OCCUPATIONAL HEALTH ASSESSMENT OF CRYSTALLINE SILICA AND RESPIRABLE DUST EXPOSURE IN TACONITE MINE WORKERS IN NORTHEASTERN MINNESOTA

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Dedication

I dedicate this work in its entirety to God, and my family, for being my support through every single phase of this process. I am forever grateful.

ABSTRACT

Introduction and objectives

This research effort investigated three study areas. Firstly, the impact of ATS/ERS "acceptability" and "repeatability" criteria for spirometry on the estimates of restrictive ventilatory defect was assessed in a population of taconite miners. The estimates of restrictive ventilatory defect were made using three different pulmonary function tests (spirometry, alveolar volume and diffusing capacity).

Secondly, the association between cumulative silica exposures in taconite mining and non-malignant respiratory disease (NMRD) outcomes was evaluated. Cumulative silica exposure was determined using current and historical exposure measurements while health outcomes were assessed from a cross-sectional screening study of taconite mine workers.

The final study area explored the joint effects of silica dust, elongate mineral particles (EMP) and non-silica respirable dust on exposure-NMRD association in miners, also using health outcomes from cross-sectional screening.

Methods

A survey of current and former taconite workers was undertaken in 2010-2011. Miners were screened with a questionnaire that focused on occupational and medical history, followed by clinic examinations including lung tests (spirometry, chest x-rays).

Current and former workers who completed the survey and performed all three pulmonary function tests (spirometry, alveolar volume and diffusing capacity) were assessed (n=1084). We applied American Thoracic Society (ATS/ERS) acceptability criteria for all tests and categorized subjects into groups according to whether they fully met, partially met, or did not meet acceptability criteria for spirometry. Obstruction and restriction were defined utilizing the lower limit of normal (lower five percent) for all tests. Mixed ventilatory defect groups were also described indicating coexisting

obstructive and restrictive ventilatory defects. When using alveolar volume, restriction was identified after excluding obstruction.

Occupational exposure assessment was performed which measured over 1,500 onsite samples for respirable dusts including silica in 28 major job functions in taconite mining. Historical exposures to dusts were estimated with data obtained from prior onsite exposure measures by existing mining operations, and from Mine Safety and Health Administration (MSHA) data for those same operations. Individual work histories from completed questionnaires were used to determine the length of time worked (years) in these jobs. Cumulative silica exposure ((mg/m^3)-years) was estimated as a product of time worked and year-specific silica dust measures for each of 28 unique job functions. Forced vital capacity (FVC) less than lower limits of normal (LLN) for age, height, race and gender was used to determine spirometric restriction in participants with “usable” spirometry. Chest x-rays were evaluated using ILO criteria for any evidence of parenchymal abnormalities of 1/0 or greater and for pleural abnormalities suggestive of pneumoconiosis by two blinded B-readers, with a third reader to arbitrate disagreements.

Prevalence ratios of association (PR), with 95% confidence intervals (CI), between silica exposures and lung disease outcomes were estimated using Poisson regression models. Regression models were adjusted for smoking, gender, age, BMI and estimation of commercial asbestos exposure.

The last area of study focused on exploring possible associations between combined silica, EMP, and non-silica respirable dust exposures and NMRD prevalence. Non-silica respirable dust includes iron oxides and particulate matter (PM) generated from mining and processing the ore. PRs of association with NMRD outcomes were calculated each for silica, EMP and non-silica respirable dust as continuous variables. Using dichotomous exposures (high versus low levels determined by the median cumulative exposure), we then estimated the PRs for silica NMRD-association within strata of EMP and non-silica dust. Relative excess risk due to interaction (RERI), attributable proportions (AP) and synergy index (SI) with 95% CIs, were then estimated to assess interaction on the additive scale. On the multiplicative scale, separate models each were used for assessing silica-EMP interaction and a second model for silica-non-silica interaction, using corresponding product terms within the models.

Results

Estimating restrictive ventilatory defect

Only 519 (47.9%) tests fully met ATS/ERS spirometry acceptability criteria. Within this group, 5% had obstruction and 6%, restriction on spirometry. In contrast, among all participants (N=1,084), 16.8% had obstruction, while 4.5% had restriction. Alveolar volume restriction showed similar results in all groups after obstruction was excluded. Impaired gas transfer (Diffusing capacity) was identified in less than 50% of restriction identified by either spirometry or alveolar volume. BMI was significantly related to spirometric restriction in all groups.

Association between silica and nonmalignant respiratory disease

Spirometric restriction occurred in 7.2%; chest x-ray parenchymal abnormalities occurred in 5.4%; chest x-ray pleural abnormalities consistent with pneumoconiosis were observed in 16.8%; and symptoms of shortness of breath (dyspnea on exertion) occurred in 11.4% of the study population. Silica exposure was associated with restrictive ventilatory defect prevalence (PR= 1.40; 95%CI=1.08-1.81) and the prevalence of parenchymal changes on chest x-ray (PR= 1.30; 95% CI=1.00-1.69).

Exploring respirable dusts joint effects in taconite mining

Assessments for silica-EMP and silica-non-silica additive and multiplicative interactions were not statistically significant. The exposure with significant association with health outcome (on spirometry), of the three exposures studied, was silica.

Conclusions

Population estimates of restriction using spirometry or alveolar volume varied by spirometric acceptability criteria. Other factors identified as important considerations in the estimation of restrictive ventilatory defect included increased BMI and gas transfer

impairment in a relatively smaller proportion of those with spirometric restriction. Spirometric assessment suggested a 40% increase in association with NMRD prevalence for workers given silica exposure. Silica exposure was also associated with parenchymal chest x-ray findings. However, these associations were dependent on the approach for estimating exposure. The presence of EMP and non-silica dust did not significantly modify the relationship between silica exposure in taconite mining and NMRD on either the additive or the multiplicative scales. Overall, these insights are important when interpreting population-based physiological data in occupational settings and understanding lung disease associations of silica and other respirable dust exposures.

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Declaration

I declare that the work presented therein is entirely mine, except stated otherwise.

It is original to me, not presented anywhere else for any degree, examination or presentation except as a form of scholarly exercise, as shown below.

This thesis was undertaken following the provision of funding for the overall Taconite Workers’ Health Study, by the State of Minnesota. The work reflected within this thesis is due to the efforts of the author and study team and do not reflect the position of the State of Minnesota.

Publications and Presentations arising from Research

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Abbreviations

ATS - American Thoracic Society

BMI - Body Mass Index

CDC - Centers for Disease Control and Prevention

CXR - Chest X-ray

DAG - Directed Acyclic Graph

DLCO - Diffusing Capacity

EMP - Elongate Mineral Particles

ERS - European Respiratory Society

FEV_1/FVC - Forced Expiratory Volume in 1st second to Forced Vital Capacity ratio

FEV_1 - Forced Expiratory Volume in 1st second of exhalation

FVC - Forced Vital Capacity

ILD - Interstitial Lung Disease

ILO - International Labour Organization

MRHAP - Mineral Resources Health Assessment Program

MSHA - Mine Safety and Health Administration

NIOSH - National Institute for Occupational Safety and Health

NMRD - Non Malignant Respiratory Disease

OR - Odds Ratio

PFT - Pulmonary Function Test

PR - Prevalence Ratio

RHS - Respiratory Health Survey

RLD - Restrictive Lung Disease

RVD - Restrictive Ventilatory Defect

SEG - Similar Exposure Group

TLC - Total Lung Capacity

TWHS - Minnesota Taconite Workers' Health Study

VA - Alveolar Volume

CHAPTER 1:

INTRODUCTION AND BACKGROUND

A. General introduction

Taconite ore has been mined from the northeastern range of Minnesota since the mid-1950's. Annually, 40 million tons of high-grade iron ore are produced from the mines, which is approximately 75 percent of total U.S. iron ore production (Minnesota Minerals Coordinating Committee, 2014). It serves as a main source of iron for steel production important in the auto, oil and gas and housing industries in the U.S. Processing this ore is known to create a dusty workplace, generating elongate mineral particles (EMP) including non-asbestiform EMP and cleavage fragments, respirable silica and other non-silica respirable dusts (Hwang, 2013b). Previous studies identified taconite miners with chest x-rays findings typical of silicosis (Clark, et al., 1980). The state department of health also identified an excess of mesothelioma cases in the taconite industry population (Minnesota Department of Health, 2003; Minnesota Department of Health, 2010). These findings increased community concerns about an association between the taconite mining industry and the occurrence of respiratory diseases in northeastern Minnesota.

Prolonged exposure to dust particles like EMPs, respirable silica and other non-silica dusts, especially in occupational settings, typically results in restrictive lung disease (RLD) but may also cause obstructive disease. The presence of lung restriction can be assessed by spirometry, chest x-rays and/or history of relevant exposure with characteristic symptoms. There is no current information on the prevalence of RLD in taconite workers in northeastern Minnesota or its association with exposure to mining dusts. In order to understand this possible association, it was also necessary to assess population characteristics that potentially act as confounders. The central hypothesis of this research was that occupational exposure to silica dust from the taconite industry is associated with restrictive lung disease.

1.1 Research aims

This central study hypothesis was examined by investigating the following three specific study areas in a sample of current and former taconite mine workers:

1. **To determine the degree of misclassification of prevalent lung disease using current spirometry testing guidelines and the potential impact on the associations with dust exposures.**
   The working hypothesis was that the current spirometry guidelines for acceptable spirometry causes exclusion of test results of older, male smokers at greater risk of restrictive lung disease from dust exposure and an error in prevalent lung disease estimates.
2. **To determine the relationship between cumulative respirable silica exposure from taconite operations and lung restriction assessed with spirometry, chest x-ray and pulmonary symptomatology.**
   The working hypothesis was that there is an association between cumulative respirable silica exposure and lung restriction determined using spirometry, chest x-ray or relevant respiratory symptoms.
3. **To explore the joint effects of silica dust, elongate mineral particles (EMP) and non-silica dust generated in taconite mining on non-malignant respiratory disease (NMRD) risk in taconite miners.**
   The working hypothesis was that the NMRD-risk from cumulative silica exposure from taconite operations is a result of joint exposure effects of EMPs and non-silica dust also generated in taconite mining operations.

1.2 Significance of thesis

First, the potential error in estimating restriction prevalence using current spirometry testing guidelines was demonstrated and an overall study protocol for determining the prevalence of restrictive ventilatory defect (RVD) was established. RVD is the more specific term describing restrictive lung disease when defined by abnormal pulmonary function testing. It can also be referred to as spirometric restriction.

This research then estimated current prevalence estimates of restrictive lung disease in potentially dust exposed current and former taconite mining workers. We determined the association between dust exposure in taconite mining and RLD while adjusting for other independent factors such as gender, age, BMI, smoking habits and commercial asbestos score. This had not been undertaken in prior research and was done to aid in understanding the burden of dust-related RLD prevalence in miners.

The last study area explored the possible joint/interaction effects of EMP and non-silica dust, also generated during the taconite mining process, on silica in silica-RLD associations. These results provide important perspectives on the association between exposure to dusts from taconite operations and RLD. This research will ultimately be useful in better understanding of exposure effects as well as enhancing clinical monitoring of miners and reducing RLD prevalence in the taconite industry.

B. Background and literature review

1.3 Silica dust, properties and occupational exposure

Silica is the most abundant surface mineral in the earth's crust (up to 20%) and a major constituent of soils (Madsen, et al., 1995; Rees & Murray, 2007). Many minerals contain SiO_2 and are called silicates. These silicates are ubiquitous and the various forms of asbestos, historically identified as causing lung disease, are also silicates (Lee, et al., 2008). There are various natural forms of silica including quartz, tridymite and critobalite, each unique in its spacing, structure and angular relationships of atoms. Silica (or quartz) refers to respirable crystalline silica dust that is usually invisible to the naked eye and less than 7 microns (µm)in diameter.

1.4 Global mining and health risk from respirable dust inhalation

Mining has been historically categorized as a dusty trade (Park, et al., 2002; National Institute for Occupational Safety and Health (NIOSH), 1991). The risk from occupational inhalation of respirable particles depends on the type of exposure, dose and susceptibility factors. Significant dose-response relationships have been demonstrated between dust and respiratory symptoms, x-ray, and lung function impairments (Beach, et al., 2001; Bio, et al., 2007; Chen, et al., 2005; Hnizdo & Sluis-Cremer, 1991; Love, et al., 1997). The greater the mechanical forces applied in exploring the earth's crust, the more likely the generation of respirable dust (Rees & Murray, 2007).

1.5 Taconite mining in northeastern Minnesota, process and risks

Iron ore mining in northeastern Minnesota was initially in the form of hematite, also known as “natural ore” which has a high composition percentage of iron (greater than 60%). This was subsequently replaced by taconite ore as hematite sources were depleted. Different transition periods from hematite to taconite ore processing are recorded for the history of the different mines on the Mesabi iron range, with most mines transitioning in the 1950’s. Taconite ore has iron content of 25% to 30%, upgraded to approximately 65% iron in iron pellets after processing (Minnesota Minerals Coordinating Committee, 2014).

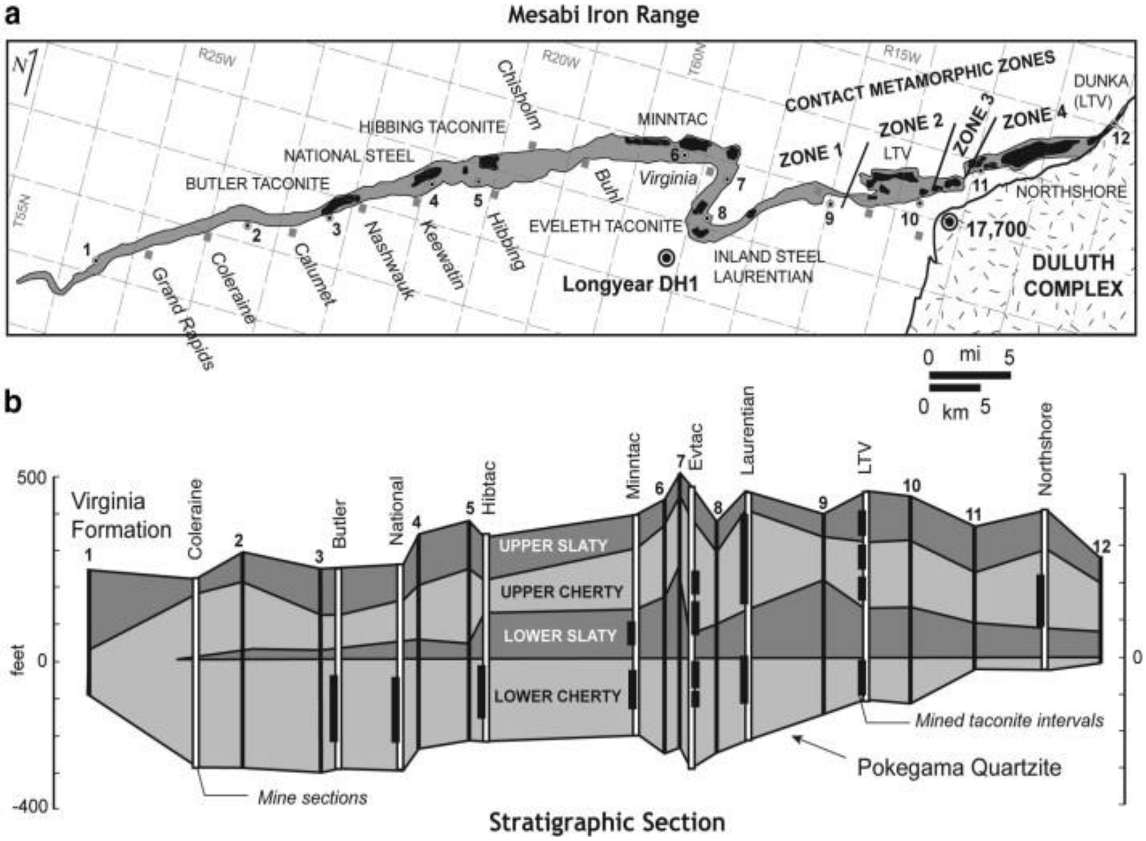


Figure 1: Geographical (a) and geological (b) descriptions of the Mesabi iron range in northeastern Minnesota.

Taconite is a hard, banded low-grade ore of iron, and is the predominant iron ore remaining in the United States. This industry produces usable concentrations of iron-bearing material by removing nonferrous rock (gangue) from low-grade iron. Ninety-nine percent of the crude iron ore produced in the United States is taconite. About ninety-eight percent of the demand for taconite comes from the iron and steel industry. Ninety-seven percent of the processed ore shipped to the iron and steel industry is in the form of pellets. Taconite ore processing consists of crushing and grinding the ore to liberate iron-bearing particles, concentrating the ore by separating the particles from the waste material (gangue), and pelletizing the iron ore concentrate.

The process of taconite mining involves the following major steps:

1. Liberation: This is the first step in taconite ore processing consisting mainly of crushing and grinding. Prior to grinding, ore is dry-crushed in up to six stages, depending on the hardness of the ore. Most taconite used today requires very fine grinding.
2. Concentration: This is the second step in taconite ore processing. Only thirty-three percent of crude taconite becomes a shippable product, a large amount of gangue is generated. Magnetic separation and flotation are the most commonly used methods for concentrating magnetic and nonmagnetic taconite ore respectively.
3. Pelletization: This is the third major step in taconite ore processing. Pelletization is generally accomplished by tumbling moistened concentrate with a balling drum or balling disc. A binder, usually powdered bentonite, may be added to the concentrate to improve ball formation and physical qualities of the “green” balls. Pellets are hardened by a procedure called induration. This involves heating in a furnace up to 1290 to 1400 degrees Celsius and then cooling. Of the three general types of indurating apparatus (vertical shaft furnace, straight grate, and grate/kiln), the grate/kiln is most commonly used (Hwang, 2013b; Environmental Protection Agency, 2012).

After processing, pellets approximately one centimeter in diameter with iron content of 65% are produced and shipped out. Dusts generated from the taconite mining process currently include respirable silica, other non-silica respirable dusts, non-asbestiform elongate mineral particles (EMP) and non-amphibole EMPs including cleavage fragments. These exposures, along with potential past exposures to asbestiform EMP, have been implicated as possibly increasing the risk of asbestosis, silicosis, lung cancer and malignant mesothelioma (National Institute for Occupational Safety and Health (NIOSH), 2011).

As part of renewed research into identifying the risk potential of particles encountered in workplaces like the taconite industry, the National Institute for Occupational Safety and Health (NIOSH) proposed research goals in their 2012 roadmap bulletin (National Institute for Occupational Safety and Health (NIOSH), 2011). This roadmap identified silica risks to human health as needed future research in occupational health and safety. This highlights the need to improve knowledge of the risks from dusts generated in this industry. With better insights into exposure-disease associations, this research effort may improve the occupational health and productivity of workers in this industry.

