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Association between Spirometric Parameters and Depressive Symptoms in New Mexico Uranium Workers

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Abstract

Background: Uranium workers are at risk of developing lung disease, characterized by low forced expiratory volume in one second (FEV₁) and/or forced vital capacity (FVC). Previous studies have found an association between decreased lung function and depressive symptoms in patients with pulmonary pathologies, but this association has not been well examined in occupational cohorts, especially uranium workers.

Methods: This cross-sectional study evaluated the association between spirometric measures and depressive symptoms in a sample of elderly former uranium workers screened by the New Mexico Radiation Exposure Screening & Education Program (NM-RESEP). Race- and ethnicity-specific reference equations were used to determine predicted spirometric indices (predictor variable). At least one depressive symptom [depressed mood and/or anhedonia, as determined by a modified Patient Health Questionnaire-2 (PHQ-2)], was the outcome variables. Chi-square tests and multivariable logistic regression models were used for statistical analyses.

Results: At least one depressive symptom was self-reported by 7.6% of uranium workers. Depressed mood was reported over twice as much as anhedonia (7.2% versus 3.3%). Abnormal FVC was associated with at least one depressive symptom after adjustment for covariates. There was no significant interaction between race/ethnicity and spirometric indices on depressive symptoms.

Conclusions: Although depressive symptoms are uncommonly reported in uranium workers, they are an important comorbidity due to their overall clinical impact. Abnormal FVC was associated with depressive symptoms. Race/ethnicity was not found to be an effect modifier for the association between abnormal FVC and depressive symptoms. To better understand the mechanism underlying this association and determine if a causal relationship exists between spirometric indices and depressive symptoms in occupational populations at risk for developing lung disease, larger longitudinal studies are required. We recommend screening for depressive symptoms for current and former uranium workers as part of routine health surveillance of this occupational cohort. Such screening may help overcome workers' reluctance to self-report and seek treatment for depression and may avoid negative consequences to health and safety from missed diagnoses.

Key Words: mining, miner, uranium, depression, mood, depressive symptoms, occupation, New Mexico, spirometry, FEV1, FVC, anhedonia,

Introduction

Uranium workers are at risk of pulmonary injury via two primary mechanisms: inhalation of radon daughters causing radiation-induced lung damage (1,2) and dust inhalation (3). Exposed workers are additionally at risk for developing cardiovascular pathology (4). Lung diseases can result in a clinically significant decline in pulmonary function and have been associated with various neuropsychiatric sequelae (5,6). Screening for and treatment of depression in interstitial lung disease (ILD) has been proposed to improve quality of life (6-8). Significant levels of depressive symptoms are described in patients with silicosis (8) and may adversely affect quality of life (9). In a study of patients with ILD, depressive symptoms correlate with dyspnea, forced vital capacity (FVC), sleep quality, and pain (7).

Presence of depressed mood or anhedonia, which is a significant decrease in deriving pleasure from the majority of one's daily activities, on most days, is requisite for diagnosis of major depressive disorder (10). Individual inquiry of depressed mood has demonstrated 85-90% sensitivity for detection of depression; and addition of another question, specific for anhedonia, raises overall sensitivity to 95% for the two-question inquiry (11).

Our objective was to evaluate the prevalence of depressive symptoms in uranium workers, to examine their association with spirometric values, and examine race/ethnicity interaction with spirometry on depressive symptoms. We studied uranium workers enrolled in the New Mexico Radiation Exposure Screening and Education Program (NM-RESEP). New Mexico workers have been significantly impacted by uranium extraction activities and many are compensated through the Radiation Exposure Compensation Act

(RECA) (12). The findings from this study may help elucidate the biopsychosocial impact of uranium-related lung abnormalities in New Mexico workers.

Methods

Study Design:

This is a cross-sectional analysis of baseline evaluation data from former New Mexico uranium workers (i.e., miners, millers, and ore transporters) voluntarily enrolled between 2004 and 2017 in NM-RESEP, a federally-funded health-screening and education program, located at the University of New Mexico (UNM) Health Sciences Center, serving Albuquerque and surrounding communities.

Data Collection:

Data were obtained from a self-reported questionnaire administered by a trained interviewer and confirmed by a physician/nurse practitioner. The questionnaire included demographics, severity of dyspnea via the modified Medical Research Council (mMRC) Dyspnea Scale (13), information on smoking history, cardiovascular status, and screening for depressive symptoms (using the modified Patient Health Questionnaire or PHQ-2) which includes two items on depressed mood and anhedonia (14). Body mass index (BMI) was calculated using measured height and weight. A prebronchodilator spirometry was obtained by trained technicians, utilizing standard guidelines from the American Thoracic Society and the European Respiratory Society (15). Test results were independently reviewed for quality by a pulmonologist. Gender- and race/ethnicity-specific reference equations were used to determine predicted normative values for spirometry (16). Abnormal values were

defined by the lower limit of normal obtained from reference standards. Data was entered into a secure web-based Research Electronic Data Capture (REDCap) database.

