | 0.04 | 7.40 | 0.04 | 0.0001 |
| PCO2 (Base) | 36.78 | 3.72 | 37.99 | 4.15 | <.0001 |
| PCO2 (Peak) | 36.77 | 4.07 | 37.84 | 4.11 | <.0001 |
| PO2 (Base) | 93.94 | 5.30 | 92.80 | 5.47 | <.0001 |
| PO2 (Peak) | 98.21 | 5.22 | 97.23 | 5.18 | <.0001 |
| A-a Gradient (Base) | 13.19 | 7.41 | 17.17 | 7.77 | <.0001 |
| A-a Gradient (Peak) | 21.33 | 10.54 | 26.08 | 10.51 | <.0001 |
| **ABG Findings in Never Smoking Miners** | **Normal $FEV_1pp$ (n = 760)** | | **$FEV_1pp$ < LLN (n = 159)** | | |
| **Variable** | **Mean** | **Std Dev** | **Mean** | **Std Dev** | ***P* value*** |
| pH at Base | 7.42 | 0.03 | 7.42 | 0.04 | 0.2098 |
| pH at Peak | 7.40 | 0.04 | 7.40 | 0.04 | 0.2489 |
| PCO2 (Base) | 36.79 | 3.73 | 38.09 | 4.38 | 0.0047 |
| PCO2 (Peak) | 36.93 | 4.25 | 37.89 | 4.58 | 0.1242 |
| PO2 (Base) | 93.68 | 5.47 | 92.64 | 5.70 | 0.1313 |
| PO2 (Peak) | 97.86 | 5.38 | 97.10 | 5.45 | 0.7615 |
| A-a Gradient (Base) | 11.97 | 6.94 | 14.73 | 7.55 | <.0001 |
| A-a Gradient (Peak) | 19.52 | 9.48 | 24.49 | 10.66 | <.0001 |

PCO2, Partial pressure of carbon dioxide; PO2, Partial pressure of oxygen; A-a Gradient, alveolar-arterial gradient for oxygen; $FEV_1$, Forced expiratory volume in one second; LLN, Lower limit of normal
*p value based on t-tests

**Table 12.** Arterial blood gas (ABG) testing findings by radiographic category of coal workers' pneumoconiosis (CWP; absent, simple CWP, or progressive massive fibrosis (PMF)) among a subset of former coal miners with both a CXRand ABG (n = 2,478).

| **ABG Findings in All Miners** | **No CWP (n = 1,432)** | | **Simple CWP (n = 866)** | | **PMF (n = 180)** | | |
|---|---|---|---|---|---|---|---|
| **Variable** | **Mean** | **Std Dev** | **Mean** | **Std Dev** | **Mean** | **Std Dev** | ***P* value*** |
| pH at Base | 7.42[a,b] | 0.03 | 7.42[a] | 0.03 | 7.43[b] | 0.03 | <.0001 |
| pH at Peak | 7.40[a,b] | 0.04 | 7.41[a] | 0.04 | 7.41[b] | 0.05 | <.0001 |
| PCO2 (Base) | 37.46[a,b] | 3.83 | 36.59[a] | 3.84 | 36.39[b] | 3.97 | <.0001 |
| PCO2 (Peak) | 37.54[a,b] | 4.08 | 36.42[a] | 4.02 | 36.17[b] | 4.20 | <.0001 |
| PO2 (Base) | 93.34[a,b] | 5.28 | 94.06[a] | 5.48 | 94.13[b] | 5.24 | 0.0011 |
| PO2 (Peak) | 97.44[a,b] | 5.30 | 98.57[a] | 5.11 | 99.04[b] | 4.85 | <.0001 |
| A-a Gradient (Base) | 13.19[a] | 7.55 | 15.59[a] | 7.84 | 14.91 | 7.05 | <.0001 |
| A-a Gradient (Peak) | 19.48[a,b] | 9.39 | 25.69[a,c] | 11.38 | 30.32[b,c] | 8.91 | <.0001 |
| **ABG Findings in Never Smoking Miners** | **No CWP (n = 589)** | | **Simple CWP (n = 254)** | | **PMF (n = 73)** | | |
| **Variable** | **Mean** | **Std Dev** | **Mean** | **Std Dev** | **Mean** | **Std Dev** | ***P* value*** |
| pH at Base | 7.42[a,b] | 0.03 | 7.42[a] | 0.04 | 7.43[b] | 0.03 | 0.0006 |
| pH at Peak | 7.40[a] | 0.04 | 7.41[a] | 0.04 | 7.41 | 0.05 | 0.0015 |
| PCO2 (Base) | 37.48[a,b] | 3.82 | 36.22[a] | 3.76 | 36.30[b] | 4.20 | <.0001 |
| PCO2 (Peak) | 37.60[a,b] | 4.19 | 36.32[a] | 4.36 | 36.12[b] | 4.66 | <.0001 |
| PO2 (Base) | 93.05[a] | 5.46 | 94.31[a] | 5.51 | 94.02 | 5.69 | 0.0030 |
| PO2 (Peak) | 97.30[a,b] | 5.39 | 98.36[a] | 5.32 | 98.80[b] | 5.42 | 0.0023 |
| A-a Gradient (Base) | 11.89[a] | 7.17 | 13.45[a] | 6.95 | 13.33 | 7.07 | 0.0041 |
| A-a Gradient (Peak) | 18.03[a,b] | 8.62 | 23.09[a,c] | 10.67 | 29.73[b,c] | 8.49 | <.0001 |