1.6 Silica-related health risks in taconite and other mining

Time weighted averages (TWA) and occupational exposure limits (OELs) exist for silica control in the workplace (Rees & Murray, 2007; Cherrie, et al., 2011). However, most OELs may not be totally protective against silica-associated diseases (Steenland, 2005). Occupational exposures to silica are associated with respiratory diseases like silicosis, lung cancer, pulmonary tuberculosis and other airway diseases (Rees & Murray, 2007; National Institute of Occupational Safety and Health, 2002; IARC , 1997).

Some challenges with determining outcomes have been raised from studies that found both over- and under-diagnosis of silicosis (Cottrell, et al., 1992; Goodwin, et al., 2003; Rosenman, et al., 2003). Silicosis may be misclassified as other lung diseases such as chronic obstructive pulmonary diseases (COPD), tuberculosis (TB), lung cancer or cardiovascular diseases (Goodwin, et al., 2003). In addition to this, non-malignant respiratory disease (NMRD) includes pneumoconiosis and also includes other inflammatory lung conditions like infection, collagen-vascular, allergic, parasitic, sarcoidosis, etc. In this setting, NMRDs encountered are primarily restrictive lung disease sequelae due to occupational dust exposure.

Recent studies have assessed the relationship between occupational dust exposure and respiratory impairment in miners. Exposure-disease associations in coal, gold, talc and tin mining as well as other forms of mineral extraction with generation of respirable dust including silica dust have been studied (Beach, et al., 2001; Bio, et al., 2007; Chen, et al., 2005; Hnizdo & Sluis-Cremer, 1991; Love, et al., 1997; Oxman, et al., 1993; Glass, et al., 2003; Gamble & Gibbs, 2008; Govender, et al., 2011).

In the taconite mining industry, there have been efforts to determine the relationship between exposure to mining dusts and lung disease. This has, up until now, mainly involved determining the association of mining with mortality and cancer incidence. These attempts have been done mainly with chest radiography in pre-mortem assessments and post-mortem examinations of lung tissue (Clark, et al., 1980; Cooper, et al., 1992; Cooper, et al., 1988; Gylseth, et al., 1981; Higgins, et al., 1983).

Besides these, studies of the impact of dusts from taconite mining on lung function are few (Clark, et al., 1980). This current research lays the foundation for understanding the non-cancer risks of taconite dust exposure. It could also serve as a framework for follow-up of working taconite miners to better tailor public health interventions.

1.7 Independent factors for health risks of silica exposure in taconite mining

Studies in current literature have established the impact of BMI and smoking on lung function in non-mining populations (Lederer, et al., 2009; Zammit, et al., 2010; Li, et al., 2003). The role of BMI and smoking in NMRD prevalence was therefore important to ascertain in this population. This helps to more accurately delineate the relationship between dust exposures in taconite mining and NMRD, without potential confounding influences. This information also increases the efficient use of spirometry as a public health tool in the longitudinal monitoring of miners' lung health. It may help inform efforts aimed at reducing the prevalence of NMRD in taconite miners by accurately determining the association of the different independent factors with disease. Though smoking is thought to cause obstructive physiological dysfunction primarily, its role as a possible effect modifier is also important. It has been described as affecting the normal clearance functions of the lungs for toxic substances (Cohen, et al., 1979). Longer and earlier smoking times may affect the ability of the lungs to manage the potential effects of dusts on lung tissue. There is however, a possible risk of bias when smoking habits are categorized as never, former or current smokers.

Other independent factors in this assessment included age, gender and a commercial asbestos score. This score was made by experienced industrial hygienists and was an estimate of potential concurrent asbestos exposure given other jobs held by participants during their taconite work history and indicated in the questionnaire information.

C. Methodology and Research Design

1.8 Study population and sampling process

The respiratory health survey (RHS) was a cross-sectional sample of current and former taconite industry workers. It was part of the Minnesota Taconite Workers' Health Survey (TWHS) aimed at studying dust exposures encountered in taconite mining, processing and shipping on the Mesabi iron range in northeastern Minnesota. It also aimed at determining the association of mining dust exposures with disease. The participants in the RHS were sampled from an employment roster of 16,990 individuals that included current and former taconite industry workers from four companies that represented seven mines located across the range. The employment roster was stratified on age and location of the mine/company to create 12 sampling categories with the proposed recruitment numbers for the study. Names were randomized and successively selected from the stratified roster to reach the pre-determined number in each sampling category. Following invitations extended to 3,310 respondents, a total of 1,353 current and former taconite workers responded with questionnaire information after the standard protocol of recruitment and of these, 1,188 completed clinic testing. Spouses of participants were also screened after consenting to participation and 497 underwent clinic testing.

Power and sample size estimates derived using the EGRET Sample size module (Cytel Software Corp, 1997), were estimated for two exposure scenarios: 1) a dichotomous exposure (high and low) in which half of the sample is in each category, and 2) a trend in effect across quartiles of exposure. Based on an assumption of prevalence of outcome of interest (pleural or parenchymal abnormalities, decreased lung function, symptoms) of three percent in the group with the lowest chance for exposure, adequate power for differences between high and low exposures (RR ≈ 2.2 with 87% power) as well as exposure response across quartiles (RR = 1.5 with about 98% power) was determined.

1.9 Clinic testing

Questionnaires were developed based on standardized questionnaires of the American Thoracic Society (Ferris, 1978), the St. George's Respiratory Questionnaire (Jones, et al., 1991), and the University of California, San Diego (UCSD) Shortness-of-Breath Questionnaire (Archibald & Guidotti, 1987). Participants were mailed the questionnaire before their scheduled appointment date and asked to bring the completed questionnaire with them to the research clinic appointment. It was reviewed at the clinic by staff nurses for completeness and consistency and by asking for and/or answering any queries they had.

Lung function testing, comprised of lung spirometry and single-breath diffusing capacity was conducted. The latter test provided two indices of lung function: 1) Diffusing capacity (DLCO), a measure of oxygen diffusion across the respiratory membrane of the lungs and 2) Alveolar volume (VA), a proxy for total lung capacity (TLC). Interpretation of these lung function tests, particularly spirometry, was necessary for the determination of RLD, the primary outcome of this research. A reduction in FVC, below the lower limit of normal (LLN) for age, sex, race and height (Hankinson, et al., 1999), indicated abnormal lung volume and lung restriction. Other spirometric outcomes include obstruction, defined as a reduction in FEV_1/FVC ratio below the LLN, and mixed disease, defined as the simultaneous identification of both restrictive and obstructive lung function.

The participants underwent standard postero-anterior (PA) chest X-ray according to the recommendations of the International Labor Organization (ILO) for the complete classification of films (International Labour Office (ILO), 2002). The quality of each chest X-ray was evaluated at the clinic by a radiological technician and poor quality films were immediately repeated. The films were initially read by a clinical radiologist to check for health conditions of immediate concern. Each film was then assessed by two B-readers for parenchymal and pleural changes and other radiographic features as specified by the ILO framework (International Labour Office (ILO), 2002). Parenchymal changes, described as profusion or opacity scores, and pleural changes, have characteristic interpretations that are indicative of RLD changes. Where there was disagreement between the two readers on the interpretation of the chest X-rays, the disputed films were sent to a third B-reader for arbitration.

Other biometric information such as weight and height were collected on physical examination by a nurse practitioner or a registered nurse. This physical examination also included chest examinations, measurements of blood pressure, pulse rate and oxygen saturation pressure. Blood samples were also drawn with participant consent at the research clinic and assessed for hemoglobin (Hgb) concentrations for the presence of anemia in the participants.

1.10 Exposure assessment

As part of the questionnaire, participants were asked to report their work history (See Appendix). This included the companies they worked in, the job title, what their activities were at this job, what year they started this employment and what year they ended. They were given an opportunity to include as many records of work histories they had over the course of their career in the taconite industry. This information was abstracted from the questionnaires and standardized for all participants using job titles and descriptions provided by the companies. Standardized job titles, similar exposure groups (SEGs) and departments of employment were analyzed for each work entry experience of each participant (See Appendix). Where information was not clearly provided by the worker, the next clear level of categorization was created. E.g., if a worker was clear about the department but not the particular job, he was considered to have missing job title information but relevant department information. This approach was used to ensure best complete data on the workers' reported work histories.

As part of the overall TWHS, concurrent exposure measurements of dusts in the workplace were taken by industrial hygienists. Personal samples were collected to measure elongate mineral particles (EMPs) using NIOSH 7400 phase contrast microscopy (PCM) for total EMPs with an aspect ratio ≥ 3:1 and length > 5 µm. Area samples of EMPs were measured using a Nano Micro-Orifice Uniform Deposit Impactor (MOUDI) instrument. These were used by a team of industrial hygienists to obtain conversion factors converting the area measurements into other exposure metrics. Respirable dust concentrations were measured using the NIOSH 600 gravimetric method while respirable crystalline silica concentrations were determined gravimetrically by X-ray diffraction (NIOSH Method 7500). These exposure measures were taken in the currently operational mines on the iron range. This was added to available historical industrial hygiene measurements of dust concentrations in the workplace over the years of taconite mining. Work exposure concentrations specific to the year of work, the SEG of employment and the company of employment were thus ascertained for the period of 1955-2010. As part of exposure measurements, various definitions of EMPs based on length and aspect ratio of particles were explored to determine if the exposure-disease relationship of EMPs vary by elongated particle definition (Hwang, 2013b; Hwang, et al., 2013a). These definitions include NIOSH, (National Institute for Occupational Safety and Health (NIOSH), 2011), Suzuki (Suzuki, et al., 2005), Chatfield (Chatfield, 2008) and cleavage fragments. Time period in this analysis corresponds to the period of mining for iron in the form of taconite ore in the taconite industry. These time measures were used to calculate cumulative exposures of the different dusts measured for the participants of the RHS.

1.11 Summary exposure measures:

i. Cumulative exposure – $CE_i = \sum_{j=1}^{Ni} Xij \times t_j$, (Kriebel, et al., 2007),

Where Xij = Average exposure concentration (here, particles/cc for EMPs; mg/cc for respirable/silica dusts) of individual ‘i’ per job group ‘j’,

t_j = time spent in job group ‘j’ (years)

N_i = number of work records for individual ‘i’

ii. Zone/Mine/Department/Job/Similar Exposure Groups (SEGs) – Qualitative descriptions of exposure in terms of work area. These qualitative exposure categories are described in increasing specificity eventually as SEGs. E.g. supervisor, electrician, pelletizing operator, etc. This exposure, modeled as ‘ever/never’, accounts for the variation in mineralogy of taconite across the iron range. The variation in work practices in the different mines and the exposure differences across jobs were also noted.

iii. Year of First employment (Start year) – This variable represents a potential way to assess earlier exposure to a toxic substance. First exposure in taconite mining might have been at different exposure levels with different engineering controls in the workplace, creating a potential cohort effect.

iv. Cumulative length of time employed (years) – Summation of the length of time spent potentially exposed to the dusts in the mining process.

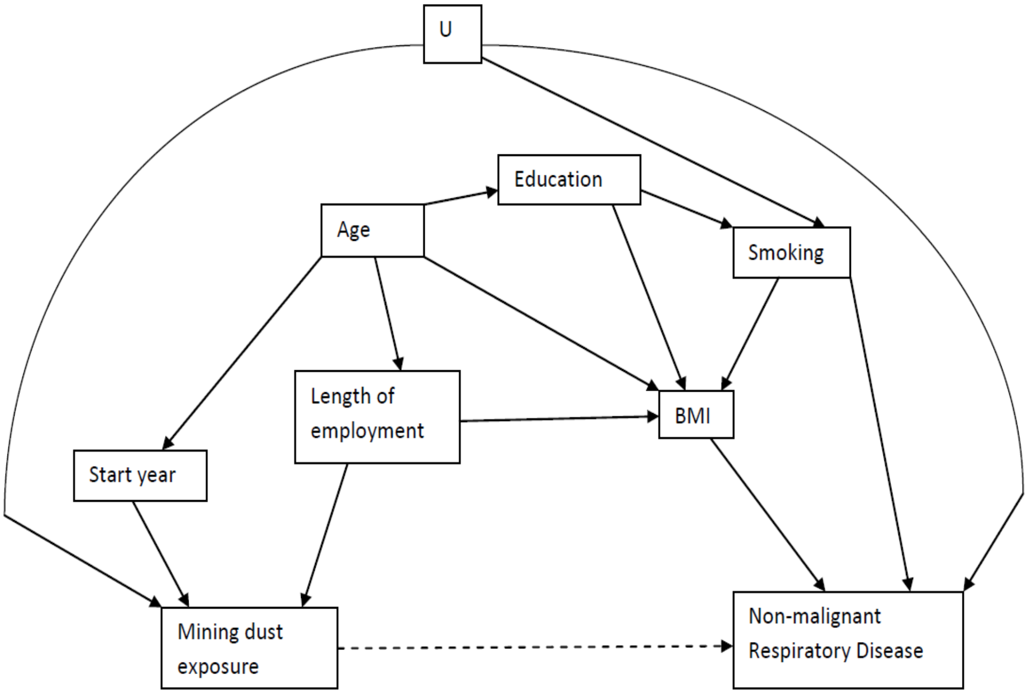


Figure 2**:** Directed Acyclic Graph Depicting Exposure-Disease relationship. U represents unmeasured factors.

1.12 Lung health outcomes assessment

Occupational health screening utilizes relevant history, symptoms, physical exam, chest x-ray and pulmonary function tests (usually spirometry) to make clinical inferences (American Thoracic Society, 2004). This is particularly important in longitudinal follow-up of workers in such industries as mining where the historical dust exposure is higher than current industry levels. Risks from cumulative respirable silica exposure have been extensively described in literature for many mineral mining occupations, especially coal mining (Beach, et al., 2001; Bio, et al., 2007; Chen, et al., 2005; Hnizdo & Sluis-Cremer, 1991; Love, et al., 1997; Oxman, et al., 1993; Glass, et al., 2003; Gamble & Gibbs, 2008; Govender, et al., 2011). In taconite mining, relationships of dusts with non-malignant respiratory diseases (NMRDs) have not been similarly studied and described. Overall understanding of the relationship between taconite mining and lung disease will be improved by describing the relationship between cumulative respirable silica exposure in taconite operations and estimated RLD. This assessment is particularly relevant for improved understanding of the how the estimates of prevalence ratios of association between dust exposure and RLD vary with different outcome measures in this population.

1. Physiological status of lung function
    - i. Non-reduced vs. reduced FVC: Non-reduced includes normal and/or obstructive lung function. Reduced FVC includes mixed function (combined restrictive with obstructive impairment). This formed the primary outcome of spirometric restriction that was used throughout the rest of the studies.
    - ii. Normal, Restrictive, obstructive and mixed disease categorical outcomes: These categories are mutually exclusive groups. (All outcomes are described in clinic testing protocols above)
    - iii. FVC (on a percentile scale) – Based on reference equations, the individual performance of participants on spirometry are standardized using reference equations from a normal population (Hankinson et al., 1999).

Here, individuals' FVC's are compared to the normal population on a percentile scale (0-100).

2. Chest Radiography
    - i. Parenchymal abnormalities- Based on profusion scores on chest x-rays as determined by two B-readers' agreement, with a third B-reader used to arbitrate disagreements on reads. Profusion scores > 1/0 are considered positive for presence of parenchymal abnormalities suggestive of restrictive lung disease.
    - ii. Pleural abnormalities- Based on presence of pleural changes on chest x-rays suggestive of restrictive lung disease. Also using the B-reader system described above for determining the presence of pleural abnormalities.
3. Shortness of breath (Dyspnea) symptoms

   Based on reported symptoms of shortness of breath reported in questionnaires that are suggestive of restrictive ventilatory function.

Using exposure and outcome measures, exposure-dose and dose-response/outcome relationships are described. A hypothesized model of association is represented using a causal diagram, also called Directed Acyclic Graph (Hernán, et al., 2002) demonstrating the role of potential covariates: age, smoking status, and BMI (Figure 2 above).

Other relevant factors in the association between exposure and outcome were considered within the statistical modeling. These other factors included sex, age smoking, BMI and commercial asbestos exposure estimated using other sources of exposure reported in the questionnaires at the time of the survey. Prevalence ratios (PRs) of association between exposures (cumulative exposure concentrations, department, onset of employment, and SEGs), in decreasing order of specificity, and categorical outcome measures were explored. As part of this analysis, this study explored the combined association of respirable silica and EMP or non-silica respirable dusts exposures with RLD outcome. This was done by including other measured dust exposures in multivariate models when assessing for the outcome associations of singular exposures. This assessed the additive and multiplicative interaction of composites of total respirable dust, including respirable silica, with outcomes determined in this study.

1.13 Ethics

Approval was obtained annually from the University of Minnesota Institutional Review Board (IRB) and from the 3,310 participants randomly selected and approached for the study.

CHAPTER 2:

ESTIMATES OF RESTRICTIVE VENTILATORY DEFECT IN THE MINING INDUSTRY. CONSIDERATIONS FOR EPIDEMIOLOGICAL INVESTIGATIONS: A CROSS-SECTIONAL STUDY.

STUDY SUMMARY

Objectives: 1) To assess the impact of ATS/ERS “acceptability” and “repeatability” criteria for spirometry on the estimates of restrictive ventilatory defect in a population of taconite miners. 2) compare estimates of restrictive ventilatory defect with three different pulmonary function tests (spirometry, alveolar volume (VA) and diffusing capacity (DL,CO)). 3) assess the role of population characteristics on these estimates.

Design: Cross-sectional study

Setting: Current and former workers in six current taconite mining operations of northeastern Minnesota were surveyed.

Participants: We attempted to enroll 3,313 participants. 1,353 responded while 1,188 current and former workers fully participated in the survey and 1,084 performed complete pulmonary function testing and were assessed.

Primary and Secondary outcome measures: We applied American Thoracic Society (ATS/ERS) acceptability criteria for all tests and categorized subjects into groups according to whether they fully met, partially met, or did not meet acceptability criteria for spirometry. Obstruction and restriction were defined utilizing the lower limit of normal for all tests. When using alveolar volume, restriction was identified after excluding obstruction.

Results: Only 519 (47.9%) tests fully met ATS/ERS spirometry acceptability criteria. Within this group, 5% had obstruction and 6%, restriction on spirometry. In contrast, among all participants (N=1,084), 16.8% had obstruction, while 4.5% had restriction. VA showed similar results in all groups after obstruction was excluded. Impaired gas transfer (reduced DL,CO) was identified in less than 50% of restriction identified by either spirometry or VA. BMI was significantly related to spirometric restriction in all groups.

