FINAL REPORT TO THE LEGISLATURE
MINNESOTA TACONITE WORKERS HEALTH STUDY

DATE: **November 24, 2014**

TO:

Sen. David Tomassoni, chair
Senate Jobs and Economic Growth Committee
317 Capitol

Sen. Tony Lourey, chair
Senate Health and Human Services Finance Division
120 Capitol

Sen. Kathy Sheran, chair
Senate Health, Human Services and Housing Committee
120 Capitol

Rep. Tim Mahoney, chair
House Jobs and Economic Development Finance & Policy Committee
591 State Office Building

Rep. Sheldon Johnson, chair
House Labor, Workplace and Regulated Industries
549 State Office Building

Rep. Tom Huntley, chair
Health and Human Services Finance Committee
585 State Office Building

Rep. Tina Liebling, chair
House Health and Human Services Policy Committee
367 State Office Building

FROM:

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COPIES:

Iron Range Legislative Delegation
Rep. David Dill
Rep. Mary Murphy
Sen. Tom Bakk
Rep. John Persell
Rep. Tom Anzelc
Sen. Tom Saxhaug
Rep. Carly Melin
Rep. Jason Metsa

November 24, 2014

Dear Legislators:

We are pleased to present the final report on our research regarding the health status of taconite workers.

This report covers the assessments made by the University of Minnesota School of Public Health (SPH). The Natural Resources Research Institute will be submitting a separate report on the environmental characterization work that they have been doing. This report contains the SPH's efforts in occupational exposure, mortality and cancer incidence, case-control studies and the respiratory health survey of taconite workers and spouses. The final NRRI report will be submitted under separate cover.

In some study areas, peer-reviewed papers have been published. Others are being prepared for journal submission and are available in the appendix of this report. We remain committed to open communication and transparency. We plan to hold at least one additional stakeholder meeting through the Minnesota Taconite Workers Lung Health Partnership on December 1, 2014 and will continue to update our website, www.taconiteworkers.umn.edu as studies become published.

We would be delighted to discuss the report at a convenient time.

We would like to thank those current and former workers who participated in our screening study. We'd also like to thank the companies and union officials for cooperating with several parts of this work. Finally, thank you for the opportunity to advance scientific knowledge on this critical issue facing Minnesota.

John R. Finnegan, Jr., PhD
Professor and Dean

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Associate Professor
Principal Investigator

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ACKNOWLEDGEMENT

This project is the result of the concerted effort of the entire Lung Health Partnership. The list of contributors to this effort are many and include the University of Minnesota investigators, graduate students, study coordinators and professional staff, the Minnesota Department of Health, the company representatives from U.S. Steel, Cliffs Natural Resources and Arcelor-Mittal, the United Steel Workers Union representatives, the legislators involved in the initial funding of this undertaking, particularly the Iron Range delegation and the participants of the Respiratory Health Survey. Our gratitude is extended to all of the people from these groups who contributed to this effort and, in so doing, helped in the effort to improve the taconite mining industry of Minnesota.

ABREVIATIONS USED IN THIS REPORT

ACGHI	American Conference of Governmental Industrial Hygienist
BMI	Body Mass Index
CVD	Cardiovascular Disease
CI	Confidence Interval
CF	Conversion Factors
EBSD	Electron Back Scattered Diffraction
EDS	Energy Dispersive X-ray Spectroscopy
EDXA	Energy Dispersive X-ray Analysis
EMP	Elongate Mineral Particle
ICD	International Classification of Disease
ISO	International Standards Organization
LTAS	Life Table Analysis System
MCE	Mixed Cellulose Ester
MCSS	Minnesota Cancer Surveillance System
MDH	Minnesota Department of Health
MIR	Mesabi Iron Range
MRHAP	Mineral Resources Health Assessment Program
MSHA	Mine Safety and Health Administration
NAAQS	National Ambient Air Quality Standard
NDI	National Death Index
NIOSH	National Institute of Occupational Safety and Health
NMRD	Non-malignant Respiratory Disease
NRRI	Natural Resources Research Institute