PCO2, Partial pressure of carbon dioxide; PO2, Partial pressure of oxygen; A-a Gradient, alveolar-arterial gradient for oxygen
*p value based on ANOVA with a post-hoc Tukey's test; Matching superscripts indicate those values that are statistically different from one another.

**Objective 4:** Link data from the CWHSP, FBLP, and NDI to the Rasmussen data to further explore progression of disease as well as associations between coal mining tenure, CMDLD severity, lung function ($FEV_1$), smoking, and time to death through Cox PHregression models. Characterize the underlying and contributing causes of death among the thousands of coal miners seen by Dr. Rasmussen between 2004 and 2015.

*FBLP, CWHSP, RASMUSSEN Data Linkage*

There were 3,094 miners seen by Dr. Rasmussen between 2004 and 2015 who could be linked to miners in the CWHSP/FBLP/NDI database. All of the linked miners were male and all but two were non-Hispanic white. Of these miners, only 283 (9%) were deceased as of Dec 31, 2016. While this represents a small percentage of the linked miners, this is not surprising as death data was obtained only through Dec 31, 2016, and the miners seen in Dr. Rasmussen's clinic were seen between 2004 and 2015.

*Lung Function Decline Among Rasmussen Miners*

The DOL FBLP does not include smoking history data for the miners in its data set. The Rasmussen data, containing examinations that comprise a subset of those performed for the

FBLP, has detailed smoking histories and allows us to examine lung function decline as it relates to coal mine employment tenure, job titles, and demographic variables while controlling for smoking.

There were 1,432 miners seen by Dr. Rasmussen who (1) linked to the FBLP/CWHSP data and (2) had serial spirometry tests for analysis. An examination of each miner's first spirometry test in these data reveals that the mean $FEV_1$ percent predicted ($FEV_1pp$) was 82.1, and 39.2% had an abnormal $FEV_1$ ($FEV_1pp$ < lower limit of normal). Among those with an abnormal $FEV_1$, 29.6% had moderately severe to very severe impairment ($FEV_1pp < 60\%$). Mean FVCpp was 87.6 in this group, and 32.7% of miners had abnormally low FVC values at their first spirometry test (Table 13).

At the time of their last spirometry test in these data, the proportion of miners with abnormally low $FEV_1$ and FVC values increased to 46.5% and 38.5%, respectively. Mean $FEV_1pp$ declined to 78.0 and mean FVCpp declined to 84.1 at the time of miners' last spirometry test.