Conclusions: Population estimates of restriction using spirometry or VA varied by spirometric acceptability criteria. Other factors identified as important considerations in the estimation of restrictive ventilatory defect included increased BMI and gas transfer

impairment in a relatively smaller proportion of those with spirometric restriction. These insights are important when interpreting population-based physiological data in occupational settings.

Introduction

The determination of population estimates for restrictive ventilatory defect (RVD) within populations exposed to mining dusts typically relies upon the use of chest x-ray and spirometry. Restrictive lung disease (RLD) refers to a decrease in total volume of the lungs due to impaired expansion from decreased lung elasticity. It is diagnosed using body plethysmography. It is a subset of what is actually measured, RVD which includes other causes of impaired expansion like decreased chest wall expansion and pulmonary vascular disease. In this paper, we measure RVD as an estimate for RLD. In the occupational setting, spirometry plays a key role in respiratory health surveillance. It can be done on-site at low cost and with minimal risk to the employee. It can assist the health professional by determining if an individual worker demonstrates a specific pattern of respiratory impairment and in occupational settings, RVD. It can also help assess the effectiveness of measures implemented to protect the worker population and can help estimate exposure patterns to known hazards within working populations (Centers for Disease Control and Prevention, 2011). An understanding of this exposure likelihood aids the interpretation of results from morbidity and mortality studies, particularly in the setting of absent or incomplete industrial hygiene information.

With the use of spirometry, the identification of RVD is complicated by several factors including low sensitivity/low positive predictive value, variation in individual performance and the impact of confounding factors, particularly obesity and the effects of cigarette smoking. Few studies have evaluated the impact of these factors on population estimates for restrictive disease within working populations.

In clinic settings lung obstruction can be identified with high reliability and validity using the American Thoracic Society and European Respiratory Society (ATS/ERS) recommendations for spirometry (Jensen, et al., 2006; Wanger, et al., 2005; Eisen, et al., 1987; Miller, et al., 2005; Pellegrino, et al., 2005). Assessing the presence of restriction can be more difficult with spirometry showing a higher negative than positive predictive value in the identification of lung restriction (positive predictive value < 60%) (Venkateshiah, et al., 2008; Aaron, et al., 1999; D'Aquino, et al., 2010; Vandevoorde, et al., 2008). Ideally, it is suggested that after conducting spirometry, the presence of lung restriction should be further defined with the use of lung volume testing (Aaron, et al., 1999; D'Aquino, et al., 2010). Given the problems of cost and access to lung volume testing, it has also been suggested that spirometry alone may be used to identify restriction without greatly compromising diagnostic accuracy (Venkateshiah, et al., 2008; Aaron, et al., 1999; Pezzoli, et al., 2003). Other methods for assessing lung function may be helpful. These include measurement of diffusing capacity (DL,CO), and the measurement of alveolar volume (VA), which is done as a part of the DL,CO test. VA, in the absence of obstruction, is more closely related to total lung capacity (TLC) (Pellegrino, et al., 2005; Rodenstein & Stanescu, 1983; O'Donnell, et al., 2010; Punjabi, et al., 1998). Although these tests are often used to enhance diagnostic accuracy in clinical practice, they are not routinely available in most clinical or occupational settings (Wanger, et al., 2005).

Individual spirometry measurement is effort-dependent and quality of test performance is variable. Some of this variability can be related to underlying morbidity, which may affect an individual's ability to adhere to ATS/ERS criteria for acceptability. In epidemiologic settings, these criteria may provide important insights into the impact of data quality on study results. For example, spirometry interpretation using 'acceptable' or 'usable' quality criteria can differentially exclude people with poor lung function from the assessment (Miller, et al., 2005). Similar to the lack of data on spirometry quality and its impact on medical decisions (Enright, 2010), an in-depth look at spirometry use in mining populations has not been undertaken with these considerations in mind.

There were three primary objectives in this study. The first was to assess the impact of ATS/ERS "acceptability" and "repeatability" criteria on estimates of RVD in a population of taconite miners. The second was to compare estimates of RVD with three different pulmonary function tests (spirometry, alveolar volume (VA) and diffusing capacity (DL,CO)). The third was to assess the role of population characteristics on these estimates.

Methods

In 2010, a survey of current and former workers in the taconite mining industry of Minnesota was conducted as an attempt to quantify the types and severity of non-malignant lung disease associated with exposure to dusts from mining operations. The survey included workers from all six current mining operations who were exposed after the 1950s (when workplace dust levels were likely higher than current levels) up to the present. A sample size of 1,200 workers was selected to provide sufficient power to explore associations between lung function and exposures of interest and to determine the prevalence of lung pattern abnormality in the overall population of workers (Petersen & Castellan, 1984).

With the help of union and company officials, we searched employment records to identify current and former miners in seven different Minnesota counties for recruitment to the study. The lists included workers who were employed at any time between 1989 and the present, regardless of when they started work. Individuals were contacted by mail or telephone and invited to participate. We obtained informed consent in accordance with a protocol approved by the University of Minnesota Human Subjects Research Committee.

Participants completed self-administered health and work questionnaires, underwent chest x-ray (CXRs) and pulmonary function tests (PFTs) which included spirometry and $D_{L,CO}$ (with VA), in that order. Testing was performed at a community clinic in a location close to the miners' homes. Estimation of the prevalence of obstruction and RVD in this population of miners was made using current ATS/ERS criteria for all test methods (Jensen, et al., 2006; Wanger, et al., 2005; Eisen, et al., 1987; Miller, et al., 2005; Pellegrino, et al., 2005). These criteria for spirometry testing included both criteria for acceptable blows, and criteria for maneuver repeatability.

Standard Approaches to Measurement Used

The use of lower limits of normal (LLN) from reference equations has been shown to have a better combination of sensitivity, specificity and predictive values (positive &

negative) as well as enhanced concordance and discordance when compared with the use of traditional cut-off points of 70% and 80% (for FEV_1/FVC ratio, FEV_1 and FVC percent predicted) (Pellegrino, et al., 2005; Ferguson, et al., 2000; Hansen, et al., 2007; Akpinar-Elci, et al., 2006; Vollmer, et al., 2009). Using the 5th percentile LLN adjusts for age-related decline in lung function so that only 5% of individuals in each age reference group is labeled as "abnormal." In contrast, using 70% or 80% absolute cut-offs potentially results in an increased proportion of false positives in older subjects (Swanney, et al., 2008).

A 10.2-litre, dry rolling seal, volume displacement spirometer (Sensormedics 1022, Occupational Marketing Inc., Houston, TX) was used to conduct spirometry while an Ultima PF system (Medical Graphics Corporation, St. Paul, MN) was used to conduct DL,CO measurements. The latter uses single-breath helium dilution for the measurement of alveolar volume (VA). The ambient temperature was recorded automatically and barometric pressure was entered manually at the beginning of each test session. Screening spirometry was performed by technicians trained in a 2-day NIOSH-certified spirometry course. These technicians were also trained to and performed diffusing capacity testing. Precautions were taken to avoid errors. These included carrying out regular quality checks of equipment and monitoring the procedural performance of technicians. Testing followed ATS/ERS recommendations (Eisen, et al., 1987; Miller, et al., 2005), except that here, five spirometry efforts were performed as a minimum. Different categories based on meeting ATS/ERS guidelines on acceptability and repeatability of spirometric maneuvers were assessed (Table 1). Measurement of DL,CO and VA were performed according to published guidelines (Rodenstein & Stanescu, 1983; Macintyre, et al., 2005). DL,CO results met criteria if a participant had a minimum of 3 valid tests without exceeding 5 attempts. A valid test required a participant to hold their breath for 8-12 seconds with an Inspiratory Vital Capacity (IVC) of ≥ 85% of Slow Vital Capacity (SVC). Repeatability criteria require that the best two DL,CO results must be within 10% of each other. For data analysis, the average of the best two results was used.

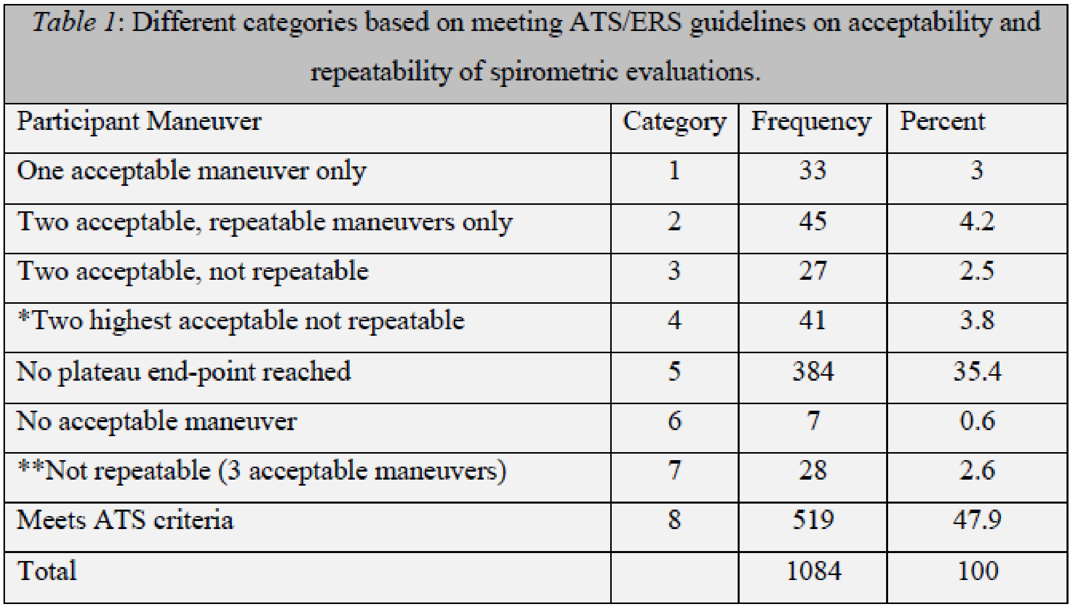


Table 1: Different categories based on meeting ATS/ERS guidelines on acceptability and repeatability of spirometric evaluations.

Participant Maneuver	Category	Frequency	Percent
One acceptable maneuver only	1	33	3
Two acceptable, repeatable maneuvers only	2	45	4.2
Two acceptable, not repeatable	3	27	2.5
*Two highest acceptable not repeatable	4	41	3.8
No plateau end-point reached	5	384	35.4
No acceptable maneuver	6	7	0.6
**Not repeatable (3 acceptable maneuvers)	7	28	2.6
Meets ATS criteria	8	519	47.9
Total		1084	100

'No plateau end-point reached' referred to the inability to achieve end-of-test volume (EOTV), an important end-of-test (EOT) criterion. In this case, the volume-time plateau was not obtained.

*Attained 3 acceptable maneuvers but, as per criteria, the two highest values were not repeatable. The lower two were repeatable and their values were used.

**Attained 3 acceptable maneuvers but, as per criteria, none were repeatable.

Several standard reference equations for FEV_1, FVC and FEV_1/FVC have been developed for the general U.S. population (Hankinson, et al., 1999; Crapo, et al., 1981; Dockery, et al., 1985; Knudson, et al., 1976; Marion, et al., 2001) and for U.S. blue collar workers (Glindmeyer, et al., 1995; Petersen & Hankinson, 1985). The reference equations of Hankinson and coworkers (1999) were used for the estimation of respective LLNs of the spirometric indices (Hankinson, et al., 1999). In addition to being recommended by ATS/ERS as the best standard for U.S population assessment (Eisen, et al., 1987; Ferguson, et al., 2000), Hankinson *et al.* stratified their analysis by gender and age, covering a broad age range (8 to 80 years) and showed good agreement with previous reference equations. It has also been shown that these reference equations for spirometry may be applied to individuals older than 80 with low risk of misclassification (Hankinson, et al., 2010).

The current recommendations for interpretation in Pulmonary Function Testing (PFT) were used (Wanger, et al., 2005; Miller, et al., 2005; Pellegrino, et al., 2005; Ferguson, et al., 2000). A subject was identified as having ‘airflow/lung/spirometric obstruction’ if the FEV_1/FVC ratio was < LLN and ‘spirometric restriction’ if their FEV_1/FVC ratio was normal (≥ LLN) but their FVC value was < LLN. A ‘mixed pattern’ was identified when both FEV_1/FVC ratio and FVC values were < LLN. A ‘mixed pattern’ may be seen in individuals with obstruction plus either superimposed restriction or air trapping, either of which can lead to a reduction in FVC. “All spirometric restriction” referred to estimates of spirometric restriction plus mixed pattern impairment identified in the population. Borderline obstruction, which may represent either very mild obstruction or a normal physiological variant, sometimes called “dysanapsis,” was identified by a low FEV_1/FVC ratio plus an FEV_1 ≥LLN (Wanger, et al., 2005; Miller, et al., 2005; Pellegrino, et al., 2005; Ferguson, et al., 2000; Mead, 1980).

Reference equations from Stocks *et al*. were used for determining the LLN for VA as recommended by ATS/ERS (Stocks & Quanjer, 1995). These were corrected for the anatomic dead space volume (VD) difference between VA and TLC (Macintyre, et al., 2005; Saydain, et al., 2004; Weibel, 1970-1971). For anatomic dead space (VD), when the BMI was < 30, the formula: VD (mL) = 2.2 × (weight in kg) was used (Weibel, 1970-1971), while when BMI was ≥ 30 the formula: $VD\ (mL) = 24 \times (\text{height in cm})^2/4545$ was used (Macintyre, et al., 2005). Reference values for DL,CO from Crapo *et al.* were utilized as recommended by ATS/ERS (Pellegrino, et al., 2005; Macintyre, et al., 2005; Cotes, et al., 2009), with an adjustment for hemoglobin (Pellegrino, et al., 2005; Macintyre, et al., 2005; Crapo & Morris, 1981).

Other Definitions Used

We used the term ‘VA restriction’ when the FEV_1/FVC ratios were normal (≥ LLN) and the VA was reduced, independently of FVC. This was done because previous studies have shown that, in the presence of lung obstruction, lung volume measured by single-breath helium dilution underestimates TLC measured by body plethysmography (VL,pleth) (Pellegrino, et al., 2005; O’Donnell, et al., 2010; Punjabi, et al., 1998). These obstructive scenarios include cysts, non-communicating bullae/air-spaces and pneumothorax and are not incorporated in the single-breath helium estimate of lung volume (VA) (Pellegrino, et al., 2005; O'Donnell, et al., 2010). However, when obstruction is excluded, lung volume estimation by single-breath helium dilution approximates VL,pleth (Rodenstein & Stanescu, 1983; O'Donnell, et al., 2010; Punjabi, et al., 1998; Ferris, 1978). For $D_{L,CO}$ estimations, the term "low $D_{L,CO}$ without obstruction" was used when $D_{L,CO}$ was reduced (< LLN) but the FEV_1/FVC ratio was normal (≥ LLN).

Participants were categorized into four non-exclusive groups (Table 2) defined by the extent to which ATS/ERS criteria for spirometric performance were met. Group 1 ("Total group") includes all tested subjects. Group 3 ("Met criteria") comprises participants who met all criteria for acceptability and repeatability (Miller, et al., 2005). Group 2 ("Exclusions") includes those who failed any of the criteria (Groups 2 and 3 were mutually exclusive). Group 4 ("Usable") uses relaxed acceptability criteria and can be thought of as allowing "usable" tests as described by ATS/ERS and included all subjects from Group 3 and some from Group 2. These "usable" tests were 1) tests with quality control (QC) grades of ≥ 'B' (at least two acceptable maneuvers with FEV_1 values repeatable within 101 - 150 ml) (Ferguson, et al., 2000), and 2) tests that did not meet end-of-test (EOT) criteria (no plateau end-point reached). The assigned FVC values in this group (no plateau end-point reached) were likely close to true FVC values that would have been attained if plateau had been reached. The EOT criteria for acceptability are related to being unable to continue further exhalation and having a volume-time curve showing no change in volume (<0.025 L) for ≥1 second and an expiratory time ≥ 6 seconds (Miller, et al., 2005; Miller, et al., 2010).

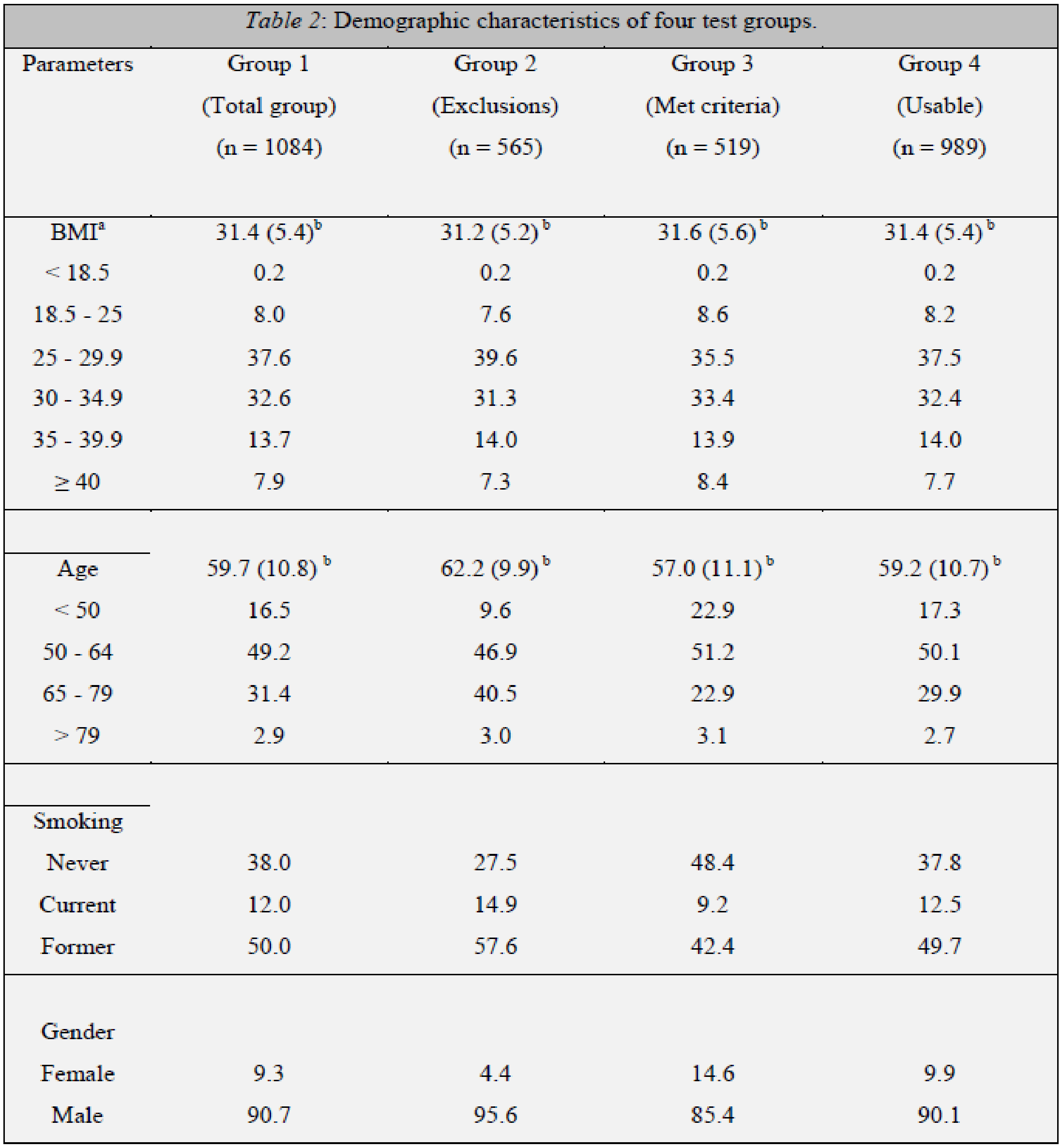


Table 2: Demographic characteristics of four test groups.