OEL	Occupational Exposure Limit
PCM	Phase Contrast Microscopy
PEL	Permissible Exposure Limit
PIXE	Proton Induced X-ray Spectroscopy
PM	Particulate Matter
RHS	Respiratory Health Survey
SAED	Selected Area Electron Diffraction
SEG	Similar Exposure Group
SEM	Scanning Electron Microscopy
SMR	Standardized Mortality Rate
SSA	Social Security Administration
TEM	Transmission Electron Microscopy
TSP	Total Suspended Particulate
TWA	Time Weighted Average
TWHS	Taconite Worker Health Study
UMN	University of Minnesota
UMD	University of Minnesota Duluth
UMTC	University of Minnesota Twin Cities

Taconite Workers Health Study: Final Report to the Minnesota Legislature

I. Overall General Summary

The following is a general summary of the Taconite Workers Health Study. Details may be found in the rest of the report and in the full component reports in the appendix.

In 2008, the University of Minnesota School of Public Health, at the request of the Minnesota Legislature, launched the Taconite Workers Health Study. The request was prompted by the discovery of an unusual number of cases of mesothelioma, a rare cancer of the lung lining, in Minnesota taconite workers.

The study asked three questions to assess occupational risks to taconite workers. The investigation has now concluded and below is a snapshot of its findings.

1. Is working in the taconite industry associated with mesothelioma and/or with other diseases, respiratory or non-respiratory?

- Taconite workers had higher than expected death rates from three diseases: mesothelioma, a cancer of the lining around the lung, lung cancer and heart disease, when compared to people in Minnesota.
- The vast numbers of other disease categories were not higher than expected or were not felt to have an occupational basis.

2. What factors, particularly dust from taconite operations, are associated with mesothelioma and other respiratory diseases?

- The length of time people worked in the industry was linked to higher levels of mesothelioma but not lung cancer.
- Exposure to a fiber-like mineral, referred to as elongate mineral particle (EMP), was linked to mesothelioma but not lung cancer. EMP exposure, as defined in this study, could be from either dust generated in mining and processing or from commercial asbestos exposure.
- Workers with above-average exposure to dust containing EMPs were twice as likely to develop mesothelioma as workers with below-average exposures.

3. Are workers at risk for common dust-related lung diseases and are their spouses at risk for the same diseases due to their partners working in the industry?

- A screening of current and former taconite workers and their spouses was conducted in 2010-11 and revealed x-ray evidence of dust-related scarring of the lung and lung lining (pleura) in workers.
- There was a link from EMP exposure in workers to scarring of the pleura.
- Spouses of taconite workers had comparable evidence of lung scarring on chest x-ray, to what's been reported for the broader general public.

Conclusions

The studies identified links to mesothelioma from working in the taconite industry and exposure to EMPs. The role of a specific EMP type of exposure is not clear. The overall risk for mesothelioma is low compared to other disease frequencies. Taconite worker spouses, as a group, showed a low frequency of lung disease on chest x-ray, comparable to the general population.

The authors of this report have made recommendations for taconite workers, the mining companies, unions and the Iron Range health care community, designed to assist in the safeguarding of future worker health.

The complete report may be found at www.taconiteworkers.umn.edu. You may direct questions about the study to **800-646-9255**.

II. Taconite Workers Health Study
Executive Scientific Summary

The Taconite Workers Health Study (TWHS) was funded by the State of Minnesota and began in 2008. The study was conducted in response to earlier findings by the Minnesota Department of Health (MDH), which described an apparent excess of mesothelioma within a cohort of iron ore workers. The taconite cohort originated from work done at the University of Minnesota (UMN) in the 1980s. At that time, all workers in the iron ore industry were identified, and included around 68,000 individuals from both taconite and hematite industries. The original cohort and subgroups have been used in several studies contained in this report. This is the final report to the legislature on the main questions asked of the study investigators in 2008 and for which these studies were designed.

An apparent excess of mesothelioma within the taconite cohort was identified by linking the cohort to the state's cancer surveillance system. Mesothelioma is considered a "sentinel disease," in that its presence suggests the possibility of other diseases occurring from the same exposure. Almost always, the exposure related to mesothelioma is asbestos, referred to in this report as elongate mineral particles (EMPs) of the asbestiform type. A prevalent mineralogy unique to the eastern Mesabi Range is the non-asbestiform EMP.