**Table 13.** Characteristics of miners seen by Dr. Rasmussen with at least two spirometry sets across either or both the Coal Worker's Health Surveillance Program or the Federal Black Lung Program, 2000-2016 (n=1,432).

| **Miner Characteristic** | **n** | **%** |
|---|---|---|
| Sex | | |
| Male | 1,432 | 100 |
| Race | | |
| Non-Hispanic White | 1,430 | 99.9 |
| Non-Hispanic Black | 2 | <0.1 |
| Smoking Status | | |
| Never-smoker | 437 | 30.5 |
| Former or current smoker | 944 | 65.9 |
| Pack years (mean, std) | 26.1 | 18.8 |
| Coal Mine Employment | | |
| Years Claimed (mean, std) | 26.4 | 8.4 |
| Years Verified[a] (mean, std) | 23.1 | 8.8 |
| Mean $FEV_1$ Percent Predicted (mean, std) | | |
| At time of initial spirometry | 82.1 | 18.3 |
| At time of last spirometry | 78.0 | 20.2 |
| Abnormal $FEV_1$ ($FEV_1$ < LLN) | | |
| At time of initial spirometry | 561 | 53.5 |
| At time of last spirometry | 666 | 46.5 |
| Abnormal FVC (FVC < LLN) | | |
| At time of initial spirometry | 468 | 32.7 |
| At time of last spirometry | 551 | 38.5 |

[a] The DOL provides both the years of coal mine employment claimed by the miner and verified by social security records.

Of those with normal $FEV_1$ at the time of their first spirometry (n = 871), 25.5% had abnormal $FEV_1$ values at the time of their last spirometry. Among those who experienced a decline in

$FEV_1$pp (n = 897), the mean (std) decline was 2.7pp per year (std 3.1pp).

We examined the relationship between $FEV_1$pp decline and the following predictors: age, years between tests, pack years, CME tenure, and radiographic disease using linear regression models in this subset of miners, as the larger FBLP/CWHSP data set lacks smoking data. As nearly all (>95%) of the miners seen by Dr. Rasmussen were Central Appalachian miners, we were unable to examine regional differences in this sub-analysis. We found that after controlling for the predictors above, only time between spirometry tests (in years) was a significant predictor of $FEV_1$pp decline in this subset of miners. The two strongest predictors of $FEV_1$pp decline in terms of estimates of effect were having radiographic coal workers' pneumoconiosis at the time of their first spirometry test and length of CME, but neither were significant in the regression models. The results of a sub-analysis among miners who reported never having smoked cigarettes (n = 437) were similar. Given that smoking pack-years (which were well-described in this sub-analysis of Dr. Rasmussen's miners) was not a significant predictor lends further support to the validity of the larger progression study performed under Task 1.1.

*Proportionate Mortality among Rasmussen Miners*

As described above, of the 3,094 miners seen by Dr. Rasmussen who could be linked to the FBLP/CWHSP data set, only 283 miners had died as of December 31, 2016. Mean age at death was 71 years (std 9.6 years), and the majority of miners in this population were born between 1930-1939. This differs substantially from the larger mortality cohort in which 69% were born prior to 1920. Also in contrast to the larger mortality cohort, the most common underlying cause of death in the Rasmussen miners was NMRD (35% compared to 20% in the larger mortality analysis). IHD and lung cancer were the underlying causes of death for 17% and 12% of these miners, respectively (Table 14). Among those with NMRD as the underlying cause of death (n = 100), the two most prevalent causes were CLRD (n = 40, 40%) and pneumoconiosis (n = 40, 40%). Pneumoconiosis was listed as the underlying cause of death in 14% of the overall population – double that seen in the larger mortality analysis – and was a contributing cause of death in 27% of deaths.

While there were relatively few miners with a determination of PMF in this sub-analysis (n = 59), these miners were significantly more likely to have NMRD or CLRD listed as the underlying cause of death than non-PMF miners (Table 14). There were no significant differences in age at death or birth cohort between the PMF and non-PMF miners in this sub-analysis. Miners in this subset of Rasmussen data worked long tenures in the coal mine industry. On average, PMF miners worked in coal mining longer than their non-PMF counterparts, but this was not a significant difference (29 vs 27 years, p = .1524). Surprisingly, only 29% of miners with PMF had pneumoconiosis listed as a contributing cause of death on their death certificates.