Parameters	Group 1 (Total group) (n = 1084)	Group 2 (Exclusions) (n = 565)	Group 3 (Met criteria) (n = 519)	Group 4 (Usable) (n = 989)
BMI[a]	31.4 (5.4)[b]	31.2 (5.2)[b]	31.6 (5.6)[b]	31.4 (5.4)[b]
< 18.5	0.2	0.2	0.2	0.2
18.5 - 25	8.0	7.6	8.6	8.2
25 - 29.9	37.6	39.6	35.5	37.5
30 - 34.9	32.6	31.3	33.4	32.4
35 - 39.9	13.7	14.0	13.9	14.0
≥ 40	7.9	7.3	8.4	7.7
Age	59.7 (10.8)[b]	62.2 (9.9)[b]	57.0 (11.1)[b]	59.2 (10.7)[b]
< 50	16.5	9.6	22.9	17.3
50 - 64	49.2	46.9	51.2	50.1
65 - 79	31.4	40.5	22.9	29.9
> 79	2.9	3.0	3.1	2.7
Smoking				
Never	38.0	27.5	48.4	37.8
Current	12.0	14.9	9.2	12.5
Former	50.0	57.6	42.4	49.7
Gender				
Female	9.3	4.4	14.6	9.9
Male	90.7	95.6	85.4	90.1

All values were percentage distributions of each parameter within the population groups.

Group 1– All workers surveyed without consideration for exclusion based on ATS/ERS test criteria for spirometry.

Group 2– All workers who did not meet all ATS/ERS criteria for spirometric assessment.

Group 3– Workers who met all ATS/ERS criteria for spirometric assessment.

Group 4– All workers with spirometry quality ≥"B" (See Methods) and repeatable tests not meeting end-of-test (EOT) criteria.

[a] Body Mass Index – Weight in kilograms/Height in meters squared (kg/m^2).

[b] These represented the mean and standard deviations (in parenthesis) for these groups.

Although the other tests (VA & DL,CO) have unique criteria for acceptability which we adhered to, we formed groups on the basis of spirometry testing only. We were most interested in spirometric classification because it is the test most available in occupational settings. Both diffusing capacity testing and spirometry are effort dependent, while diffusing capacity (and VA) has the drawback of performing inconsistently in the presence of lung obstruction.

Description of the different groups was done and the only two mutually exclusive groups (Groups 2 and 3) were compared using t-test and chi-square analysis. Crude prevalence estimates of obstruction and restriction by spirometry were determined. Exact (Clopper-Pearson) 95% confidence intervals were derived for the all estimates of lung function impairment. This method has the advantage of calculating conservative confidence interval estimates when assessing binomial proportions. Prevalence estimates of RVD determined by combining tests were presented to show increased likelihood of restriction determination (Table 3) (Pellegrino, et al., 2005). The combination of these three tests also represented the lower bound for RVD prevalence estimates. When estimates were based on any of the three tests being abnormal (“Or”), this represented the upper bound for RVD estimates.

To explore the impact of obesity on the apparent prevalence of restriction in this population, we performed a multivariate analysis to determine the association of BMI with FVC. For this analysis, FVC was converted to a percentile value for each participant based on normal reference equations (Hankinson, et al., 1999). This percentile is the FVC of each participant, standardized to the NHANES III population-based distribution of normal lung function. This is different from percent predicted which is a ratio of the FVC to the median predicted value for each participant (race, age, height and gender adjusted). This association was determined with a generalized linear model both unadjusted and adjusted for age and gender in all the described groups.

Results

We attempted to enroll 3,313 potential participants. A total of 1,353 subjects responded and provided consent and questionnaire information and of these, 1,188 current and former workers fully participated in the survey. Of the 1,188 workers, 1084 performed complete pulmonary function testing. Their data comprised the data set analyzed for this assessment.

The participants lived in seven different counties in northeastern Minnesota and ranged in age from 36 to 89 years with a mean age of 59.7 yrs. (SD = 10.8 yrs.). Most participants were male (90.7%), with current smokers comprising 12%, never-smokers, 38% and former smokers, 50% of the population tested. Of the 1084 participants assessed, 519 (47.9%) fully met ATS/ERS criteria of 3 acceptable and 2 repeatable maneuvers for spirometry (Miller, et al., 2005). The others had criteria for exclusion as shown in Table 1. Of the tests that were potentially excluded, the majority were due to failure to meet end-of-test (EOT) criteria by reaching an adequate plateau (Miller, et al., 2005). This latter category comprised 68% of potentially excluded tests.

Table 2 shows the demographics of all groups. While BMI was distributed similarly among all groups, Group 3 was younger, had a higher proportion of women and a higher proportion of individuals who had never smoked. Comparison of groups 2 and 3 (“Exclusions” vs. “Met criteria”) showed a significantly higher mean testing age in group 2, a higher proportion of males, a higher mean FEV_1 and a significantly higher proportion of ever smokers (current and former). All p-value estimates were <0.0001 and mean BMI was not significantly different between the two groups.

Table 3 presents the lung abnormality estimates for obstruction and RVD by spirometry, restriction by alveolar volume (VA restriction) and mixed disease by spirometry for all groups. It also presents estimates of abnormal lung function characterized by a $D_{L,CO}$ < LLN (Pellegrino, et al., 2005) (low $D_{L,CO}$ without obstruction) after patients with obstruction on spirometry were excluded. Estimation of the prevalence of restriction using VA ranged from 5% to 6.9% across the different groups. Estimation of RVD using spirometry had a wider range across the four groups ranging from 3.2% to 6.0%. When participants with a mixed pattern were included, the range of estimates of RVD (FVC < LLN) across these four groups were less (6.9% to 7.8%). Spirometric obstruction varied the most, ranging from 5% to 27.6% depending on adherence to ATS/ERS guidelines. Prevalence estimates of RVD using a combination of available tests ranged from 0.5% in Group 2 using the “&” classification and all the tests to 9.4% in Group 3 using the “Or” classification for all the tests (after excluding obstruction).

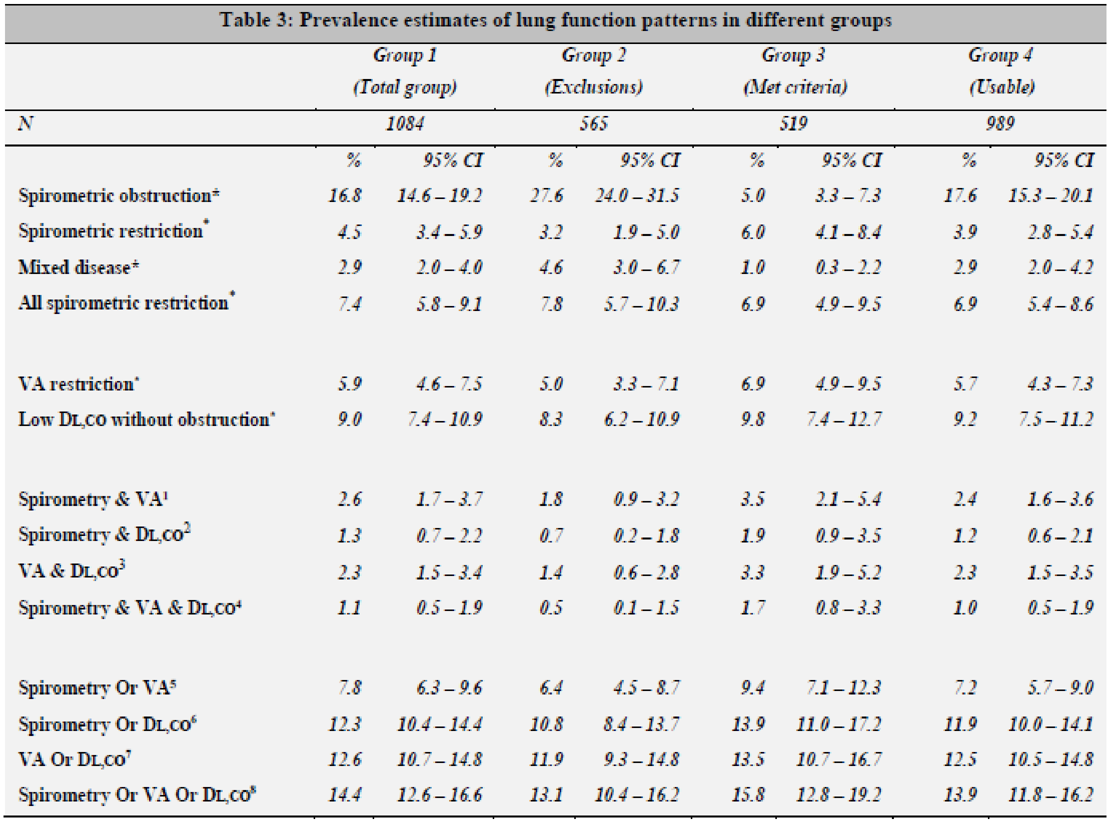


Table 3: Prevalence estimates of lung function patterns in different groups

	Group 1 (Total group)		*Group 2 (Exclusions)*		*Group 3 (Met criteria)*		*Group 4 (Usable)*	
N	*1084*		*565*		*519*		*989*	
	%	*95% CI*	*%*	*95% CI*	*%*	*95% CI*	*%*	*95% CI*
Spirometric obstruction*	*16.8*	*14.6 – 19.2*	*27.6*	*24.0 – 31.5*	*5.0*	*3.3 – 7.3*	*17.6*	*15.3 – 20.1*
Spirometric restriction*	*4.5*	*3.4 – 5.9*	*3.2*	*1.9 – 5.0*	*6.0*	*4.1 – 8.4*	*3.9*	*2.8 – 5.4*
Mixed disease*	*2.9*	*2.0 – 4.0*	*4.6*	*3.0 – 6.7*	*1.0*	*0.3 – 2.2*	*2.9*	*2.0 – 4.2*
All spirometric restriction*	*7.4*	*5.8 – 9.1*	*7.8*	*5.7 – 10.3*	*6.9*	*4.9 – 9.5*	*6.9*	*5.4 – 8.6*
VA restriction*	*5.9*	*4.6 – 7.5*	*5.0*	*3.3 – 7.1*	*6.9*	*4.9 – 9.5*	*5.7*	*4.3 – 7.3*
Low DL,CO without obstruction*	*9.0*	*7.4 – 10.9*	*8.3*	*6.2 – 10.9*	*9.8*	*7.4 – 12.7*	*9.2*	*7.5 – 11.2*
Spirometry & VA[1]	*2.6*	*1.7 – 3.7*	*1.8*	*0.9 – 3.2*	*3.5*	*2.1 – 5.4*	*2.4*	*1.6 – 3.6*
Spirometry & DL,CO[2]	*1.3*	*0.7 – 2.2*	*0.7*	*0.2 – 1.8*	*1.9*	*0.9 – 3.5*	*1.2*	*0.6 – 2.1*
VA & DL,CO[3]	*2.3*	*1.5 – 3.4*	*1.4*	*0.6 – 2.8*	*3.3*	*1.9 – 5.2*	*2.3*	*1.5 – 3.5*
Spirometry & VA & DL,CO[4]	*1.1*	*0.5 – 1.9*	*0.5*	*0.1 – 1.5*	*1.7*	*0.8 – 3.3*	*1.0*	*0.5 – 1.9*
Spirometry Or VA[5]	*7.8*	*6.3 – 9.6*	*6.4*	*4.5 – 8.7*	*9.4*	*7.1 – 12.3*	*7.2*	*5.7 – 9.0*
Spirometry Or DL,CO[6]	*12.3*	*10.4 – 14.4*	*10.8*	*8.4 – 13.7*	*13.9*	*11.0 – 17.2*	*11.9*	*10.0 – 14.1*
VA Or DL,CO[7]	*12.6*	*10.7 – 14.8*	*11.9*	*9.3 – 14.8*	*13.5*	*10.7 – 16.7*	*12.5*	*10.5 – 14.8*
Spirometry Or VA Or DL,CO[8]	*14.4*	*12.6 – 16.6*	*13.1*	*10.4 – 16.2*	*15.8*	*12.8 – 19.2*	*13.9*	*11.8 – 16.2*

% - Prevalence of lung function patterns in each population group in percentage.

95% CI – Clopper-Pearson (Exact) 95% Confidence Limits of prevalence estimates.

Group definitions are as described in the Methods section

* Definitions described in the Methods section.

[1] After excluding spirometric obstruction, both FVC and VA were < LLN.

[2] This is the proportion of spirometric restriction that also had a reduced (<LLN) DL,CO.

[3] This is the proportion of VA restriction that also had a reduced (<LLN) DL,CO.

[4] After excluding spirometric obstruction, FVC, VA and DL,CO were < LLN.

[5] After exclusion of spirometric obstruction, either FVC or VA were < LLN.

[6] After exclusion of spirometric obstruction, either FVC or DL,CO were < LLN.

[7] After exclusion of spirometric obstruction, either VA or DL,CO were < LLN.

[8] After exclusion of spirometric obstruction, either FVC or VA or DL,CO were < LLN.

BMI was ≥ 30 in 54.2% of study participants. In Table 4, BMI was significantly associated with FVC percentiles in all four groups when unadjusted or adjusted for age and gender ($p < 0.0001$). BMI was observed to account for 8.8 – 9.2% of variation in percentile values when unadjusted. When adjusted for age and gender, this range increased to 9.3 – 10.6% with the highest value seen in Group 3. The association in both adjusted and unadjusted models demonstrated a trend of decreasing FVC percentile with increased BMI.

Table 4: Linear Regression of Forced Vital Capacity (Percentiles*) by Body Mass indices (BMI)

Test Criteria Groups	**Estimate**	**R^2 (%)**
Group 1[a] (Total group)	-0.018	9.1
Group 2[b] (Exclusions)	-0.019	9.2
Group 3[c] (Met criteria)	-0.017	9.0
Group 4[d] (Usable)	-0.017	8.8

*Percentiles of spirometry performance are expressed as the FVC of each participant, standardized to the NHANES III population-based distribution of normal lung function. This is different from percent predicted which is the ratio of the FVC to the median predicted value for each participant (race, age, height and gender adjusted).

All crude and multivariate linear regression models had significant p-values at <0.0001.

Multivariate models involved adjusting for Age and Gender.

Groups are as described in the Methods Section.

- a- Adjusted estimate : -0.018; R^2 (%) : 9.5
- b- Adjusted estimate : -0.019; R^2 (%) : 9.5
- c- Adjusted estimate : -0.016; R^2 (%) : 10.6
- d- Adjusted estimate : -0.017; R^2 (%) : 9.3

Discussion

The use of pulmonary function testing to estimate the prevalence of restrictive ventilatory defect (RVD) in a dust-exposed population of workers has uncertainties about it. These uncertainties relate to individual performance on testing, testing errors, group characteristics of the participants tested and representativeness of the group tested. The focus of this investigation was to highlight the potential range of estimates of lung impairment depending on how spirometry acceptability criteria were applied and by the different pulmonary function tests used while considering population characteristics.

The overall response rate in this study was 40.8%. We would expect similar factors to affect variability in estimates of RVD despite the degree of study participation. Estimates could vary upwards or downwards depending on the degree of underlying illness within the study participants.

The application of spirometry acceptability criteria to test results was an important factor in assessing abnormality. Acceptability criteria for spirometry impacted the prevalence estimates for RVD, especially lung obstruction and, consequently, mixed disease. Our assessment showed a high prevalence of obstructive patterns in those not meeting acceptability criteria, compared to those fully meeting criteria (27.6% vs. 5%). Identifying lung obstruction in this mining population is relevant because of the recognized role of heavy dust exposure in causing lung obstruction (non-pneumoconiotic effect).

A key criterion for the recommended exclusion of a spirometric maneuver (“acceptable” vs. “usable”) was not meeting end-of-test (EOT) criteria. Among the participants, 35.4% (68% of potentially excluded tests) did not meet EOT criteria for acceptability. Current ATS/ERS guidelines recommend not using maneuvers not meeting all acceptability criteria except where they may still contain useful information (“usable” maneuvers) (Miller, et al., 2005). This recommendation referred to assessments for morbidity important for clinical care of patients. In this epidemiologic assessment, most test curves not meeting EOT criteria were repeatable and represented the subjects’ best performance. Even though EOT criteria were not met, these results were included in groups 1, 2 and 4. Group 3 excludes these results. We regarded them as a necessary inclusion for epidemiologic assessment (Group 4), meeting the “usability” criteria. Including these tests (not meeting EOT criteria) increased test success from 47.9% to 83.3%. The diagnosis of “true restriction” (Restrictive Lung Disease-RLD) is usually based on demonstrating a reduced total lung capacity (TLC) measured by body plethysmography (VL,pleth). This is considered the gold-standard for the diagnosis of RLD (Wanger, et al., 2005; Pellegrino, et al., 2005; Aaron, et al., 1999; Ferguson, et al., 2000; Vandevoorde, et al., 2005). This test is not widely available in occupational or clinical settings, is costly and not portable (Wanger, et al., 2005). Though some studies have shown VL,pleth to be comparable to lung volume measured by single-breath helium dilution (VA), current guidelines point out that VA underestimates TLC in the setting of moderate to severe obstructive disease (Pellegrino, et al., 2005; D'Aquino, et al., 2010; Rodenstein & Stanescu, 1983; O'Donnell, et al., 2010; Punjabi, et al., 1998). This is a key limitation of using VA as an approximate for TLC. For these reasons, use of VA (and DL,CO) in this study was limited to participants without obstruction (FEV_1/FVC ≥ LLN). In the same sub-population in all four groups (after excluding obstruction), VA restriction proportion was consistently higher than spirometric restriction proportion. This is thought to reflect the higher positive predictive value (PPV) of VA than spirometry in detecting restriction.