Since EMPs of the asbestiform type are also strongly related to lung cancer and lung scarring, also known as non-malignant respiratory disease (NMRD), UMN researchers thought that all of these diseases should be evaluated. Unfortunately, no one study design accounts for all of these conditions. Accordingly, the research team developed a multi-pronged strategy which included the following study designs: 1) an assessment of the major exposures from dust in taconite operations (EMPs, silica and respirable dust) 2) a mortality (cause-of-death) study to examine a variety of diseases and their frequency 3) an incidence study for all cancer types 4) mesothelioma and lung cancer case-control studies where exposures to dusts from the workplace could be studied in more detail and 5) a medical screening of current and former workers (and spouses) for NMRD. This last study included information on other exposures and on smoking. Although all of these study types are important, the case-control studies are generally accepted as the most insightful investigations. Collectively, all of these studies form the TWHS. Additional investigations were conducted by the Natural Resources Research Institute (NRRI) and were done to characterize exposures in the non-working community. The final NRRI report will be submitted under separate cover.

The collective TWHS approach was designed to answer three specific questions:

1. Is working in the taconite industry associated with mesothelioma and/or other diseases, respiratory and non-respiratory?
2. What factors, particularly exposure to dust from taconite operations, are associated with mesothelioma and other respiratory diseases?
3. Are spouses of taconite workers at risk for respiratory diseases as a result of their partners working in the industry?

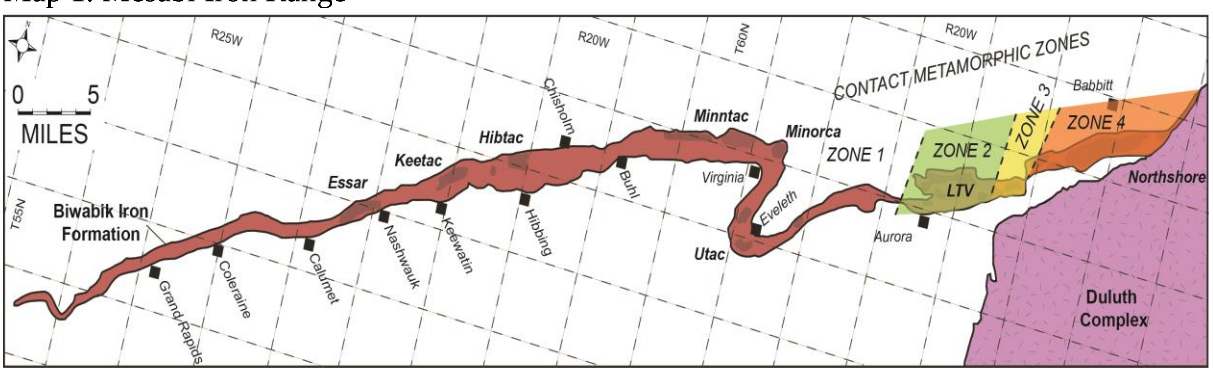
As of this writing, we are providing insights to each of these questions. As in most investigations of this nature, this work has also raised additional questions, which go beyond the original scope of this work. Several of these new issues are being pursued through additional grant procurement or are mentioned in the list of recommendations at the end of the Executive Summary.

These are the unique findings from each of the TWHS components:

- Occupational exposure assessment

Over 2000 current, on-site samples were collected by study investigators in 2010-11. Samples included personal and area types for elongate mineral particles (EMPs), silica and respirable dust. The latter two are the most prevalent exposures in the industry and were gathered for that reason. Silica is an important consideration since it has known toxicity in the lung and has been implicated as a lung carcinogen. The term "EMP" refers to any mineral particle with a minimum aspect ratio of 3:1 that is of inhalable size. EMPs were gathered because of the known relationship of one type (asbestiform) with mesothelioma and lung cancer. Area samples for EMPs included the use of a cascade impactor with size fractions ranging from 36 nanometers to 56 microns in length. These dimensions were measured by phase contrast and electron microscopy and counted using several dimension-based definitions of EMPs. Based on the use of the NIOSH definition of EMPs, most on-site, current measurements were within the recommended federal exposure limits. Measurements indicated that when excursions did occur, they were more likely to be in the eastern part (zone 4) of the Mesabi Range (Map 1). The east range measurements also identified non-asbestiform amphibole EMPs, which were not present on the west range. There were no asbestiform EMPs identified in any of the samples, defined by NIOSH as silicate minerals from the serpentine and amphibole groups that grow in a fibrous habit. Although detected in the east, the non-asbestiform amphibole EMP measurements were typically a magnitude or more below the current NIOSH Recommended Exposure Limit (REL). Based on current measurements, silica exposures had more excursions (over the ACGIH TLV).

Map 1. Mesabi Iron Range



Historical EMP measurements (n=682) were identified from two sources: (a) the Mine Data Retrieval System maintained by the Mine Safety and Health Administration (MSHA), and (b) the internal industrial hygiene monitoring databases of U.S. Steel, and Cliffs Natural Resources, two of the currently operating taconite mining companies. By combining comprehensive on-site exposure concentrations with the relatively fewer historical data, we generated exposure concentration matrices that were used to estimate cumulative exposures for individual workers. Using the measured data and regression model estimates, we reconstructed the exposure for each similar exposure group (SEG) for each mine and for each year between 1955 and 2010 for all three exposure types. Based on these estimates, EMP exposures were likely to have been higher in the earlier days of the industry. This exposure information was then used in the case-control and Respiratory Health Survey studies.

- Occupational cohort mortality study

To obtain a general picture of mortality in the cohort, a standardized (by age and gender) analysis of the causes of death was undertaken for those individuals who worked a year or more in the taconite industry and who were born in 1920 or later. Approximately 31,000 individuals were included in this investigation. This study did not contain information on exposure measurements or smoking. Three causes of mortality were significantly higher than expected, compared to causes of death for the rest of Minnesota, not including the counties that include the Mesabi Range. These included mesothelioma, lung cancer and cardiovascular death. Mesothelioma was a rare disease in comparison to other disease frequencies in the cohort. These three diseases were all elevated at sites across the Mesabi Range.

- Cancer incidence study

A standardized incidence ratio (SIR) analysis was undertaken for the cohort, to determine cancer morbidity using the Minnesota Cancer Surveillance System (MCSS). This added to the mortality analysis because it included people who were diagnosed with cancer but living for study purposes and allowed an analysis of more detailed subtypes of cancer. A total of 5,700 cancers were identified in the study cohort including 51 mesotheliomas and 973 lung cancers. The incidence of cancer types in the cohort was compared to that of other Minnesotans. After adjusting for out-of-state migration, the SIR for lung cancer and mesothelioma was 1.3 (95% CI: 1.2-1.4) and 2.4 (95% CI: 1.8-3.2) respectively. Other elevated cancers included stomach (SIR = 1.4, 95% CI: 1.1-1.6), laryngeal (SIR = 1.4, 95% CI: 1.1-1.7), and bladder (SIR = 1.1, 95% CI: 1.0-1.2). Adjusting with a bias factor for smoking attenuated the lung cancer SIR (SIR = 1.1, 95% CI: 1.0-1.1). No variation in risk was seen for subtypes of lung cancer.

- Mesothelioma case-control study

This case-control study originated within the occupational mortality cohort (nested study). It was designed to evaluate whether exposures from within the taconite industry, specifically EMPs, could explain some or all of the excess number of mesotheliomas. For 57 cases that worked in the taconite industry, each year worked in the industry resulted in a 3% increase of mesothelioma frequency. Cumulative exposure to EMPs (NIOSH 7400 definition) was associated with a 10% increase in mesothelioma for each EMP/cc/year of employment. One EMP/cc/year could be 10 years of average exposure to 0.1 EMP/cc or 1 year of average exposure to 1.0 EMP/cc. This finding was marginally significant, statistically. There were approximately twice the numbers of cases for the group in the upper exposure range compared to the lower range, using the median exposure as the dividing point. Assessing the impact of small fibers was complicated by a high correlation with other EMP definitions.