Predictor and Outcome Variables:

The outcome included a positive response for PHQ-2 item on either depressive symptom, i.e., depressed mood or anhedonia. Predictor variables included spirometric parameters and race/ethnicity, including the absolute and percent-predicted values for FVC), forced expiratory volume in one second (FEV1), and the absolute value of the FEV1/FVC ratio. Lower limits of normal obtained from the reference standards from the Third National Health and Nutrition Examination Survey (NHANES III) were used to define abnormal spirometric values (16).

Statistical Methods:

Frequencies, percentages, means, and standard deviations in a univariate analysis were reported. For the purpose of analyses, the outcome variable was endorsement of either depressive symptom. Chi-Square tests were used to analyze categorical outcome variables and generate p-values to determine significance of the findings. In the multivariable logistic regression analysis, variables that were evaluated for potential confounding included smoking status and pack-years.

Ethical Approval and Funding:

This study was approved by the UNM Institutional Review Board or Human Resources Protections Office (14-058). The study was supported by NM-RESEP, which is funded by the Health Resources Services Administration (HRSA), and UNM Health Science Center CTSC Grant Number: UL1TR001449.

Results

Subject characteristics are shown in Table 1. Of the 570 uranium workers, 97.1% were men, 66.7% were of racial/ethnic minority with the largest group being American Indian (36.6%). Most workers were older (mean age of 68.5 ± 8.1 years) with BMI values in the overweight or obese categories (82.1%). 7.6% of workers reported at least one depressive symptom, with 7.2% and 3.3% reporting depressed mood and anhedonia, respectively. The prevalence of at least one

depressive symptom in Hispanic, American Indian, and non-Hispanic White workers were 11.4%, 7.2%, and 4.1%, respectively ($p=0.14$ for all race/ethnicity group comparison) and post-hoc comparison between Hispanic and non-Hispanic White workers was significant ($p=0.001$) (not shown in Table 1). 66.9% of workers were either former or current smokers. With regards to previous pulmonary history, 15.3% and 10.0% of workers reported positive history of COPD and asthma, respectively.

Table 1. NM-RESEP Uranium Workers (2004-2017).

Characteristics		N (%) or Mean (SD) 570 (100%)
Gender	Female	16 (2.88%)
	Male	539 (97.12%)
Race/Ethnicity	Hispanic	160 (29.74%)
	Non-Hispanic White	175 (32.53%)
	American Indian	197 (36.62%)
	Non-Hispanic Black	2 (0.37%)
	Other	4 (0.74%)
BMI Category	Underweight/Normal	96 (17.94%)
	Overweight	225 (42.06%)
	Obese	214 (40.00%)
≥1 Depressive Symptom	No symptoms	501 (92.44%)
	At least one symptom	41 (7.56%)
Depressed Mood	No	503 (92.80%)
	Yes	39 (7.20%)
Anhedonia	No	524 (96.68%)
	Yes	18 (3.32%)
mMRC Dyspnea Score	0-1	324 (58.59%)
	≥2	229 (41.41%)
Smoking Status	Never	183 (33.09%)
	Former	295 (53.35%)
	Current	75 (13.56%)
Pack-Years Smoking		21.86 (27.11)
Abnormal FVC	No	405 (79.10%)
	Yes	107 (20.90%)
Abnormal FEV1	No	430 (83.98%)
	Yes	82 (16.02%)
Abnormal FEV1/FVC Ratio	No	466 (90.49%)
	Yes	49 (9.51%)
Self-reported COPD	No	471 (84.71%)
	Yes	85 (15.29%)
Self-reported Asthma	No	503 (89.98%)
	Yes	56 (10.02%)
FVC (Liters)		3.70 (1.52)
FEV1 (Liters)		2.75 (0.70)
FEV1/FVC Ratio		0.75 (0.10)
FVC (% predicted)		94.01 (39.10)
FEV1 (% predicted)		93.82 (21.42)

Both unadjusted univariate and adjusted multivariable analyses revealed that workers with abnormal FVC were at least 2.9 times more likely to endorse at least one depressive

symptom. No associations were found between abnormal FEV1 or abnormal FEV1/FVC ratios and depressive symptoms (Table 2).

Table 2. Unadjusted and Adjusted Associations of the Presence of Depressive Symptoms on Spirometric Indices.