**Table 14.** Descriptive characteristics of deceased miners participating in the Coal Workers' Health Surveillance Program or applying for Federal Black Lung Program benefits between 1970 – 2017, by PMF status[a]. All miners were seen by Dr. Rasmussen in his Black Lung Clinic in West Virginia between 2004 and 2015.

| | **All Deceased Miners (n = 283)** | | **Non-PMF Miners (n=224)** | | **PMF Miners (n=59)** | | |
|---|---|---|---|---|---|---|---|
| **Variable** | **n** | **%** | **n** | **%** | **n** | **%** | **p-value*** |
| Age at Death | | | | | | | |
| 45-65 | 70 | 24.7 | 53 | 23.7 | 17 | 28.8 | 0.713 |
| 65-74 | 105 | 37.1 | 84 | 37.5 | 21 | 35.6 | |
| ≥75 | 108 | 38.2 | 87 | 38.8 | 21 | 35.6 | |
| Birth Cohort | | | | | | | |
| <1920 | 37 | 13.1 | 30 | 13.4 | 7 | 11.9 | 0.554 |
| 1920-1929 | 81 | 28.6 | 67 | 29.9 | 14 | 23.7 | |
| 1930-1939 | 165 | 58.3 | 127 | 56.7 | 38 | 64.4 | |
| Underlying Cause of Death[b] | | | | | | | |
| NMRD | 100 | 35.3 | 69 | 30.8 | 31 | 52.5 | 0.002 |
| CWP | 34 | 12 | 24 | 10.7 | 10 | 17 | 0.190 |
| Pneumoconioses | 40 | 14.1 | 29 | 13.0 | 11 | 18.6 | 0.264 |
| CLRD | 40 | 14.1 | 25 | 11.2 | 15 | 25.4 | 0.005 |
| Lung Cancer | 35 | 12.4 | 30 | 13.4 | 5 | 8.5 | 0.307 |
| IHD | 48 | 17 | 30 | 13.4 | 4 | 6.8 | 0.165 |
| Contributing Causes of Death[c] | | | | | | | |
| NMRD | 183 | 64.7 | 144 | 64.3 | 39 | 66.1 | 0.795 |
| CWP | 64 | 22.6 | 49 | 21.9 | 15 | 25.4 | 0.562 |
| Pneumoconioses | 76 | 26.9 | 59 | 26.3 | 17 | 28.8 | 0.703 |
| CLRD | 97 | 34.3 | 71 | 31.7 | 26 | 44.1 | 0.075 |
| Lung Cancer | 41 | 14.5 | 35 | 15.6 | 6 | 10.2 | 0.290 |
| IHD | 63 | 22.3 | 55 | 24.6 | 8 | 13.6 | 0.071 |

[a] Progressive massive fibrosis (PMF) as determined through the Federal Black Lung Benefits Program claims process.
[b] Non-malignant respiratory disease (NMRD) category contains coal workers' pneumoconiosis (CWP), all pneumoconioses, emphysema, and chronic obstructive pulmonary disease (COPD) categories.
[c] Categories are not mutually exclusive. Individuals are categorized based on underlying and contributing causes of death.
* P-value based on results of Chi-square test of proportions

*Survival Analysis of Miners seen by Dr. Rasmussen*

Using the subset of miners seen by Dr Rasmussen that also linked to the larger FBLP/CWHSP data set, we performed Cox PH modeling to address this task. We found that $FEV_1$pp, age, smoking status (nonsmoker vs former/current smoker), severity of radiographic CWP, and whether the miner had won their DOL claim were significant predictors of probability of death. Hypertension and total coal mine employment were included in the model but were not significant predictors of mortality.

Having an abnormal $FEV_1$ ($FEV_1pp$ < LLN) was significantly associated with having over three times the probability of death compared to those with a normal $FEV_1$, even after controlling for smoking status (HR 3.03, 95% CI 2.33, 3.95). Conversely, higher $FEV_1pp$ was significantly associated with increased survival (HR 0.73, 95% CI 0.69, 0.78 for every increase of 10 $FEV_1pp$). One of the strongest predictors of increased mortality was winning one's DOL claim (HR 1.80, 95% CI 1.37, 2.36), which likely reflects the greater ease with which severe disease claims are awarded. Mortality probability was significantly increased for those with simple CWP (HR 1.47, 95% CI 1.12, 1.93) and PMF (HR 3.92, 95% CI 2.65, 5.81) compared to those without radiographic evidence of coal workers' pneumoconiosis.