- Lung cancer case-control study

This case-control study originated within the occupational mortality cohort (nested study). It attempted to identify exposures from within the taconite industry that could explain some or all of the excess number of lung cancers. Cases and controls were assessed for exposure to EMPs and to silica, both of which have been associated with risk for lung cancer in other studies. Lung cancer cases (n=1706) were identified through the cohort mortality study and through linkage with the Minnesota Cancer Surveillance System. Through the latter case identification process, histological cell type was available for each lung cancer for 973 cases. For the overall lung cancer group, exposure to EMPs and silica were not associated with cases. For the cell-specific group, no cell type was associated with these exposures. Evaluation by work location on the Mesabi Range (east vs. west range) did not reveal significant differences. Smoking information was not available for this study.

- Respiratory Health Survey (RHS)

In order to better understand the most typical exposures in the industry and their impact on common lung conditions, a screening of current and former taconite workers was conducted. This study utilized data obtained by the exposure assessment (above). Smoking information was also available through the use of an occupational/medical questionnaire. The screening included spouses of workers, to assess the likelihood of "take-home" exposures. There were 1188 workers who participated and 496 spouses in the complete screening (occupational/medical history, pulmonary function testing and chest x-ray). Within the worker group restrictive lung function on spirometry, an indication of dust exposure occurred in 4.5 % of those workers screened. Obstructive lung function occurred in 16.8% with another 2.9% having mixed (obstructive and restrictive) function. Chest x-ray abnormalities, defined by a consensus of two B-readers, suggested that abnormalities of the lung substance, another indication of dust exposure, occurred in 5.4% of those workers screened. Also in workers 16.7% demonstrated pleural abnormalities. Spousal chest x-rays showed 0.6% parenchymal findings and 4.5% pleural abnormalities, suggesting a similar amount of abnormalities as described within the general population (Appendix 8). Associations with cumulative silica and respirable dust, using onsite and historical estimates, were not revealing. Exposure to EMP was associated with pleural abnormalities, most likely suggesting exposure to asbestiform EMPs in the past.

Original Questions of Interest:

1. **Is working in the taconite industry associated with mesothelioma and/or other diseases, respiratory and non-respiratory?**

The mortality and cancer incidence investigations were important in assessing whether other diseases were occurring in excess within the entire industry of taconite workers. In the mortality study, excesses were found for mesothelioma, lung cancer and cardiovascular mortality (specifically from ischemic heart disease). (Mesothelioma most often occurs in the setting of asbestiform EMP exposure and is addressed in question 2.) Lung cancer has a high attributable risk from smoking, which in other studies accounts for 80% or more of cases. The case-control study of lung cancer, where workplace exposures were evaluated in detail, did not show EMP or silica exposure associated with the lung cancer cases. Increased cardiovascular mortality was an unexpected finding, given that most work forces are healthier than the general population and usually have lower cardiovascular mortality than the reference population. This finding could indicate that a lifestyle issue is contributing to cardiovascular mortality but could also indicate exposure to small particulates, which have recently been found to increase mortality from this disease. It was not investigated further. Other causes of death were comparable to the overall Minnesota population. In the cancer incidence evaluation, other disease categories that occurred higher than expected included laryngeal, bladder and stomach. The first two also have associations with smoking but bladder cancer has also been associated with some occupational exposures (certain dyes). Asbestos has been included in this group, although the suggestion for additional research by the investigators was made (Silverman, 1989[(1)]). Stomach cancer studies have shown the strongest risk factor to be from *H. pylori* infection with smoking also playing a role (Shibata and Parsonnet, 2006[(2)]. An occupational basis for stomach cancer has not been demonstrated. Other than these disease categories, with the likely explanations above, the cohort did not have higher observed numbers of death or other cancers compared to a Minnesota population of the same age and gender.