Spirometric Index		Univariate Analysis				Multivariable Analysis*			
		At Least One Depressive Symptom				At Least One Depressive Symptom			
		N (%)	OR (unadjusted)	95% CI	P	OR (adjusted)	95% CI	P	
Forced Vital Capacity (FVC)	Abnormal	16/107 (15.0%)	2.94	(1.49, 5.83)	<0.001	2.90	(1.21, 6.93)	0.02	
	Normal	22/405 (5.6%)							
Forced Expiratory Volume in 1 second (FEV1)	Abnormal	10/82 (12.2%)	1.92	(0.89, 4.12)	0.09	1.85	(0.68, 5.04)	0.23	
	Normal	28/430 (6.8%)							
FEV1/FVC ratio		Abnormal	4/49 (8.2%)	1.08	(0.37, 3.19)	0.89	1.19	(0.32, 4.35)	0.80

*Covariates in the above multivariable model using logistic regression analysis included: smoking status and smoking pack-years.

**Further adjustment for the following covariates: age, gender, and race/ethnicity did not change results in the multivariable model (FVC OR: 2.86, 95% CI: 1.18-6.96, p=0.02).

Although the associations between spirometric indices and depressive symptoms appeared stronger among Hispanic workers than other race/ethnicity subgroups, this was not borne by a formal test of interaction between race/ethnicity and spirometric

indices on either depressive symptom. However, interaction testing identified a trend towards significance for Hispanic workers between abnormal FEV1 and self-reporting of depressive symptoms (p=0.07) (Table 3).

Table 3: Interaction between Spirometric Indices and Race/Ethnicity on Depressive Symptoms.

Predictor Variables		Depressive Symptoms (At Least One Depressive Symptom)			Main Interaction	Interaction for Race/Ethnicity Subgroups
		OR adj	95% CI	P	p-value	p-value
Abnormal FVC		2.85	(1.42, 5.72)	<0.001	0.35	-
Race/Ethnicity	Non-Hispanic White	1.00	-	-		-
	Hispanic	4.37	(1.69, 11.29)	<0.001		0.15
	American Indian	1.89	(0.69, 5.18)	0.22		0.35
Abnormal FEV1		1.74	(0.80, 3.81)	0.16	0.17	-
Race/Ethnicity	Non-Hispanic White	1.00	-	-		-
	Hispanic	4.28	(1.66, 11.00)	<0.001		0.07
	American Indian	1.91	(0.70, 5.22)	0.21		0.47
Abnormal FEV1/FVC Ratio		0.96	(0.32, 2.89)	0.93	0.91	-
Race/Ethnicity	Non-Hispanic White	1.00	-	-		-
	Hispanic	4.41	(1.72, 11.32)	<0.001		0.97
	American Indian	1.85	(0.68, 5.07)	0.23		0.97

*Logistic regression analysis was used.

Discussion

A minority of uranium workers sampled in this secondary analysis self-reported at least one depressive symptom (7.6%). Depressed mood was reported over twice as much as anhedonia was reported (7.2% vs 3.3%). Abnormal FVC on spirometry was found to be associated with depressive symptoms after adjustment for covariates. There was no significant interaction between race/ethnicity and spirometric indices on depressive symptoms.

Uranium ore extraction in New Mexico occurs in open pit or underground mines. Subsequently, uranium is isolated from ore via milling or heap leaching (17). Most of the workers in this study were subjected to hazardous working conditions marked by lack of provision of personal protective equipment (including respirators) to handle uranium and inhalational dust exposure. Inadequate ventilation in underground mines also led to increased radon and dust exposure and workers were not adequately informed of these occupational exposures by mining companies or federal agencies (i.e. US Atomic Energy Commission, Nuclear Regulatory Commission, US Department of Energy) (12).

Uranium enters the human body primarily via inhalation and ingestion (18). It deposits primarily in the lungs and skeleton (insoluble uranium) and kidneys (soluble uranium) (19) where it causes chemical and radiological damage to these organs (20). In a murine study, uranium was found to enter the central nervous system, crossing the blood-brain barrier and accumulating in the hippocampus, resulting in detrimental neurophysiological effects and changes in REM sleep patterns (21). A case study involving 81 American Indian uranium workers found anxiety and depression to be the most common mental health problems,

and respiratory complaints and skin rashes were the most common physical health issues (22). Radon gas, a byproduct of the uranium decay process, attaches to dust particles and when inhaled into the lungs the alpha radiation released by radon daughters damages lung tissue. Like non-uranium industry workers engaged in other types of mining-related activities, uranium workers are at risk for occupational pneumoconiosis, presenting with features similar to silicosis (23), and chronic fibrotic ILD (3).