With our inclusion of tests not meeting EOT criteria, VA restriction could have included some subjects with obstruction. The addition of DL,CO to spirometry increases the accuracy of functional lung disease determination (Pellegrino, et al., 2005). It further characterizes restriction identified by spirometry by providing a quantitative measure of gas transfer in the lungs (Stocks & Quanjer, 1995). In this study, the prevalence of "low DL,CO without obstruction" was higher than "VA restriction" in all groups. While DL,CO may be a sensitive indicator of early interstitial lung disease, it is not a measure of lung volume. It is rather, a product of DL,CO/VA ratio and VA. DL,CO can also be abnormal in conditions unrelated to dust exposure such as pulmonary vascular abnormality (e.g. pulmonary hypertension), or early emphysema not detected by spirometry (Pellegrino, et al., 2005; Crapo, et al., 1981; Saydain, et al., 2004; Hegewald, 2009). It may also be falsely reduced by maldistribution of inspired gas when measuring VA in obstructive disorders (Macintyre, et al., 2005). A systematic error in measurement using VA and DL,CO was also possible since they are measured using similar technique (single-breath gas dilution) and on the same maneuver.

Although smoking does not result in RVD, the high prevalence of current & former smokers in this cohort could result in a greater estimate of mixed disease. Including the mixed category increases the estimate of RVD and is important for assessing restriction on that basis. Groups 2 and 3 represent the most disparate estimates for RVD, likely due to the higher prevalence (Group 2) versus the lower prevalence (Group 3) of mixed disease. The Group 2 participants were shown to be significantly older than Group 3, had significantly higher male proportions and higher amounts of current/former smoking.

The variation in estimates of abnormality across groups and the uniqueness of the potentially excluded group (Group 2) highlights the problems of accurately estimating abnormality prevalence in the total group of workers. If only assessments that strictly met all ATS/ERS acceptability criteria were used, many older and potentially sicker participants' tests would not be utilized, resulting in a biased estimate of the prevalence of RVD. Overall, the prevalence estimates determined using Group 4 reflected a reasonable compromise in the application of ATS/ERS acceptability criteria. This assumes that the differences in obstruction prevalences observed between Groups 3 and 4 represent the sicker, older miners, as suggested by the differences in mean age, BMI and current smoking proportions. Group 4 contained tests not meeting EOT criteria but were still usable in determining prevalence estimates. Exclusion of the potentially sicker population is avoided (Group 3), while still excluding tests of poor quality, which Group 1 would include. The minor differences in abnormality estimates between Groups 1 and 4 may be accentuated in populations with a higher burden of underlying disease.

The prevalence of RVD determined with either spirometry or VA in combination ('&') with isolated reduction in DL,CO represented RVD likely caused by interstitial lung disease (See footnotes in Table 3 for test combinations). The results showed that RVD with impaired gas transfer (DL,CO < LLN) represented less than 50% of estimated lung restriction by either spirometry or VA or both, together. This suggests that more than 50% of estimated restriction (by spirometry or VA) may be from extra-pulmonary causes not affecting gas transfer in the lungs (e.g. obesity). The effect of using multiple tests, including VA and DL,CO, should enhance the estimates of RVD (Aaron, et al., 1999; Rodenstein & Stanescu, 1983).

The effect of obesity on the apparent prevalence of RVD in an occupational group with dust exposure has obvious implications in studying such populations. Obesity can result in chest wall restriction that can affect the estimation the prevalence of RVD. In this study, 10% of the variation in FVC was accounted for by body mass index (BMI). This is not surprising given the high percentage of overweight participants across all acceptability groups.

The estimate of restriction with spirometry was closest to the VA estimate of restriction in Group 3. In this group, restriction estimates from the combination of Spirometry, VA and $D_{L,CO}$ likely represented the best estimate of true lung restriction. It comprises the least amount of obstruction, while theoretically better approximating TLC. This insight, along with the ease of administration suggests that spirometry is a reasonable approach for the identification of lung restriction in this setting, particularly when taking chest wall issues, like obesity, into account. Since spirometry is commonly used in assessing lung health in occupational settings, it is important to characterize estimates of varying conditions in cross-sectional studies. The further understanding of its performance in longitudinal settings will also enhance its use.

Conclusions

Factors identified as important in the estimation of restrictive ventilatory defect in this group of miners included BMI, gas transfer impairment and spirometric acceptability criteria. High BMI was identified in a large proportion of the group and was strongly correlated with spirometry-identified RVD. Gas transfer impairment, in combination with spirometry, was likely helpful in more accurately identifying intrinsic restrictive ventilatory defect. Estimates for RVD also varied by spirometric acceptability criteria with more representative results occurring in those classified as “usable”. These findings will be useful in future efforts to understand qualitative and quantitative exposure-disease relationships in these miners.

CHAPTER 3:

THE ASSOCIATION OF CUMULATIVE SILICA EXPOSURE WITH LUNG DISEASE OUTCOMES IN TACONITE MINERS

STUDY SUMMARY

Introduction

We examined the association between cumulative silica exposures in taconite mining and non-malignant respiratory disease (NMRD) outcomes using a comprehensive assessment of current and historical exposures in taconite mining using a cross-sectional screening study of Minnesota taconite mining workers.

Methods

A survey of current and former taconite workers was undertaken in 2010. Miners were screened with a questionnaire that focused on occupational and medical history, along with lung tests (spirometry, chest x-rays). An occupational exposure assessment was performed which measured over 1,500 onsite samples for respirable dusts including silica in 28 major job functions. Historical exposures to dusts were estimated with data obtained from prior onsite exposure measures by existing operations, and from the Mining Safety and Health Administration. Individual work histories were used to determine the length of time worked (years) in these jobs. Cumulative silica exposure ((mg/m^3)-years) was estimated as a product of time worked and year-specific silica dust measures for the 28 job functions. Forced vital capacity less than lower limits of normal for age, height, race and gender was used to determine restrictive ventilatory defect (RVD). Chest x-rays were evaluated using ILO criteria for any evidence of parenchymal abnormalities of 1/0 or greater and pleural abnormalities suggestive of pneumoconiosis by two B-readers, with a third reader to arbitrate disagreements. Prevalence ratios (PR) of exposure-outcome association, with 95% confidence intervals (CI), were estimated using Poisson regression, adjusting for smoking, gender, age, BMI and commercial asbestos exposure.

Results

Spirometric restriction (RVD) occurred in 7.2% of participants; chest x-ray parenchymal abnormalities occurred in 5.4%; chest x-ray pleural abnormalities consistent with pneumoconiosis were observed in 16.8%; and symptoms of shortness of breath (dyspnea on exertion) occurred in 11.4% of the study population. Silica exposure was significantly associated with RVD prevalence (PR = 1.40, 95% CI= 1.08 – 1.81) and prevalence of parenchymal abnormalities on chest x-ray (PR = 1.30, 95% CI= 1.00 – 1.69).

Conclusions

Study results suggest as much as a 40% increase in RVD risk in taconite workers given silica exposure. Silica exposure was also associated with parenchymal chest x-ray findings. However, these associations were dependent on the approach for estimating exposure. When exposures were defined using actual available historical values obtained, no associations were observed between silica exposure and any outcomes. With the more rigorous measurement techniques used in the current exposure assessment, the association observed between silica exposure and lung disease outcomes presents an important insight into the silica exposure impacts in taconite mining.

Introduction

The mining of iron ore (taconite) in northeastern Minnesota has been found to result in several predominant exposures including silica, non-silica dust like iron oxide dusts, and elongate mineral particles (EMP) (Hwang, 2013b). The health risks of exposure to silica are of particular concern due to its occurrence in taconite and its propensity to cause scarring of the interstitium of the lungs (Balmes & Speizer, 2012).

Taconite ore has been mined in northeastern Minnesota since the early 1950's. When refined through processing, the iron content is increased from about 25% to 65% (Kohn & Specht, 1958; Manuel, 2013; Minnesota Minerals Coordinating Committee, 2014). The iron from the Minnesota's Mesabi Range contributes 75% of the iron utilized in North American steel production (Minnesota Minerals Coordinating Committee, 2014). Crystalline silica (silica, respirable silica) is ubiquitous in the earth's crust and is encountered as a component of respirable dust generated in metal mining, including taconite ore mining. Quartz is the most common form encountered in mining (Joy, et al., 2014). According to the U.S. Bureau of Mines, silica is present in nearly all mining operations (Glenn, 2005). Non-malignant respiratory disease (NMRD), includes pneumoconiosis, a well-described result of occupational dust exposure (Antão, et al., 2007). It also includes other inflammatory lung conditions like infection, allergic, infective and immune-mediated, like sarcoidosis. In occupational settings however, with respirable dust exposures, pneumoconioses is mainly prevalent. There is a dose-dependent effect, usually occurring after 15-20 years of exposure (Balmes & Speizer, 2012). In occupations where silica dust is encountered, characteristic lung problems have been described (Fanning, 2004). The lung health risks from silica dust exposure are dependent on the proportion of silica in airborne dust and the duration of exposure (Joy, et al., 2014; Fanning, 2004; Chen, et al., 1989).

Prolonged exposure to respirable silica is associated with parenchymal scarring, observed on chest imaging, and subsequent physiologic limitation of lung function, which can be assessed using spirometry. Earlier investigation into NMRD in this population done over 30 years ago also found little NMRD (Higgins, et al., 1983; Clark, et al., 1980). Previous attempts at describing NMRD in this population did not have the benefit of the quantitative assessment of exposure utilized for this study (Hwang, 2013b; Hwang, et al., 2013a). Overall, little is known about the silica dust exposure among taconite workers or its impact on NMRD in this population.

The main goal of this study was to estimate the association between cumulative silica exposures and NMRD outcomes among a cross-section of current and former taconite miners. This is the first study to look at multiple NMRD outcomes along with detailed exposure measurements.

Methods

Approval was obtained annually from the University of Minnesota Institutional Review Board (IRB) and from the 3,310 participants randomly selected and approached for the study.

Study population and sampling process

This study was a cross-sectional assessment of current and former taconite industry workers and was one component of the larger Minnesota Taconite Workers' Health Study (TWHS). The participants in the RHS were sampled from an employment roster of 16,990 individuals comprising current and former taconite miners across the iron range of northeastern Minnesota. From this group, 3310 study participants were invited, after selection by stratified random sampling based on age, with oversampling of older individuals to increase the chances of identifying dust-related lung disease. A sample size of 1,200 workers was determined to provide adequate power for detection of differences between exposure groups and associations with lung disease outcomes assessed in the study.

Exposure assessment

The exposure assessment has been described in more detail elsewhere (Hwang, 2013b; Hwang, et al., 2013a; Hwang, et al., 2014). Work information was abstracted from study questionnaires and mapped in a standardized fashion for all participants using job titles and descriptions of previous work and dust exposures in the taconite industry to create 28 similar exposure groups (SEGs) (Hwang, 2013b; Sheehy & McJilton, 1987). These SEGs and departments of employment were analyzed for each work entry experience of each participant (Hwang, et al., 2013a). Historical exposures to silica were obtained from all active companies' records and records from Mining Safety and Health Administration (MSHA) monitoring (Minnesota Taconite Workers Health Study, 2014). Current exposure measures were ascertained for taconite mines operating from 2010 to 2011. Respirable silica levels were measured using the NIOSH 7500 analytic method.

Using regression techniques to account for gaps in historical monitoring, the combination of current measurements and historical estimates allowed the creation of a job-exposure matrix (JEM). This matrix consisted of estimated annual exposures to silica exposures specific for each SEG. A person's work history, reported in the questionnaires, was used to determine the amount of time worked in a specific SEG. From this, respective cumulative exposures were summed up for silica exposures. The product of employment years and mine/job/SEG-specific exposure level was determined as cumulative silica exposure for each participant. Where work history information provided by participant was unclear on specific job worked, the average exposure level for the department was used to calculate cumulative exposure.

From the foregoing, two cumulative silica exposure profiles were estimated as representing the possible exposure experience of workers. A "current-only" profile used recently measured, onsite silica levels projecting those values into the past to calculate individual cumulative silica exposure. The historical profile utilized both the current onsite exposure measures and actual historical measures obtained from records from companies and MSHA to calculate individual cumulative silica exposure.

Clinic testing

The survey included a detailed self-administered questionnaire, which determined health, smoking, military and occupational histories, along with in-clinic physiologic pulmonary function tests (PFT) and chest x-ray evaluation on all participants. Questionnaires were developed based on standardized questionnaires of the American Thoracic Society, (Ferris, 1978) the St. George's Respiratory Questionnaire (Jones, et al., 1991), and the University of California, San Diego (UCSD) Shortness-of-Breath Questionnaire (Eakin, et al., 1994). Questionnaires were self-administered and completed in advance of the two-hour clinical evaluation. It contained an assessment of common respiratory symptoms (American Thoracic Society, 1995).

For this study, lung function was assessed using lung spirometry. A reduction in FVC, below the lower limit of normal (LLN) for age, sex, race and height (Hankinson, et al., 1999), indicated abnormal lung volume and lung restriction (Restrictive Ventilatory Defect-RVD). Other spirometric outcomes included obstruction, defined as a reduction in FEV_1/FVC ratio below the LLN, and mixed disease, defined as combined restrictive and obstructive lung function patterns (Hankinson, et al., 1999; Odo, et al., 2013).

The participants underwent standard postero-anterior (PA) chest X-ray according to the recommendations of the International Labor Organization (ILO) for the complete classification of films (International Labour Office (ILO), 2002). The quality of each chest X-ray was evaluated at the clinic by a radiological technician and poor quality films were immediately repeated. The films were initially read by a clinical radiologist to check for health conditions of immediate concern. Each film was then read blindly by two independent NIOSH-certified B-readers for parenchymal and pleural changes and other radiographic features as specified by the ILO framework (International Labour Office (ILO), 2002). Parenchymal abnormalities, described as profusion or opacity scores greater than 1/0, and pleural abnormalities (e.g. plaques, thickening), are characteristic interpretations that are indicative of interstitial lung disease (ILD) changes (Clark, et al., 1980; International Labour Office (ILO), 2002; Farzaneh, et al., 2009). Where there was disagreement between the two readers on the interpretation of the chest X-rays, the disputed films were sent to a third B-reader for arbitration. Dyspnea (shortness of breath) is characteristic of compromised lung function. A common cause of this compromised function is restrictive lung disease, possibly from significant dust exposure. This entailed a "yes/no" response to the question, "Do you ever have to stop for breath when walking at your own pace on level ground?" The prevalence of dyspnea was estimated from information provided by participants in the survey questionnaires to this question (Ferris, 1978; Jones, et al., 1991).

Other variables important for understanding the association between cumulative silica dust exposures and NMRD outcomes included BMI, age (36-55, 56-64, & 65-90), smoking status at the time of the study, gender, as well as commercial asbestos score. Commercial asbestos was used in the maintenance and building of the mines, but no quantitative data existed for their levels within the mines. This maximum asbestos score was a score estimation of the likelihood of commercial asbestos exposure given job description and mine location reported in questionnaires. To account for potential commercial asbestos exposure in the mines, each SEG was assigned a subjective commercial asbestos score of low, medium, or high by an experienced industrial hygienist, based on the combined probability of exposure and frequency of contact with asbestos.

Statistical Analysis

Descriptive analyses, using univariate and bivariate statistics, examined the demographic and clinical characteristics of workers who completed the questionnaire and clinic visit by level of silica exposure. A descriptive comparison was also conducted between participants in the study, "responders" and the sample population that did not respond to invites to participate, "non-responders." Exposure measures were obtained from the Mineral Resources Health Assessment Program (MRHAP) database, with cut-off of exposure measurements ending in 1982. Only completely available exposure records were utilized for this comparison. In addition, sampling information such as age, gender and distance from the facility (in minutes) were compared between the two groups. Descriptive analysis and comparisons were conducted using Chi-square, T-test, and ANOVA estimations for appropriate variables.

Poisson regression models with robust standard errors were used to estimate the relationship between cumulative silica exposure and NMRD (Spiegelman & Hertzmark, 2005; Coutinho, et al., 2008). Two cumulative exposure profiles derived were used to estimate cumulative silica exposure NMRD-risk in this study. Separate Poisson models were fit for each NMRD outcome (spirometric restriction, dyspnea, parenchymal and pleural chest x-ray abnormalities) and prevalence ratios (PR) and 95% confidence intervals (CI) were estimated from each model. All models were adjusted for age in categories (35-54, 55-64, 65-90), BMI, smoking (current, former, non-smoker), gender, and asbestos score.

Results

Of 3,310 participants randomly selected and approached for the study, a total of 1,353 current and former taconite workers responded with questionnaire information after the standard protocol of recruitment. Of these, 1,188 completed clinic testing. A group of 134 individuals responded to the questionnaire only without taking part in the clinical testing, designated as “partial responders” in the study. Table 1 shows a comparison of cumulative silica in responders and non-responders as described in methods. Available information on responders shows higher average exposure levels than in non-responders. Responders were both significantly older (66.4 vs. 58.1 yrs.) and lived closer to test sites (62.5 vs. 143.3 mins.)

Table 2 shows crude associations between covariates of interest (age, BMI, gender, smoking status and asbestos scores) and cumulative exposure estimates. A look at start year of employment with a cut-off at 1980 demonstrated a significantly lower mean cumulative silica exposure in taconite workers after 1980. These tables compare mean cumulative silica levels in participants with lung health outcomes versus participants without the outcomes.

Table 3 shows results of multivariate Poisson regression analysis of the association between cumulative silica exposure and NMRD outcomes (spirometric restriction, parenchymal abnormalities, pleural abnormalities and dyspnea). These models were adjusted for age, BMI, gender, smoking status and asbestos scores with PRs and 95% CIs shown. This model utilized onsite exposure measurements from mines operational at the time of the study as well as actual historical values from mines. These historical values were measured workplace silica levels obtained from available company industrial hygiene records of dust levels in the mines. These models showed no association between cumulative silica exposure and any NMRD outcomes assessed in this study.

Table 4 shows similar exposure-disease models as seen in Table 3. Here, cumulative silica exposure was estimated using only onsite exposure measurements from mines operational at the time of the study. These current measures were used to model and assign estimates of past exposure in the mines through the target period. We observed associations between cumulative silica exposures and spirometric restriction (PR = 1.40; 95% CI = 1.08-1.81) and between silica and parenchymal abnormality (PR = 1.30; 95% CI = 1.00-1.69).