## 6.0 Publication Record and Dissemination Efforts

We have made considerable efforts to disseminate our research findings to all relevant stakeholders, including federal agencies, the scientific community, miners, and the general public. The results of these efforts are presented below.

**6.1** Published and planned manuscripts

1. Almberg KS, Halldin CN, Friedman LS, et al. Increased odds of mortality from non-malignant respiratory disease and lung cancer are highest among U.S. coal miners born after 1939. *Occup Environ Med*. 2023; 80: 121-128. doi:10.1136/oemed-2022-108539
2. Go LHT, Almberg KS, Rose CS, Cohen RA. Relationship between radiographic disease, spirometry findings, and diffusion capacity in a population of former U.S. coal miners. *Occup Environ Med* (*in preparation)*.
3. Almberg, KA et al. Survival Analysis of U.S. Coal Miners: Risks and protective factors. (*in progress*).
4. Cohen, RA et al. Physiologic impairment associated with coal mine employment: beyond spirometry. (*planned*).

**6.2** Peer reviewed presentations at national and international scientific conferences

1. Almberg KS, Go LHT, Rose CS, Zell-Baran L, Friedman L, Cohen RA. Relationship Between Radiographic Disease, Spirometry Findings, and Diffusion Capacity in a Population of Former U.S. Coal Miners. American Thoracic Society International Conference Abstracts. American Thoracic Society; B105 Advances in Occupational Lung Disease; 2023; 209.
2. Almberg KS, Halldin CN, Friedman LS, Go LHT, Rose CS, Cohen RA. Excess Mortality from Chronic Lower Respiratory Disease, Lung Cancer, and Pneumoconiosis Is Increasing in US Coal Miners. American Thoracic Society International Conference Abstracts. American Thoracic Society; 2021; 203:A3036.

**6.3** Invited presentations at national and international meetings

1. Almberg, KS. "Research Update: The Changing Burden of Radiographic, Physiologic and Mortality Among Former Miners." The National Coalition of Black Lung & Respiratory Disease Clinics Conference. St. Louis, Missouri. September 28, 2022.
2. Almberg, KS. "Long term Pathologic and Epidemiologic Trends in Black Lung." The National Coalition of Black Lung & Respiratory Disease Clinics Conference. *Virtual*. September 22, 2021.

**6.4** Dissemination of findings via the media

1. Almberg, KS and Cohen, RA. "Modern Coal Miners Have Higher Death Rates From Lung Diseases Than Their Predecessors." NIOSH Science Blog, CDC.

February 27, 2023. https://blogs.cdc.gov/niosh-science-blog/2023/02/27/mining-lung-disease/

2. Stump, J. “Black lung is on the rise in Appalachia; deregulation of the coal mine industry is the main culprit.” Virginia Mercury. March 21, 2023. https://www.virginiamercury.com/2023/03/21/black-lung-iblack-lung-deregulation-of-coal-mine-industry-leads-to-black-lung-spike-in-appalachia/
3. Vogelsong, S. “Modern Kentucky Coal Miners Face Higher Mortality Risk Than Predecessors.” CityBeat. March 6, 2023. https://www.citybeat.com/news/modern-kentucky-coal-miners-face-higher-mortality-risk-than-predecessors-14874334
4. Pollard, T. “CDC shares new research: For miners, death rate from lung disease is higher than ever before.” Appalachian Voices Press Release. February 27, 2023. https://appvoices.org/2023/02/28/coal-miner-death-rate/

## 7.0 Conclusions and Impact Assessment

While occupational exposure to respirable coal mine dust can cause a broad spectrum of respiratory diseases, encompassed by the term CMDLD[2], much of the work to date on CMDLD has relied almost exclusively on radiographic evidence of disease, which does not reflect the true burden of CMDLD among U.S. coal miners. Furthermore, there has been scant examination of rates of disease progression, both radiographically and physiologically, over the lifetime of the miner. This body of work reflects the most comprehensive effort to date to characterize the full spectrum of CMDLD among U.S. coal miners and elucidate longitudinal trends in their cardiopulmonary health as a result of their occupational exposures.