2. **What factors, particularly exposure to dust from taconite operations, are associated with mesothelioma and other respiratory diseases?**

Study findings suggest that mesothelioma risk is linked to length of time employed in the industry. The role of specific dusts from taconite operations in the mesothelioma cases is less clear. An association with exposure to EMPs (type not specified) was demonstrated with twice the number of mesotheliomas occurring in the high exposure group vs. the low. Because mesothelioma is a rare disease it is helpful to consider these results in the context of lifetime risk of mesothelioma. An average person who lives to be 80 years old has on average a 0.144 percent chance of developing mesothelioma in their lifetime, or about 1.4 cases per 1,000 individuals. A taconite miner who worked for 30 years in the taconite industry has on average a 0.333 percent chance of getting mesothelioma in their lifetime or about 3.33 cases per 1,000 taconite miners working for 30 years and living to be 80 years old. Even though attempts were made to control for the effect of commercial asbestos exposure, the investigators were not able to state with certainty that the association with EMPs and mesothelioma was related to the ore dust or to the use of commercial asbestos or both. The predominant exposure in this industry is to shorter, non-asbestiform EMPs, in the range of 1-3 microns (μm) in length. EMPs in this category have been described as less pathogenic than longer, asbestiform EMPs. However, in this study we found that shorter EMPs were highly correlated with longer EMPs, making it difficult to determine size-related effects. Analyses of where cases worked showed higher rates for mesothelioma in the western most portion of the Mesabi Iron Range (zones 1 and 2) compared to east. However, this finding did not correlate with the exposure concentrations that were measured and/or estimated in the east and west range plants and remains unexplained. Exposure to dust from taconite operations as a cause of the excess lung cancer is not supported by the case-control study for lung cancer. In that study, no significant relationship was found between the case group (lung cancer) and cumulative EMP exposure. There was an association found between pleural abnormalities in current and former taconite workers (Respiratory Health Survey) and cumulative EMP exposure that could indirectly support the mesothelioma-cumulative EMP association. The importance of this finding in support of the mesothelioma cases having a potential association to dusts from taconite operations requires further evaluation.

(1)Silverman DT, Levin LI, Hoover RN. Occupational risks of bladder cancer in the United States: I. White men. J Natl Cancer Inst 1989, 81:1472-1480

(2)Shibata A, Parsonnet J. Chapter 37: Stomach Cancer. In Cancer Epidemiology and Prevention, 3rd Edition (2006). Edited by Schottenfeld and Fraumeni. Oxford University Press. New York, N.Y. Pages 707-720

3. **Are spouses of taconite workers at risk for respiratory diseases as a result of their partners working in the industry?**

Based on the screening findings from the Respiratory Health Survey, spouses had a low prevalence of chest x-ray and spirometry abnormalities. There was no indication that spouses had high exposures to dusts generated from mining based on findings measured by spirometry and chest x-ray. Although exposures in the communities could obviously have changed over the years, the current exposure potential in the communities appears to be low, based on these findings.

Given the combined assessments from all TWHS investigations, the following recommendations are suggested:

1. If not currently being undertaken, comprehensive exposure assessment and monitoring for the major exposures in the industry should be done routinely for a broad cross-section of workers.
2. If not already in place, electronic data systems that involve exposure monitoring and employment (*e.g.* job groupings) should be updated with the idea of using these data for future epidemiological purposes.
3. Given the rate of death from cardiovascular disease, efforts to control known risk factors should be made by the companies, unions and communities. Consideration of the potential for cardiovascular disease to be related to dust exposure should be made.
4. The cause of death study should be updated every five years or so, using the existing mortality statistics available from the Minnesota Department of Health.
5. The state's cancer surveillance system (MCSS) should update the cohort's mesothelioma and lung cancer listing periodically. This could be done as a routine function of MCSS, without the incorporation of more complicated exposure data. Depending on the frequency of findings from this investigation, additional exposure-disease studies could be considered.
6. Given the known hazards in mining, the process of avoiding exposures generated in the mining and processing of taconite ore is critical. Exposure avoidance is the most effective way to minimize disease risk. Improvement in engineering exposure control technology should continue to be a priority. Educational activities involving the use of personal protective equipment (PPE) should also continue. The use of PPE in unusual circumstances where exposure potential is high and/or unknown should be included in these activities. Consideration should be given to mandatory use of PPE in high-exposure circumstances, if not in effect already.
7. Given the potential for lung disease to be impacted by workplace exposures and smoking, a comprehensive approach should be placed on smoking cessation, if this is not already in place.
8. Given the higher potential for dust-related lung disease in this industry, consideration should be given to an evaluation of existing medical surveillance (monitoring) programs with an emphasis on participation rates by exposure potential categories. This could include an independent review of existing company chest x-rays, by experienced B-readers, to further clarify the magnitude of NMRD in workers.
9. Consideration should also be given to identifying a post-1982 cohort and evaluating it with exposure and epidemiology approaches.
10. In view of community health concerns, a reevaluation of spouses should be considered in the future.