Discussion

The mining occupation is traditionally a dusty trade. The drilling and processing of ore has been associated with significant health risk. (Haibing, et al., 2006; International Agency for Research on Cancer, 1997; Ross & Murray, 2004) A common problem in dust-exposed workers, non-malignant respiratory disease (NMRD), is a result of significant occupational exposure to particulates and dust. NMRD typically results after 15-20 years of exposure and is characterized by symptoms of shortness of breath (dyspnea), restrictive pattern on pulmonary function testing (PFT) and small rounded opacities in the upper lobes of the lungs on chest x-rays. (Balmes & Speizer, 2012) Silica is one respirable dust component commonly encountered in mining and has the most potential for toxicity with a characteristic sequelae called silicosis. (Balmes & Speizer, 2012; Farzaneh, et al., 2009) Other major forms of NMRD from mining exposure include asbestosis from asbestos exposure, and coal workers' pneumoconioses (CWP) from coal mining.

For this study, a comprehensive industrial hygiene silica exposure characterization was carried out as a key step in assessing exposure-risk for NMRD (Hwang, 2013b). In this taconite mining population, though studies have assessed mortality risk from lung cancer none have assessed NMRD risk with the benefit of this exposure assessment approach (Higgins, et al., 1983; Clark, et al., 1980). This study is the first investigation to date with detailed silica exposure assessment in combination with multiple NMRD end-points and potential covariates of exposures.

Findings from this study show that cumulative silica exposure using current-only exposure profile (Table 3) during the taconite mining process is associated with increased risk of spirometric restriction (PR- 1.40; 95% CI- 1.08-1.81). A borderline association was also observed between cumulative silica and parenchymal abnormalities on chest x-ray (PR- 1.30; 95% CI- 1.00-1.69). With the rigorous approach used for the current exposure assessment and possible errors in historical records collection and keeping, the current-only exposure profile is likely a more reliable estimate of exposures in the mines. Hence, our findings suggest that there is significant NMRD risk in this population. In addition, the two endpoints (restrictive pattern on spirometry and parenchymal abnormality on chest x-ray) have been most consistently associated with dust exposure in literature (Balmes & Speizer, 2012).

This study aimed to assess the association between cumulative silica exposure and NMRD risk in taconite mining that requires that sufficient time elapse between exposure and disease measurement. An important impression from the descriptive analyses was significant bivariate relationships between start year of employment and dyspnea, parenchymal and pleural chest x-ray abnormalities. There was also a trend of decreasing prevalence of NMRD outcomes observed in workers who began working in mining later. This apparent cohort effect likely suggests that higher exposure occurred earlier in mining. This is also likely why previous studies of this population detected low silicosis risk (Clark, et al., 1980). Another implication of this investigation, is that data collected only on employed workers may underestimate silicosis incidence (Pearce, et al., 2007). For this reason, the cross-sectional design for this study utilized employment information from both current and former miners.

Two cumulative exposure profiles were derived and used to estimate cumulative silica exposure NMRD-risk in this study. A “current-only” profile used recently measured, onsite silica levels projecting those values into the past to calculate individual cumulative silica exposure. The historical profile utilized both the current onsite exposure measures and actual historical measures obtained from records from companies and MSHA to calculate individual cumulative silica exposure. While higher average cumulative silica exposure was observed with historical data (Table 2), the use of either exposure profile resulted in varied NMRD association estimates. Potential errors inherent to actual historical exposure measures including changes to monitoring equipment and subsequent differences in equipment accuracy, inconsistent measurement rationale, lost records and sparse measurements. For these reasons, combined with the more comprehensive nature of the current, onsite measurements, these could be a better reflection of actual exposure representation in the taconite industry. The current-only approach was considered comprehensive and covered all major job categories in the industry (Minnesota Taconite Workers Health Study, 2014). However, due to the likelihood of higher exposures in the past, use of the current approach was a likely under-estimation of exposure.

Covariates assessed in this study were chosen *a priori* based on demonstrated impact on NMRD risk in similar studies of occupational dust effects (Haibing, et al., 2006; Ross & Murray, 2004). Particularly, analyses in this study demonstrated the importance of smoking and obesity on NMRD risk in silica exposure. Studies suggest an additive effect of dust exposure and smoking while body fat has been shown to mimic pleural abnormalities, as well as result in mild restrictive pattern on PFT (Lederer, et al., 2009; Santamaria, et al., 2011). Other factors that result in pleural disease like asbestiform fiber exposure may explain the increase in pleural chest x-ray abnormalities in miners with employment start date after 1980 (Table 2).

The study approach was particularly important for minimizing the healthy worker effect, which is possibly the most common source of bias in occupational studies (Pearce, et al., 2007). By studying both current and former miners, the potential bias from selection of unhealthy workers from the workforce was thought to be lessened. However, the amount of improvement is unknown. The thorough exposure assessment, combining employment histories from the questionnaires and conducting onsite exposure measurements, further minimized exposure errors. Though bias from unmeasured confounding cannot be completely eliminated, the study approach assessed for the more common sources of confounding for dust exposure risk in mining like age, gender, BMI, smoking, asbestos score. However, there is still likely differential and non-differential misclassification in the study and the possible direction of residual bias cannot be stated definitely.

With the study's cross-sectional design, disease is assessed at one point in time only. Hence it is not ideal for estimation of cause and effect. With an overall response rate of about 39.9%, response rate bias may also limit inferences from study results. It is also possible that those who are sick and unhealthy elected to participate. Preliminary analyses shown in Table 1 comparing responders to non-responders in this study suggest that distance from the test site was an important factor in participation. Other analyses comparing responders to partial responders (filled questionnaires only, but did not completely participate by having a clinical assessment), suggest comparable respiratory symptom prevalence. There is the added probability that this population was depleted by death from other chronic comorbidities with similar latencies like heart disease or COPD.

NMRD end-points used in this study, traditionally utilized in occupational studies, are sources of possible outcome misclassification. To reduce bias from outcome misclassification with spirometric restriction, only usable tests were used in these analyses as this improves validity of spirometry assessment (Odo, et al., 2013). Ascertaining chest x-ray outcomes was by at least 2 of 3 B-readers, as this has been shown to provide more accurate estimates of radiographic classification of abnormalities (Larson, et al., 2012). Dyspnea, though specific, has lower specificity for NMRD because it is more subject to response bias and is characteristic of other cardiopulmonary diseases like COPD, heart failure, asthma or other non-dust related lung diseases.

The delineation of possible mixed dust effects exploring confounding, interaction or effect modification by other dust fractions of respirable dust is the topic of additional investigation. These other fractions, such as EMP, iron dust and other non-silica dusts, have different pathophysiologic mechanisms in causing lung disease. However, silica remains the most commonly encountered pathogenic dust exposure in mining, and the focus of NMRD-risk studies.

Conclusions

This study showed the occurrence of NMRD in these taconite workers. Spirometric assessment suggested a 40% increase in NMRD association for workers given silica exposure. Silica exposure was also associated with parenchymal chest x-ray findings. These findings suggest an association between the dusty nature of work in this industry and NMRD prevalence in miners.

Table 1: Responder versus Non-Responder comparison

	Responders	Non-responders
Exposure parameters	N = 680	N = 884
Cum silica (mg/m3-yrs)	0.33 (0.29)	0.30 (0.26)
Cum non-silica (mg/m3-yrs)	1.87 (1.95)	1.70 (1.70)
EMP (emp cc-yr)	1.62 (2.13)	1.27 (1.92)
Other parameters	N = 1188	N = 907
Age (yrs.)	66.4 (11.11)	58.1 (11.99)
Gender		
Male	1084 (91.25)	732 (80.71)
Female	103 (8.67)	62 (6.84)
Unknown	1 (0.08)	113 (12.46)
Time to facility (mins)[b]	62.5 (158.6)	143.3 (351.9)

Cumulative exposures were assessed from the Mineral Resources Health Assessment Program (MRHAP) database, with cut-off in 1982, and using all historical data available.

a – “Unknown” category was excluded in calculating p-values for gender proportions between groups.

b – The facility of reference is the Virginia facility.

All values are mean (standard deviations) except for gender which is N (column percent)

Mean and frequency estimations were tested using chi-square and T-test estimations.

Table 2a: Descriptive table of measured independent variables and cumulative silica exposure

	N (%)	Cumulative silica exposure ((mg/m^3)-years)[a]			Cumulative silica exposure ((mg/m^3)-years)[b]		
Variables		Mean	Std.Dev		Mean	Std.Dev	
BMI categories[d]							
Underwt (<18.5)	2 (0.17)	0.3165	0.1261		0.8558	0.1862	
Normal (18.5-25)	102 (8.63)	0.4463	0.4582		1.0630	0.6475	
Overwt (>25-30)	441 (37.31)	0.4889	0.6036		1.1031	0.6092	
Obesity I (>30-35)	379 (32.06)	0.4694	0.6099		1.0808	0.6540	
Obesity II(>35-40)	166 (14.04)	0.4473	0.4346		1.1024	0.6619	
Obesity III (>40)	92 (7.78)	0.5121	0.5633		1.1391	0.6660	
Age categories							
1 (36-54)	340 (28.62)	0.4129	0.5634		0.8172	0.6189	
2 (55-64)	404 (34.01)	0.4881	0.5452		1.2017	0.6560	
3 (65-90)	444 (37.37)	0.5135	0.5982		1.2061	0.5668	
Smoker							
Current	141 (12.03)	0.4810	0.5225		1.0087	0.5765	
Former	591 (50.17)	0.4927	0.5685		1.1699	0.5955	
Never	445 (37.80)	0.4496	0.5863		1.0234	0.6992	
Gender							
Male	1076 (90.5)	0.4880	0.5775		1.1310	0.6339	
Female	112 (9.5)	0.3618	0.5000		0.7312	0.5517	
Commercial Asbestos score							
Low	340 (28.72)	0.5621	0.6932		0.9660	0.6680	
Medium	569 (48.06)	0.4491	0.5615		1.2009	0.6258	
High	273 (23.23)	0.4308	0.3904		1.0352	0.5727	
Start year							
Before 1980	952 (80.20)	0.5137	0.5857		1.2318	0.6170	
After 1980	235 (19.80)	0.3256	0.4840		0.5366	0.3446	

Table 2b: Descriptive table of lung disease outcomes and cumulative silica exposure

	N (%)	Cumulative silica exposure ((mg/m^3)-years)[a]			Cumulative silica exposure ((mg/m^3)-years)[b]		
Variables		Mean	Std.Dev		Mean	Std.Dev	
Spirometric restriction[e]							
Yes	76 (7.27)	0.6299	0.7970		1.1761	0.7387	
No	969 (92.73)	0.4709	0.5595		1.0912	0.6356	
Parenchymal abnormality[f]							
Yes	64 (5.41)	0.6233	0.8634		1.2445	0.6623	
No	1118 (94.59)	0.4685	0.5506		1.0873	0.6350	
Pleural abnormality[g]							
Yes	198 (16.79)	0.4827	0.5609		1.2062	0.6305	
No	981 (83.21)	0.4755	0.5756		1.0740	0.6375	
Dyspnea[h]							
Yes	135 (11.37)	0.5407	0.7215		1.0584	0.5864	
No	1052 (88.63)	0.4678	0.5496		1.0966	0.6426	

a - Cumulative silica exposures are measured in (mg/m^3)-years based on current onsite exposure measures and modeled to estimate past exposure levels.

b - Cumulative silica exposures measured in (mg/m^3)-years using historical onsite measures obtained from company records.

c – Continuous variable relationship with cumulative silica exposure.

d – For BMI category relationship with cumulative silica exposure, underweight category was omitted.

e – Defined as FVC < LLN (includes mixed ventilatory defects) using usable spirometry results (N = 1045).

f – Defined as a consensus read of 1/0 or greater by the ILO categorization.

g – Defined as consensus CXR read indicating the presence of pleural abnormalities characteristic of pneumoconiosis.

h – Shortness of breath defined as having to stop for breath when walking at own pace on level ground.

Mean estimations were tested with the student’s T-test & ANOVA estimations, while continuous associations with regression estimations

Percentages (%) are column percent values of the frequencies.

Table 3: Association between cumulative silica exposure (including actual historical data) and lung disease outcomes.

Lung Disease Outcomes (N)	Prevalence Ratios (PRs)	95% Confidence Intervals (CIs)
Spirometric Restriction (76/969) [a]	1.14	0.76 – 1.70
Parenchymal abnormalities (64/1116) [b]	0.97	0.60 – 1.57
Pleural abnormalities (198/980) [c]	1.06	0.85 – 1.31
Dyspnea (135/1052) [d]	0.79	0.58 – 1.09

N- Number of cases/non-cases.

Cumulative silica exposures are measured in (mg/m^3)-years incorporating historical onsite measures obtained from company records.

Models are adjusted for age categories, BMI, smoking, gender and maximum asbestos score.

a – Defined as FVC < LLN (includes mixed ventilatory defects) using usable spirometry results (N = 1045).

b – Defined as a consensus read of 1/0 or greater by the ILO categorization.

c – Defined as consensus CXR read indicating the presence of pleural abnormalities characteristic of pneumoconiosis.

d – Shortness of breath defined as having to stop for breath when walking at own pace on level ground.

Table 4: Association between cumulative silica exposure (current onsite-based) and lung disease outcomes.

Lung Disease Outcomes (N)	Prevalence Ratios (PRs)	95% Confidence Intervals (CIs)
Spirometric Restriction (76/969) [a]	1.40	1.08 – 1.81
Parenchymal abnormalities (64/1116) [b]	1.30	1.00 – 1.69
Pleural abnormalities (198/980) [c]	0.96	0.76 – 1.22
Dyspnea (135/1052) [d]	1.19	0.94 – 1.51

N- Number of cases/non-cases.

Cumulative silica exposures are measured in (mg/m^3)-years based on current onsite exposure measures only and modeled to estimate past exposure levels.

Models are adjusted for age categories, BMI, smoking, gender and maximum asbestos score.

a – Defined as FVC < LLN (includes mixed ventilatory defects) using usable spirometry results (N = 1045).

b – Defined as a consensus read of 1/0 or greater by the ILO categorization.

c – Defined as consensus CXR read indicating the presence of pleural abnormalities characteristic of pneumoconiosis.

d – Shortness of breath defined as having to stop for breath when walking at own pace on level ground.

CHAPTER 4:

HEALTH EFFECTS OF SILICA DUST IN THE SETTING OF MIXED DUST EXPOSURES IN TACONITE MINING

STUDY SUMMARY

Objective: The objective of this study was to explore the joint effects of silica dust, elongate mineral particles and non-silica dust on non-malignant respiratory disease risk in taconite miners.

Methods: The Respiratory Health Survey was a cross-sectional study of current and former Minnesota taconite industry miners comprised of a health assessment (medical questionnaire, chest x-ray and pulmonary function testing) in combination with an exposure assessment. Respirable dust fractions studied included silica dust, the primary exposure of interest, non-silica dust, and elongate mineral particles. Prevalence ratios were calculated for health outcomes associated with silica and other dusts individually and with silica within exposure specific strata. Finally, additive and multiplicative exposure interactions were estimated adjusting for age categories, BMI, gender, smoking and possible commercial asbestos exposure.

Results: The prevalence of spirometry determined restriction was 7.2%. Chest x-ray parenchymal abnormalities occurred in 5.4% of participants. Silica exposure was significantly associated with Restrictive Ventilatory Defect (RVD) prevalence (PR = 1.40, 95% CI= 1.08 – 1.81) and prevalence of parenchymal changes on chest x-ray (PR = 1.30, 95% CI= 1.00 – 1.69). Assessments for silica-EMP and silica-non-silica additive and multiplicative interaction were not statistically significant.

Conclusions: These analyses suggest that the presence of either elongate mineral particles or non-silica dust does not significantly modify the relationship between silica exposure in taconite mining and non-malignant respiratory disease on either the additive or the multiplicative scales at levels experienced in this work setting.

Introduction

Lung health is an important public health goal in mining. Respirable dusts generated during mining come in different sizes, shapes and mineral compositions. Since these dusts have variable compositions and different exposure potential with varying mining processes, the health risks also vary (Banerjee, et al., 2006). Respirable dusts generated from the Minnesota taconite mining process include respirable silica (usually quartz), elongate mineral particles (EMP) and other non-silica respirable dusts like iron oxide dust (Hwang, 2013b). Respirable silica is usually the major component of total respirable dust generated in mining and has typical chest x-ray and spirometric patterns. EMPs refer to minerals with aspect (length to width) ratio of 3:1 or greater and may be classified as amphibole or non-amphibole (NIOSH, 2011). Amphibole EMPs may be further classified as asbestiform or non-asbestiform. In this taconite mining industry, non-asbestiform EMPs and cleavage fragments were predominant. Non-silica dusts constitute the other “impurities” found while mining for iron ore and these non-silica dust may contain iron oxides. Other impurities found in iron mining include clay minerals like alumina, lime, magnesium and zinc (Banerjee, et al., 2006). Exposure to some of these dust impurities may potentiate acute or chronic lung scarring with accompanying morbidity and mortality.

Exposure of miners to respirable dusts in the workplace results in nonmalignant respiratory diseases (NMRD) (Driscoll, et al., 2005). In the workplace, NMRD describes the lung disease sequelae of exposure to airborne agents including particulates, chemical agents like chlorofluorocarbons, alcohols or their salts and fumes, and biological agents (Driscoll, et al., 2005). These exposures occur in different stages of processing of ores in mining like gold, iron, and copper, as well as various stages of manufacturing and building/construction. Of possible NMRDs encountered in the workplace, pneumoconioses is a concerning and preventable type. Of the workplace exposures, silica has been most associated with inflammation and damage of the lung parenchyma causing, most notably, silicosis (Antão, et al., 2007; Balmes & Speizer, 2012; Fanning, 2004; Glenn, 2005). Silicosis is a lung disease caused by the inhalation and deposition of respirable silica particles (i.e., particles less than 10 micrometers in diameter) (IARC, 1987). Silicosis and associated restrictive lung disease (RLD) are well-established consequences of prolonged, intense exposures to respirable crystalline silica (Checkoway, et al., 1997). An important factor in the development of silicosis is the “dose” of silica-containing dust in the workplace- that is, the product of the concentration of respirable silica in the workplace air, the duration of exposure, and the percentage of respirable silica in the total dust (US Department of Health and Human Services, 2002).

Mixed dust effects may exist due to the presence of other constituents or “impurities” other than respirable silica in mining (Banerjee, et al., 2006; Leung, et al., 2012; Love, et al., 1997; Chen, et al., 2005). These effects may result in increased inflammatory and damaging effects of respirable silica on the lung parenchyma, specifically, silicosis (Chen, et al., 2006; Ng & Chan, 1992). Potential confounding of silica-NMRD relationships by concurrent exposure to known or suspected agents is a concern in mining (Checkoway, et al., 1997). Possible synergistic effects of silica and asbestos on lung cancer has been suggested in other studies (Checkoway, et al., 1997). Given the higher prevalence of NMRD in mining, the question arises as to the role of the other constituents of respirable dust generated during taconite ore mining and processing (Driscoll, et al., 2005; Antão, et al., 2007; Balmes & Speizer, 2012; US Department of Health and Human Services, 2002).