Our findings on radiographic progression demonstrate that CWP can develop and/or progress rapidly to PMF absent further coal mine dust exposure. We found that 42% of miners who had no evidence of CWP at their baseline CXR had developed simple CWP and 3% had developed PMF by the time of their FBLP claim. For those with baseline CXRs indicating simple CWP while they were actively working, 23% progressed to category 2 or 3 simple CWP and 12% progressed to PMF (n = 18) by the time of their final FBLP claim. Likelihood of progression to PMF was most significantly associated with increasing small opacity profusion on earlier CXR, controlling for region and coal mine employment tenure. This finding underscores the importance of identifying current, active miners at the earliest stages of disease and reducing or preventing further coal mine dust exposure. Importantly, the absence of radiographic pneumoconiosis after dust exposure has ceased does not preclude development of PMF at a later time. Our findings suggest that former coal miners, especially those with at least 10 years of coal mine dust exposure, should continue to participate in regular medical surveillance.

In our examination of progression of lung function decline, we found that having mined in Central Appalachia was associated with worsening mean $FEV_1$pp compared to miners from the rest of the U.S., controlling for age, years between tests, and CMEtenure. When we examined this in the subset of miners for whom we could control for the confounding effect of smoking, we found that the time between spirometry tests was the strongest predictor of progression, suggesting that former miners should receive frequent lung function testing to monitor and/or intervene to impede the loss of further lung function. Our findings also suggest that former miners with evidence of radiographic coal workers' pneumoconiosis and long coal mine tenures should be prioritized for frequent screening.

The findings from our mortality study, the largest and most comprehensive to date, demonstrate that U.S. coal miners experience excess mortality from respiratory diseases including pneumoconiosis, chronic lower respiratory diseases, and lung cancer compared to total U.S. and Central Appalachian populations. Of great concern, these associations are highest in the most recent birth cohort, consistent with current reports of increasing prevalence of CMDLD and PMF in younger miners. Importantly, our work highlights the increased relative contribution of obstructive lung disease to CMDLD mortality and underscores the importance of coal mine dust exposure as an important cause of occupational obstructive lung disease. Our most recent analysis shows an increase in mortality associated with simple CWP, a finding not previously demonstrated. Prior work primarily showed that PMF was associated with increased mortality.

Using data from Dr. Rasmussen's WV black lung clinic, we have demonstrated that additional tests beyond spirometry and chest radiography, including diffusion capacity, ABGs, and CPET, are critical for understanding the true burden of disease and impairment in this population of workers. In particular, CPET can identify abnormalities that are not identified in resting studies alone. These miners had high rates of lung function impairment (33%) and relatively high rates of PMF (7%), including among never smokers, consistent with previous findings from Central Appalachian miners. Moderate to severe diffusion impairment was frequently observed in this large population of former coal miners, even among those with normal $FEV_1$. These findings demonstrate that measurement of DLCO in coal miners identifies an additional population of former coal miners with pulmonary impairment associated with coal mine dust exposure beyond that identified using chest radiographs and spirometry alone. Our findings support the addition of DLCO testing to the battery of studies required as part of Department of Labor for Black Lung evaluations.

## 8.0 Recommendations for Future Work

We believe the following areas for future research are particularly important for understanding the breadth of occupational diseases in U.S. coal miners and for monitoring the longitudinal health trends of this workforce, both with the intention of informing interventions and policies to protect the health of our nation's coal miners.

1. The findings in this report, coupled with data from federally-funded black lung clinics,[47] demonstrate that the prevalence of CWP, PMF, and lung function impairment is increasing in the U.S. This challenges the assumption that current regulatory limits, particularly for respirable silica, are inadequate to protect worker health. Consequently, research and interventions are needed into (a) regulatory compliance with exposure limits; (b) targeted dust control efforts with a focus on respirable silica dust reduction; and (c) the relationship between dust violations and safety violations in mining operations.