Pneumoconiosis has been associated with increased risk of other pulmonary conditions, including pulmonary emboli (24), lung carcinoma (23), chronic obstructive pulmonary disease (COPD) (26), tuberculosis (27), and clinically significant decline in lung function (28).

Many chronic pulmonary conditions such as asthma, COPD (29), bronchiectasis (30), and lung cancer (31) are associated with depressive symptoms. In a prospective study of patients with bronchiectasis, low FEV1 values were observed among patients with depressive symptoms (30). In a study of French dairy farmers, Guillien (32) found depression was associated with lower FEV1. A 2013 systematic review and meta-analysis revealed that the relationship between COPD and depression is bidirectional (33). Our study did not contain information regarding history of a prior or current diagnosis of depression for enrolled patients, thus our secondary analysis is not a like-for-like comparison to existing literature on this topic. Our study involved individuals with mostly normal lung function, indicating that the association between abnormal FVC and depressive symptoms may be seen relatively early in the disease course.

Psychosocial factors may play a role in the development of workplace-associated disability in workers with respiratory

impairment, but evidence-based guidance to address these psychosocial factors is limited (34). The low prevalence of depressive symptoms in our study may reflect the high proportion of men enrolled (97.1%), as overall prevalence of depression in men is approximately half that of women (35). Alternatively, men may under-report due to a lack of awareness and understanding of depression and fear of stigmatization for self-reporting amongst coworkers or wider society. Additionally, use of the standard PHQ-2 and DSM diagnostic criteria in American Indians may not produce reliable results due to potential cultural and linguistic differences (36). The rate of depression in American indigenous populations has found to be 8.9% (which is higher than all other racial/ethnic groups except biracial individuals) and can range from 10-30% (37), however, the prevalence of depressive symptoms in American Indian workers in our study was 7.2%. To the best of our knowledge, no validation studies have been performed for use of any version of the PHQ-2 in New Mexican American Indian populations. The PHQ-2 has been validated in English- and Spanish-speaking Hispanic Americans (38). Perini found ethnic minorities diagnosed with “chronic nonspecific lung disease” exhibited higher absolute prevalence of depressive symptoms than the ethnic majority (29). Our study findings partially agree with Perini’s findings in that Hispanic uranium workers were more likely to endorse depressed mood than non-Hispanic White workers. Our study was a cross-sectional, secondary analysis of an occupational cohort of mostly elderly, former uranium workers enrolled in NM-RESEP. Longitudinal analysis of this association may further elucidate the direction of the association. Our study could benefit from culture-specific depression

diagnostic criteria paired with spirometric measures to specific pulmonary diagnoses. While anhedonia has customarily been associated with loss of pleasure (10), the construct has recently expanded to include interest in activity, effort, and discrimination between anticipation and consummatory forms of pleasure. New approaches for anhedonia assessment are in development (39). Our assessment of anhedonia may have been limited and a more robust screening tool that screens for additional depressive symptoms beyond depressed mood and anhedonia, such as the PHQ-9 or Hospital Anxiety and Depression Scale (HADS) rather than the PHQ-2, could improve result validity. As depression has a complex nature, a more rigorous biopsychosocial assessment would help in determining the role pulmonary pathology plays in depression in this study sample. To the best of our knowledge, this is the first study to examine the association of spirometric indices with depressive symptoms in former uranium workers. The strengths of our study include the robust participation of minority workers due to use of a mobile screening unit, its clinical relevance in light of ongoing uranium-associated activity, and potential future impact on health. Further study on this topic is merited as untreated depression in workers poses potential risks to workplace safety. As industrial use of nuclear material continues in the United States and other countries such as Kazakhstan, Canada, and Australia, this area of study is relevant to occupational health on a global scale. We recommend screening for depressive symptoms in current and former uranium workers as part of routine health surveillance to better address reluctance to self-report and seek treatment for depression, as well as to avoid potential negative consequences to health and safety from a missed diagnosis.

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Abbreviation List

BMI: body mass index
COPD: chronic obstructive pulmonary disease
CTSC: Clinical and Translational Science Center
DSM: Diagnostic and Statistical Manual of Mental Disorders
FEV1: forced expiratory volume in one second
FVC: forced vital capacity
HADS: Hospital Anxiety and Depression Scale
ILD: interstitial lung disease
mMRC: modified Medical Research Council
NHANES III: The Third National Health and Nutrition Examination Survey
NM-RESEP: New Mexico Radiation Exposure Screening and Education Program
PHQ-2/PHQ-9: Patient Health Questionnaire-2/Patient Health Questionnaire-9
RECA: Radiation Exposure Compensation Act
REDCap: Research Electronic Data Capture
UNM: University of New Mexico

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