The objective of this study was to explore the individual and joint effects of cumulative silica, cumulative EMP and cumulative non-silica dust on the NMRD risk in taconite miners.

Methods

Approval was obtained annually from the University of Minnesota Institutional Review Board (IRB) and from the individuals who participated in the study.

Study population and sampling process

This study was a cross-sectional assessment of current and former taconite industry workers. It was aimed at determining the relationship between taconite mining dust exposure and NMRD. The survey included a detailed self-administered questionnaire, which determined health, smoking, military and occupational histories, along with in-clinic physiologic pulmonary function tests (PFT) and chest x-ray evaluation on all participants. The participants in the RHS were sampled from an employment roster of 16,990 individuals comprising current and former taconite miners across the iron range of northeastern Minnesota. From this group, 3310 study participants were invited, after selection by stratified random sampling based on age, with oversampling of older individuals to increase the chances of identifying dust-related lung disease. A sample size of 1,200 workers was determined to be adequate for detection of respiratory symptoms in exposed versus unexposed workers.

Clinic testing

Questionnaires were developed based on standardized questionnaires of the American Thoracic Society (Ferris, 1978), the St. George's Respiratory Questionnaire (Jones, et al., 1991), and the University of California, San Diego (UCSD) Shortness-of-Breath Questionnaire (Eakin, et al., 1994). Questionnaires were self-administered and filled in advance of the two-hour clinical evaluation. It contained medical, occupational, military and smoking history. It also contained a list of common respiratory symptoms (American Thoracic Society, 1995). Incomplete or missing questionnaire information was addressed with the use of experienced interviewers at the time of clinical testing.

Lung function was assessed using screening spirometry. A reduction in FVC, below the lower limit of normal (LLN) for age, sex, race and height (Hankinson, et al., 1999), indicated abnormal lung volume and lung restriction (Restrictive Ventilatory Defect-RVD). Other spirometric outcomes determined included obstruction, defined as a reduction in FEV_1/FVC ratio below the LLN, and mixed disease, defined as combined restrictive and obstructive lung function patterns (Hankinson, et al., 1999; Odo, et al., 2013).

The participants underwent standard postero-anterior (PA) chest X-ray according to the recommendations of the International Labor Organization (ILO) for the complete classification of films (International Labour Office (ILO), 2002). The quality of each chest X-ray was evaluated at the clinic by a radiological technician and poor quality films were immediately repeated. The films were initially read by a clinical radiologist to check for health conditions of immediate concern. Each film was then read blindly by two independent NIOSH-certified B-readers for parenchymal and pleural changes and other radiographic features as specified by the ILO framework (International Labour Office (ILO), 2002). Parenchymal abnormalities, described as profusion or opacity scores greater than 1/0, and pleural abnormalities (e.g. plaques, thickening), are characteristic interpretations that are indicative of interstitial/restrictive lung disease (ILD/RLD) changes (International Labour Office (ILO), 2002; Clark, et al., 1980; Farzaneh, et al., 2009). Where there was disagreement between the two readers on the interpretation of the chest X-rays, the disputed films were sent to a third B-reader for arbitration.

The outcomes utilized in this study were restrictive ventilatory defect (RVD) measured by spirometry and applying established rules for usable tests (Odo, et al., 2013), and chest x-ray reports of parenchymal changes (International Labour Office (ILO), 2002). Covariates assessed for multivariate modeling included BMI, age categories (36-55, 56-64, & 65-90), smoking status at the time of the study (current, former or non-smoker), gender and maximum asbestos score. This maximum asbestos score was a score estimation of the likelihood of commercial asbestos exposure given job description and mine location reported in questionnaires. Commercial asbestos was used in the maintenance and building of the mining facilities, but no quantitative data existed for their levels within the facilities. To account for potential commercial asbestos exposure in the mines, each SEG was assigned a commercial asbestos score of low, medium, or high. This was done in a blinded fashion, by an experienced industrial hygienist, based on the combined likelihood and frequency of asbestos exposure and verified by an additional industrial hygienist.

Exposure assessment

The exposure assessment is described elsewhere and briefly here (Hwang, 2013b; Hwang, et al., 2013a; Hwang, et al., 2014). Work information was abstracted from study questionnaires and mapped in a standardized fashion for all participants using job titles and descriptions of previous work and dust exposures in the taconite industry to create 28 similar exposure groups (SEGs) (Hwang, 2013b; Sheehy & McJilton, 1987). These SEGs and departments of employment were analyzed for each work entry experience of each participant (Hwang, et al., 2013a). Respirable silica was analyzed using the NIOSH 7500 analytic method. Current exposure measures were ascertained for all current taconite mines operating from 2010 to 2011. Historical exposures to silica and EMPs were obtained from all active companies' records and records from Mining Safety and Health Administration (MSHA) monitoring (Minnesota Taconite Workers Health Study, 2014). Using regression techniques to account for gaps in historical monitoring, the combination of current measurements and historical estimates allowed the creation of a job-exposure matrix (JEM). This matrix consisted of estimated annual exposures to all three exposures (silica, EMP, non-silica dust), specific for each SEG. A person's work history, reported in the questionnaires, was used to determine the amount of time worked in a specific SEG. From this, respective cumulative exposures were summed up for all three exposures for each individual in the study. The product of employment years and mine/job/SEG-specific exposure level was determined as cumulative silica exposure for each participant. Where work history information provided by participant was unclear on specific job worked, the average exposure level for the department was used to calculate cumulative exposure. In those instances where department information was missing, the average cumulative exposure for the plant was used.

Statistical analysis

Prevalence ratios (PR) for lung disease were estimated to determine the individual associations of silica, EMP and non-silica dust with lung disease outcomes (spirometric restriction and parenchymal abnormalities). Using dichotomous exposures (high versus low levels by the median cumulative exposure), PRs for silica-related NMRD risk were estimated within dichotomous strata of EMP, and non-silica dust. Relative excess risk due to interaction (RERI), attributable proportions (AP) and synergy index (SI) with 95% CIs, were estimated to assess interaction on the additive scale (Knol & VanderWeele, 2012). For measures of additive interaction (RERI, AP and SI), 95% CIs were estimated using the delta method (Knol & VanderWeele, 2012). These measures assess if two or more risk factors act together (interact) in causing an outcome of interest, also called joint effects (Richardson & Kaufman, 2009). These measures provide useful metrics for assessing departure from additivity and are useful for different study designs (Richardson & Kaufman, 2009; de Mutsert, et al., 2009). On the multiplicative scale, one model each was used for silica/EMP interaction, and for silica/non-silica dust interaction including product terms for each to assess for multiplicative interaction. All multivariate analyses were conducted using Poisson regression modeling with robust variance adjusted for age categories, BMI, gender, smoking and commercial asbestos exposure (Spiegelman & Hertzmark, 2005; Coutinho, et al., 2008). Standard errors for parameter estimates were included to control for possible violation of the distribution assumption in the modeling approach.

Results

Based on exposure assessment, the mean percentage of silica was approximately 14% of total dust across the mines (Hwang, 2013b). Many exposure values were assessed in the different SEGs that comprise the departments. Table 1 present the highest geometric mean measured SEG exposure value in each department. Here, all mines had some SEGs above the ACGIH TLV for respirable silica (0.025 mg/m^3) (Hwang, et al., 2013a). The taconite EMPs were predominantly non-amphibole EMPs as concentrations of amphibole EMPs were well controlled across the mines and well below the NIOSH REL of 0.1 particles/cm^3 (Hwang, et al., 2013a).

7.2% of the population had spirometric restriction and 5.4% parenchymal abnormalities with B-reader consensus. The PR (95% CI) of silica-spirometric restriction association was 1.41 (1.09-1.81) and for silica-parenchymal abnormality, 1.30 (1.00-1.69). Table 2 also presents the non-silica dust-NMRD and EMP-NMRD associations.

Table 3 presents the prevalence ratios (PR) for interaction terms for silica/non-silica dust and silica/EMP for spirometric restriction and parenchymal abnormalities. These estimates show non-significant multiplicative interactions in the models.

In Table 4, silica-NMRD associations were stratified by dichotomous levels of EMP and non-silica dust. At high (above median) non-silica dust exposure levels, silica-spirometric restriction association was PR = 1.43 (1.10-1.86) and silica-parenchymal abnormality, PR = 1.42 (1.05-1.92). At high (above median) EMP exposure, silica-spirometric restriction association was PR = 1.59 (1.23-2.05).

RERI, AP and SI estimates are shown in Table 5 and presented non-significant statistical relationships.

Discussion

Historically, studies looking into the dust effects in mining have assessed one dust component. For example, asbestiform EMP have been shown to increase lung disease risk resulting in both pleural disease and parenchymal lung disease (Driscoll, et al., 2005; NIOSH, 2011). Silica has been associated with silicosis as well as lung cancer (Antão, et al., 2007; Checkoway, et al., 1997; Fanning, 2004; Finkelstein, 2000; Leung, et al., 2012; IARC, 1997). However, these different dusts, including non-silica dust, are encountered and potentially inhaled simultaneously in the mining workplace. Non-silica dust can contain a variety of minerals depending on the geology of the rock being mined. It includes iron oxide dust that is a product of the taconite mining process and has generated increased interest in scientific studies (Banerjee, et al., 2006; Cullen, et al., 1997). Depending on the type of mineral being mined (coal, granite, zinc, beryllium, diamonds, and iron), other components of the mineralogy of the geological structure may play a role in compromised respiratory function and lung diseases seen after exposure (Banerjee, et al., 2006).

Given the real-life scenario of these different impurities being encountered simultaneously in the workplace, this assessment of interaction is important to comprehensively assess NMRD risk in this workplace. Some important factors include potentiation of silica effects by non-silica dusts or EMP, as well as different silica related NMRD-risk at potential high levels of non-silica or EMP exposures not observed in this study. This study is the first attempt in this industry at shedding light on the possible joint effects that may exist between EMPs or non-silica dusts and silica.

Silica-spirometric restriction association at high EMP level was significant at PR-1.59; 95% CI: 1.23-2.05. However, further exploration of additive and multiplicative interactions showed no significant joints effects by either non-silica dust or EMP (Tables 3, 4, 5). For the association of silica with lung disease, this study suggests that the silica-NMRD association is driven primarily by silica exposure, at least at exposure levels encountered in this workplace. Exposure assessment in this study overall showed low EMP levels of mainly non-asbestiform EMP form. Based on recommended exposure limits (REL) for EMP and threshold limit values (TLV) for respirable dust and respirable silica exposures set by NIOSH and ACGIH respectively, silica exposures were the highest dust exposure in the taconite industry (see Table 1).

As part of an attempt at a comprehensive exposure assessment in taconite mining, a number of different dust components were identified and measured (Hwang, 2013b; Hwang, et al., 2013a; Hwang, et al., 2014). This study tested the possible association these exposures, singly and combined, with two outcome measure, spirometric restriction and parenchymal abnormality, both a potential manifestation of dust exposure. Silica exposures may result in parenchymal changes on chest x-ray characteristic of interstitial fibrosis (Balmes & Speizer, 2012; International Labour Office (ILO), 2002). It may also result in impaired physiologic lung function on pulmonary function testing (PFT) when significant numbers of breathing units (alveoli) are affected (Balmes & Speizer, 2012; Hankinson, et al., 1999; Carta, et al., 1996; Humerfelt, et al., 1998; Ng & Chan, 1992). This results in restrictive ventilatory defect on PFT.

Studies have suggested and described synergistic effects between EMP and silica dust in causing cancer and parenchymal disease respectively (Chen, et al., 2005; Chen, et al., 2006; Harrison, et al., 2005). There is a sparse literature reporting on the possible combined effects of different dust components specifically of mining processes causing

NMRDs. In public health, studies of particulate inhalation have shown that different particles, inhaled concurrently, can result in combined effects of the individual disease risk of the each particle type (Chen, et al., 2006). This combination of effects may be additive or multiplicative. Additive effects of concurrent exposures have been described as more useful for intervention purposes (Knol & VanderWeele, 2012; VanderWeele, 2009; VanderWeele & Robins, 2007). Techniques have been described to identify the presence of these joint, interaction or effect measure modification effects where they are present (Knol & VanderWeele, 2012; VanderWeele, 2009; VanderWeele & Robins, 2007). Examples of identified occupational exposure-related interactions in public health include asbestos and smoking, as well as silica and smoking (Checkoway, et al., 1997; Cohen, et al., 1979; Hnizdo, et al., 1990).

While some rock formations may have high silica dust components and lower EMP components, some may have the reverse proportion with varying composition of other dust components like iron oxide, clay, magnesium oxides and other particulate matter. Studies suggest that in industries like the taconite industry, where iron ore is the mineral of interest, lung health risk from prolonged exposure/inhalation of iron oxide dust may be significant (Banerjee, et al., 2006). However, after exposure assessment, levels of EMP were shown to be largely low and below the NIOSH recommended exposure threshold levels (REL) of 0.1 particles/cm^3 (Table 1) (Hwang, et al., 2013a; Hwang, et al., 2014). This NIOSH REL is intended for regulated asbestiform EMP and for their non-asbestiform EMP analogs. The EMPs detected in this study comprised mainly the non-asbestiform type that has been shown to pose relatively lower lung disease risk than the asbestiform EMP (Gamble & Gibbs, 2008). Non-silica respirable dust was also shown to comprise low levels in total respirable dust, with the iron oxide particles, therefore, at low levels as well (Hwang, 2013b; Hwang, et al., 2013a). Silica, on the other hand, had more excursions over the permissible exposure limit. The lack of synergy could be related to these relative levels of air contaminants.

Study pros and cons

The cross-sectional study design limits the ability of this study to make causal inferences from these results. This is because the outcomes are prevalent outcomes, assessed at one point in time only. To reduce the impact of these limitations, the design improved on outcome determination by applying usability criteria for spirometry outcomes (Odo, et al., 2013), and using the best two of three B-reader assessments to determine chest x-ray outcomes. Also inherent in the study design, length of time from exposure to developing disease presents a possible source of misclassification of disease as well as posing questions on the temporality of NMRD-risk estimated in the study results. This length of time of employment was incorporated in estimating cumulative exposures and considered adjusted for when determining possible interaction between exposures.

Table 4 shows increased PRs in high exposure strata of EMPs and non-silica dust from baseline (Table 2) with the most significant being silica-spirometric restriction association at high EMP level. However, further analysis using metrics for assessing interaction (RERI, AP, and SI) in Table 5 shows non-significant departures from additivity. Given that cumulative exposure is a continuous variable and categorization is arbitrary (here based on the median), results in Table 5 showing non-additivity were considered more reliable. With three interaction assessments (RERI, AP and SI) demonstrating non-significant departure from additivity, a stronger assertion of non-significant departure from additivity is reasonable. These results are consistent with other occupational studies on the strength of association and are therefore plausible and useful as sources of inference and additional evidence as to the true relationships of dust exposure and NMRD prevalence.

The study approach was important for minimizing the healthy worker effect, which is a common source of bias in occupational studies (Pearce, et al., 2007). With an overall response rate of about 40.8%, response rate bias may also limit inferences from study results. By studying both current and former miners, the potential bias from selection of unhealthy workers from the workforce as well as non-response was thought to be lessened. It is possible that those who are sick and unhealthy elected to participate.

Preliminary analyses suggest that non-responders had twice average travel time to clinic than participants, however, prevalence of symptoms in participants did not differ significantly from partial responders. There is the added possibility that this population was depleted by death from other chronic comorbidities with similar latencies like heart disease or COPD.

The detailed exposure assessment, combining employment histories from the questionnaires and conducting onsite exposure measurements, further minimized exposure errors. This exposure assessment consisted of over 1,500 onsite measures, along with historical data, and was the first to be incorporated in epidemiologic studies of this population. Though bias from unmeasured confounding cannot be completely eliminated, the study approach assessed for the more common sources of confounding for dust exposure risk in mining like age, gender, BMI, smoking, asbestos score. It is still possible that differential or non-differential misclassification exists in the study, but the direction of this potential residual bias cannot be stated definitely. In assessing non-silica dust, the possible minerals comprising this component were not assessed individually. These limitations may also present a source of unmeasured confounding in the form of uncharacterized exposures.

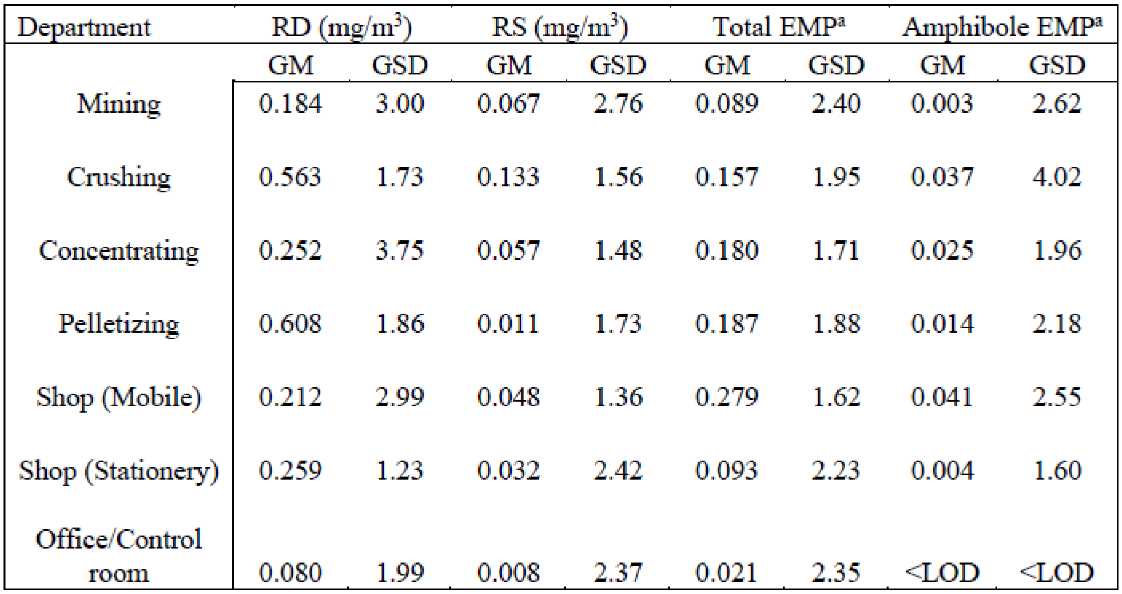
NMRD end-points used in this study, traditionally utilized in occupational studies, are sources of possible outcome misclassification. To reduce bias from outcome misclassification with spirometric restriction, only usable tests were used in these analyses as this improves validity of spirometry assessment (Odo, et al., 2013). Ascertaining chest x-ray outcomes was by at least 2 of 3 B-readers, as this has been shown to provide more accurate estimates of radiographic classification of abnormalities (Larson, et al., 2012). A strong correlation has also been demonstrated between spirometric restriction and parenchymal abnormalities on chest x-ray (Larson, et al., 2012). However, there may be an underestimation of the prevalence of parenchymal abnormality. Study findings comparing CT scans and chest x-ray studies of lung disease have demonstrated that CTs detect 4-5 times the number of abnormalities as chest x-rays (Miller, et al., 2013; Kazerooni, 2001). As lung function decline typically follows structural changes from disease, the true disease prevalence is likely higher than either spirometry or chest x-ray findings suggest in this study. It is also important to note that chest x-ray findings show interstitial changes characteristic of interstitial lung disease (ILD). ILD is correlated with RLD and not all ILD, like NMRD, is from mining dust exposure. Considering these limitations, true associations between exposure and disease are likely stronger than detected in these analyses.