2. Given the growing burden of severe disease in this workforce, additional research into treatments is imperative. For miners with fibrotic lung disease, including pneumoconiosis and silicosis, there is no cure and treatment options are limited. Improved understanding of the basic pathophysiology of silicosis and the availability of specific antagonists for several of the many cytokines, chemokines and other mediators involved in the pulmonary fibrotic response may allow the use of anti-fibrotic treatments for patients with silicosis in the future. For example, IL-1 blockade using anakinra,[48] or tyrosine kinase blockers such as nintedanib[49] may be effective in preventing progressive disease.

3. Pulmonary rehabilitation can be a useful treatment for those with CMDLD and associated conditions. The evidence supportive of pulmonary rehabilitation relates mainly to those with COPD, for whom it has been shown to reduce dyspnoea, increase exercise capacity, and improve quality of life. But by contrast, there are few studies of the efficacy of pulmonary rehabilitation specifically in individuals with pneumoconioses. Consequently, there is an opportunity for further research about the role of pulmonary rehabilitation programs for those with pneumoconiosis. The few existing studies of the efficacy of

pulmonary rehabilitation in those with pneumoconiosis, and specifically silicosis, suggest that it can reduce dyspnoea, anxiety, and the occurrence of respiratory infections and health care utilization. It has been shown to increase skeletal muscle strength, maximum exercise capacity, and quality of life in some individuals with silicosis. Sustained benefits from 4- to 8-week programs are not apparent, which would suggest long-term maintenance programs may be needed to maintain functional capacity in those with silicosis. In addition to this research, efforts to make pulmonary rehabilitation more widely available are needed.

4. We are currently working on an updated mortality study that would bring our previous analysis through 2022. We are in the midst of a historic rise in CMDLD in the U.S., a trend we saw mirrored in our mortality analysis. This future work will be iterative and monitor the trend in mortality for this workforce to identify the rest of this trend and identify regional hotspots.

5. We plan to examine the relationship between DLCO, ABG, and CPET results and whether FBLP benefits were awarded to former miners, controlling for radiographic disease and spirometry impairment. Specifically we want to investigate whether these tests have made material differences in identifying compensable impairment using the Rasmussen and FBLP data. This would be important evidence as to why the DOL may require or encourage the use of these tests more broadly in their DOL Black Lung evaluations.

6. In addition to these cardiopulmonary health outcomes, there is an urgent need to understand the prevalence of mental health disorders within the mining workforce. Researchers from one federally-funded black lung clinic found alarmingly high rates of depression, anxiety and suicidality among their coal miner population, which raised the alarm about this previously unstudied health outcome in this population. We are currently engaged in a large mixed-methods study of depression, anxiety, post-traumatic stress disorder, and substance misuse among coal miners seen through the federal network of black lung clinics, funded by the Alpha Foundation to understand the prevalence of these outcomes nationally.

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## 10.0 Abbreviations

| | |
|---|---|
| ABG | Arterial blood gases |
| BMI | Body mass index |
| CLRD | Chronic lower respiratory disease |
| CMDLD | Coal mine dust lung disease |
| CME | Coal mine employment |
| COPD | Chronic obstructive pulmonary disease |
| CPET | Cardiopulmonary exercise test/testing |
| CVD | Cardiovascular disease |
| CWHSP | Coal Workers' Health Surveillance Program |
| CWP | Simple coal workers' pneumoconiosis |
| CXR | Chest radiograph |
| DLCO | Diffusing capacity of the lungs for carbon monoxide |
| DOL | U.S. Department of Labor |
| FBLP | Federal Black Lung Program |
| $FEV_1$ | Forced expiratory volume in one second |
| FVC | Forced vital capacity |
| GLI | Global Lung Function Initiative |
| HR | Hazard ratio |
| IHD | Ischemic heart disease |
| ICD | International Classification of Diseases |
| ILO | International Labour Office |
| IRB | Institutional Review Board |
| MOR | Mortality odds ratio |
| NDI | National Death Index |
| NIOSH | National Institute for Occupational Safety and Health |
| NMRD | Nonmalignant respiratory disease |
| NVSS | National Vital Statistics System |
| PCO2 | Partial pressure of carbon dioxide |
| PFT | Pulmonary function test |
| PH | Proportional hazards |
| PMF | Progressive massive fibrosis |
| PO2 | Partial pressure of oxygen |
| pp | Percent predicted |
| SSN | Social security number |
| TLC | Total lung capacity |