Conclusions

These analyses suggest that the presence of EMPs and non-silica respirable dust do not seem to significantly alter the relationship between silica exposure in taconite mining and NMRD, at least at levels described in this industry. The minimization of NMRD in this industry could be enhanced by efforts focused at reducing silica exposure.

Tables

Table 1: Summary statistics of silica, respirable dust, total and amphibole EMPs per department measured and aggregated from all mines



Department	RD (mg/m^3)		RS (mg/m^3)		Total EMP[a]		Amphibole EMP[a]	
	GM	GSD	GM	GSD	GM	GSD	GM	GSD
Mining	0.184	3.00	0.067	2.76	0.089	2.40	0.003	2.62
Crushing	0.563	1.73	0.133	1.56	0.157	1.95	0.037	4.02
Concentrating	0.252	3.75	0.057	1.48	0.180	1.71	0.025	1.96
Pelletizing	0.608	1.86	0.011	1.73	0.187	1.88	0.014	2.18
Shop (Mobile)	0.212	2.99	0.048	1.36	0.279	1.62	0.041	2.55
Shop (Stationery)	0.259	1.23	0.032	2.42	0.093	2.23	0.004	1.60
Office/Control room	0.080	1.99	0.008	2.37	0.021	2.35	<LOD	<LOD

*adapted from (Hwang, 2013b)

a – unit is particles/cm^3

RD – Respirable dust

RS – Respirable silica

EMP – Elongate mineral particles

GM – Geometric mean exposures

GSD – Geometric standard deviation

NIOSH REL for EMP = 0.1 particles/cm^3

ACGIH TLV for RD = 0.025 mg/m^3 TWA

ACGIH TLV for RS = 3 mg/m^3 TWA

Table 2: Associations between respirable dust fractions and Lung disease outcomes

Spirometric Restriction		
Exposure	PR	95% C.I.
Silica	1.41	1.09-1.81
Non-silica	0.99	0.96-1.01
EMP	1.01	0.93-1.09

Parenchymal abnormalities		
Exposure	PR	95% C.I.
Silica	1.30	1.00-1.69
Non-silica	1.02	1.00-1.04
EMP	0.98	0.91-1.06

Cumulative dust exposures (silica, non-silica dust) are measured in (mg/m^3)-years based on current onsite exposure measures and modeled to estimate past exposure levels.

Cumulative elongate mineral particles (EMP) exposure are measured in (particles/m^3)-years based on current onsite exposure measures and modeled to estimate past exposure levels.

Models are adjusted for age categories, BMI, smoking, gender and maximum asbestos score.

Spirometric restriction – Defined as FVC < LLN (includes mixed ventilatory defects) using usable spirometry results (N = 1045).

Parenchymal abnormalities – Defined as a consensus read of 1/0 or greater by the ILO categorization.

Table 3: Assessing interaction using multiplicative terms of continuous exposure

Spirometric Restriction		
Interaction Exposure	PR	95% CI
Silica*non-silica dust	1.02	0.99-1.04
Silica*EMP	1.04	0.98-1.11

Parenchymal abnormalities		
Interaction Exposure	PR	95% CI
Silica*non-silica dust	1.00	0.96-1.03
Silica*EMP	1.04	0.96-1.12

Cumulative dust exposures (silica, non-silica dust) are measured in (mg/m^3)-years based on current onsite exposure measures and modeled to estimate past exposure levels.

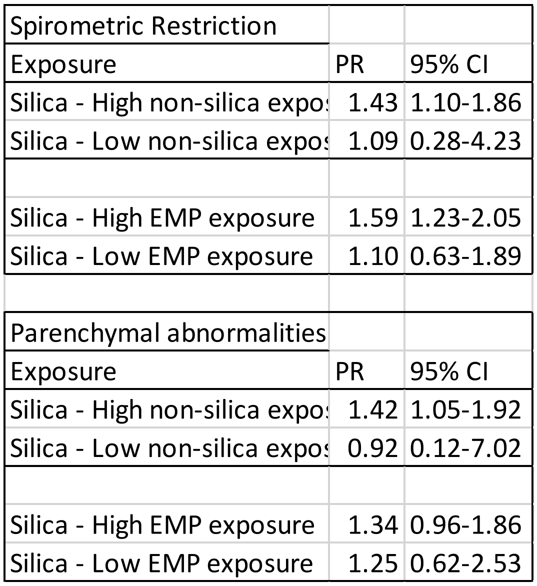
Cumulative elongate mineral particles (EMP) exposure are measured in (particles/m^3)-years based on current onsite exposure measures and modeled to estimate past exposure levels.

Models are adjusted for age categories, BMI, smoking, gender and maximum asbestos score.

Spirometric restriction – Defined as FVC < LLN (includes mixed ventilatory defects) using usable spirometry results (N = 1045).

Parenchymal abnormalities – Defined as a consensus read of 1/0 or greater by the ILO categorization.

Table 4: Silica-parenchymal/spirometric restriction associations in strata of EMP/non-silica dust



Spirometric Restriction		
Exposure	PR	95% CI
Silica - High non-silica expo	1.43	1.10-1.86
Silica - Low non-silica expo	1.09	0.28-4.23
Silica - High EMP exposure	1.59	1.23-2.05
Silica - Low EMP exposure	1.10	0.63-1.89

Parenchymal abnormalities		
Exposure	PR	95% CI
Silica - High non-silica expo	1.42	1.05-1.92
Silica - Low non-silica expo	0.92	0.12-7.02
Silica - High EMP exposure	1.34	0.96-1.86
Silica - Low EMP exposure	1.25	0.62-2.53

Cumulative dust exposures (silica, non-silica dust) are measured in (mg/m^3)-years based on current onsite exposure measures and modeled to estimate past exposure levels.

Cumulative elongate mineral particles (EMP) exposure are measured in (particles/m^3)-years based on current onsite exposure measures and modeled to estimate past exposure levels.

Models are adjusted for age categories, BMI, smoking, gender and maximum asbestos score.

Spirometric restriction – Defined as FVC < LLN (includes mixed ventilatory defects) using usable spirometry results (N = 1045).

Parenchymal abnormalities – Defined as a consensus read of 1/0 or greater by the ILO categorization.

High versus low exposures are determined with a cut-off of median cumulative exposure.

Table 5: Assessing dust fraction interactions using continuous exposure measures

Spirometric Restriction		Parenchymal abnormality	
Silica-Non-silica dust		Silica- Non-silica dust	
RERI	95% CI	RERI	95% CI
0.01	(-0.02, 0.05)	0.001	(-0.03, 0.03)
AP	95% CI	AP	95% CI
0.01	(-0.03, 0.05)	0.001	(-0.02, 0.02)
SI	95% CI	SI	95% CI
1.10	(0.55, 2.21)	1.00	(0.92, 1.09)
Silica-EMP		Silica-EMP	
RERI	95% CI	RERI	95% CI
0.04	(-0.01, 0.10)	0.03	(-0.05, 0.12)
AP	95% CI	AP	95% CI
0.04	(-0.03, 0.10)	0.03	(-0.06, 0.12)
SI	95% CI	SI	95% CI
1.35	(0.30, 6.06)	1.79	(0.001, 2560.97)

Key	Description	Null value
RERI	Relative Excess Risk due to Interaction	0
AP	Attributable Proportion due to interaction	0
SI	Synergy Index	1

Cumulative dust exposures (silica, non-silica dust) are measured in (mg/m^3)-years based on current onsite exposure measures and modeled to estimate past exposure levels.

Cumulative elongate mineral particles (EMP) exposure are measured in (particles/m^3)-years based on current onsite exposure measures and modeled to estimate past exposure levels.

Models are adjusted for age categories, BMI, smoking, gender and maximum asbestos score.

Spirometric restriction – Defined as FVC < LLN (includes mixed ventilatory defects) using usable spirometry results (N = 1045).

Parenchymal abnormalities – Defined as a consensus read of 1/0 or greater by the ILO categorization.

Overall Future Directions

A number of possible ideas for further research and information gathering exist. This study could form the foundation on which future studies will look more definitively at causes of non-malignant RLD. This is because there is little prior research on the occurrence of non-malignant RLD and its association with dust exposures in taconite mining occupations. This can also set the framework for modification of previous studies of exposure-specific relationships in mining and other occupations with dust exposures.

These further studies may include gold-standard tests like high-resolution computed tomography (HRCT) and body plethysmography. This will enable the comparison of these tests of restrictive disease with the commonly available assessments used in screening (lung function, chest x-rays and respiratory symptoms). This is particularly needed in populations like the taconite mining industry with occupational exposure to respirable particles.

Longitudinal follow-up of this cohort using these same screening tools can provide more knowledge about the reliability of these tools over time. In this suggested approach, trends in both individual performance and test reliability can be identified and better understood.

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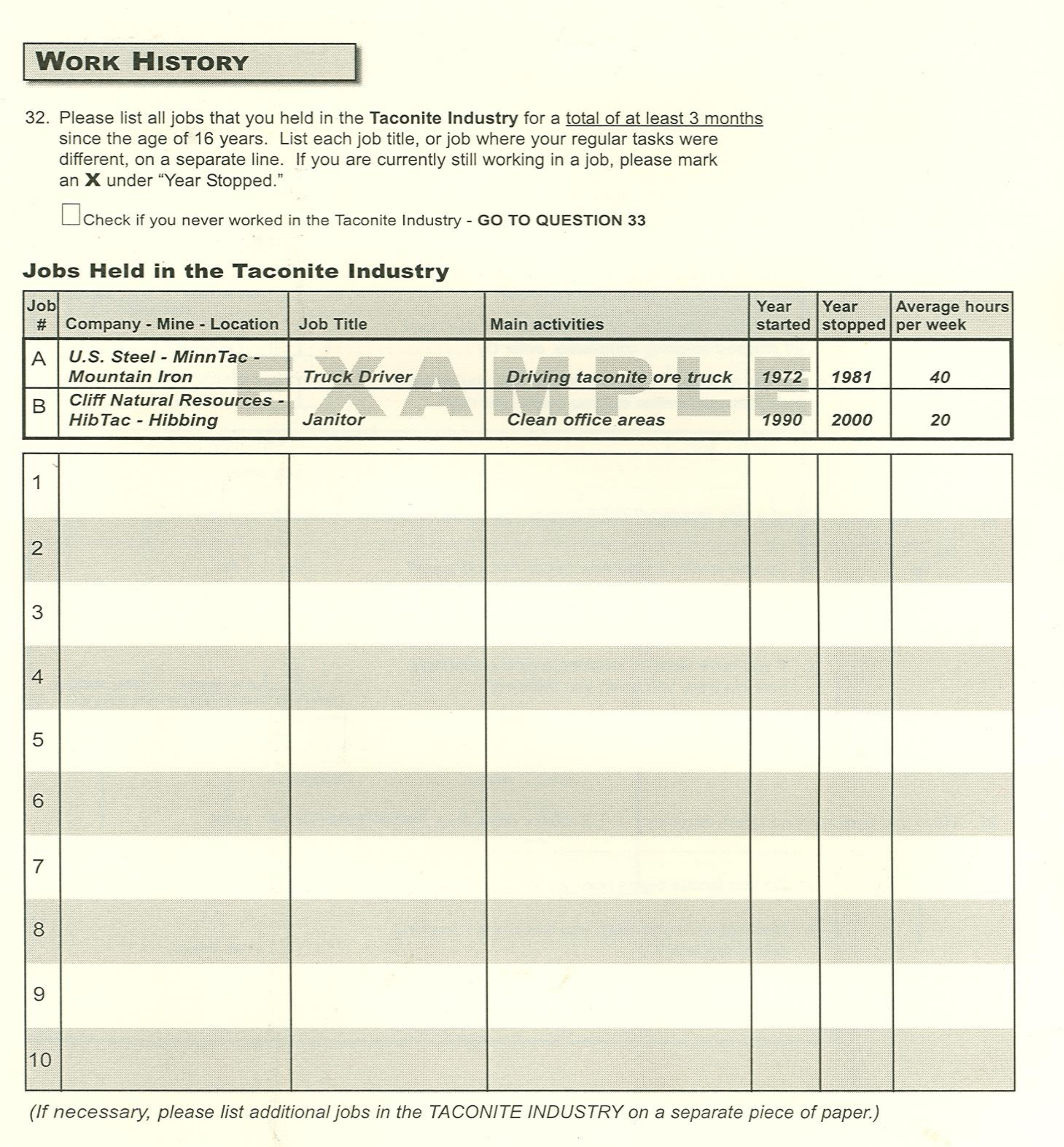
APPENDICES

Appendix A: Survey Questionnaire- Work History Section.



Work History

32. Please list all jobs that you held in the **Taconite Industry** for a total of at least 3 months since the age of 16 years. List each job title, or job where your regular tasks were different, on a separate line. If you are currently still working in a job, please mark an **X** under "Year Stopped."

☐ Check if you never worked in the Taconite Industry - **GO TO QUESTION 33**

Jobs Held in the Taconite Industry

EXAMPLE

Job #	Company - Mine - Location	Job Title	Main activities	Year started	Year stopped	Average hours per week
A	*U.S. Steel - MinnTac - Mountain Iron*	*Truck Driver*	*Driving taconite ore truck*	*1972*	*1981*	*40*
B	*Cliff Natural Resources - HibTac - Hibbing*	*Janitor*	*Clean office areas*	*1990*	*2000*	*20*

1						
2						
3						
4						
5						
6						
7						
8						
9						
10						

(If necessary, please list additional jobs in the TACONITE INDUSTRY on a separate piece of paper.)

Appendix C: Similar Exposure Groups Exposure Assessment for Taconite Study

Department	SEGs	Job titles
Mining (N=4)	Mining operator 1	Backhoe Operator
		Brakeman
		Cage/equipment tender
		Load haul dump
		Driller
		Excavator
		Bull/powder gang
		Dump man
		Churn Drill Operator
		Grader Operator
		Jet drill operator
		Helper
		Front end loader operator
		Blaster
		Jet piercing change operator
		Loader
		Pitman
		Rotary Drill Helper
		Bank Trimmer
	Mining operator 2	Equipment operator
		Bulldozer operator
		Scraper operator

		Shuttle car operator
		Washer operator
		Tail truck driver
		Crane car operator
		Forklift operator
		Tractor operator
		Rubber bull operator
		Truck driver
		Shovel engineer
		Shovel operator
	Basin operator	Basin operator
	Rail road	Switchboard operator
		Yard engine operator
		Flagman
		Transfer house
		Rail road crusher maintenance
		Locomotive operator
Crushing (N=3)	Crusher operator	Crusher operator
		Bin man
		Primary/Secondary attendant
		Crusher screen operator
		Mill Supply Conveyor Operator
		Pan feeder operator
		Turn bin attendant
		Feeder man

		Tunnel man
		Down/up attendant
		Dry screen plant operator
		Finisher attendant
		Separator operator
		Dry Cobb
	Crusher maintenance	Car dump
		Crusher welder
		Ventilation crew
		Crusher sweeper
		Skip dumper
		Material car unloader
		Crusher maintenance
	Operating technician	Chainman
		Conveyor attendant
		Belt Man
Concentrating (N=2)	Concentrator operator	Grinding mill operator
		Rod charger
		Mill man
		Deck man
		Pump attendant
		Rod mill operator
		Ball charger
		Screen/scalper operator
		Balling mill operator
		Concentrator

		Grinding attendant
		Plant operator
		Coal Mill Operator
	Concentrator maintenance	Concentrator maintenance
		Millwright
		Hybrid
		Concentrator service attendant
Pelletizing (N=5)	Pelletizing operator	Agglomerator operator
		Rover
		Slurry mix operator
		PP helper
		Filter bag renewer
		Chip regrind attendant
		Bagging operator
		Green feed attendant
		Filter operator
	Pelletizing maintenance	Pelletizer pallet repair
		Hydrating plant operator
		Hybrid
		Lube maintenance
		Pelletizing maintenance
	Balling drum operator	Balling attendant
		Balling Drum Operator

	Furnace operator	Ashman
		Furnace Operator
		Burner operator
		Kiln operator
		Metallurgical clerk
	Dock man	Material handler operator
		Coal unloader
		Yards/Docks
		Car shake out operator
		Labor matt handler
		Pellet load out
		Bentonite unloader
		Dock man
Shop mobile (N=8)	Carpenter	Carpenter
		Cement/concrete man
		Mason
		Disc Sweeper Operator
	Electrician	Electrician
		Pit electrician
		Plant electrician
		Floor man
	Pipefitter/Plumber	Pipefitter
		Plumber
	Maintenance technician	Mechanic
		Millwright

		Painter
		Machinist
		Instrument man
		Engineer
		Fuel station attendant
		Rougher man
		Welderman
	Repairman	Brickman
		Building repair maintenance
		Repairman
		Iron worker
		Instrument Repairman
		Lamp maintenance
		Tool room attendant
	Lubricate technician	Lubricate technician
		Shovel oiler
		Primary mill oiler
		Oil house attendant
	Boiler technician	Boiler Attendant
		Boiler Maker
	Supervisor	Foreman
		Shift manager
		Team leader
		Fire chief
		First Aid Man
		Safety engineer

		Maintenance coordinator
		Maintenance supervisor
Shop stationary (N=4)	Warehouse technician	Warehouse technician
	Lab analyst	Analyst
		Sample grinder
		Dust/Plant sampler
		Utility person
		Cost analyst
		Geologist
		Lab technician
	Auto mechanic	Auto mechanic
		Motor man
		Truck shop operator
		Tire man
		Equipment cleaner
		Car dropper
	Janitor	Light Fixture Cleaner
		Cleanup attendant
		Janitor
		Guest Housekeeper
		Timekeeper
Office/Control room (N=2)	Office staff	Account
		Airman
		Human resources administrator
		Biller

		Clerk/Schedule planner
		IT administrator
		Draftsman
		Messenger
		Counterman
	Control room operator	Computer programmer
		Control room operator
		Area control operator
		Programmer
Total 7 Departments	**Total 28 SEGs**	**Total 181 Job Titles**