III. Taconite Workers Health Study
Exposure Assessment Study (component summary)

The workplace exposure assessment strategy was to gather exposure information from all existing mining sites that could be used in epidemiologic investigations. This was done using a combination of current, on site measurements, historical measurements taken by the mining companies and measurements obtained by the Mining Safety and Health Administration as part of their regulatory function. Exposure assessment involved three major exposures that included elongate mineral particles (EMPs), respirable dust and respirable silica.

The three main goals for the exposure assessment effort related to EMPs were:

1. Assess present-day exposures of workers to EMPs in dust from taconite operations in relation to current occupational exposure limits;
2. Assess historical exposures of workers to EMPs in the taconite industry for the time period 1955-present;
3. Evaluate existing practices and methods to reduce worker exposures in this industry and, where appropriate, suggest improvements in these methods.

Present day exposures to EMPs are addressed in Hwang *et al.*, 2013 (Appendix 1). Briefly, 28 unique, similarly exposed work groups (SEGs) were established from approximately 180 job descriptions. The SEGs were consistent across all mines. Personal samples were collected for exposures at six active mines in the Mesabi Iron Range for each of the 28 SEGs. The samples were analyzed using the NIOSH 7400 method (phase contrast microscopy) along with the NIOSH 7402 method (transmission electron microscopy) for 20% of the samples. Methods incorporated additional methods to distinguish amphibole from non-amphibole EMPs and, if amphibole, whether they were asbestiform or non-asbestiform types. (Some of these methods were for study purposes and did not represent the approach used in the regulation of EMPs.) Findings from these samples (n=1298) indicated that, for many SEGs in several mines, the exposure levels of total EMP were higher than the NIOSH Recommended Exposure Limit (REL) for EMPs. However, the total EMP classification does not necessarily refer to regulated asbestiform EMP because the NIOSH 7400 method can’t differentiate between asbestiform and non-asbestiform EMPs. In fact, there were no asbestiform EMPs identified in any of the onsite samples. The concentrations of amphibole EMPs were well-controlled across all mines and were a magnitude lower than the concentrations of total EMPs, indicating that amphibole EMPs are not major components of taconite EMPs (Figures 1 and 2). Although the eastern Mesabi Iron Range was the only area where amphibole EMP was found, the levels were all under the recommended exposure limit.

Different dimensions of elongate mineral particles (EMPs) have been proposed as being relevant to respiratory health end-points such as mesothelioma and lung cancer. A methodology for converting personal EMP exposures measured using the NIOSH 7400/7402 methods to exposures based on other size-based definitions was developed (Hwang *et al*., 2014; appendix 2). The highest fractions of EMP concentrations were found for EMPs that were 1–3 µm in length and 0.2 – 0.5 µm in width. Therefore, the current standard NIOSH method 7400, which only counts EMP > 5 µm in length and ≥ 3 in aspect ratio, will underestimate shorter EMP exposures. At the same time, there was a high degree of correlation between the exposures estimated according to the different size-based metrics.

The second major component of the exposure assessment involved the reconstruction of historical EMP measures, also to be used for epidemiologic purposes. A person's total exposure was comprised of the current exposure plus their historical exposure, summed to provide a cumulative exposure measure (EMP/cc/years). Some of the historical data for EMP measurements involving early time periods were sparse. This was particularly true for the time prior to the regulatory era (pre-1970s). This was also a time when exposure control methodology was not as effective as current control methods. This suggested that exposures were likely to have been higher in the earlier part of the taconite industry's history. Around 700 historical EMP measurements were extracted from databases maintained by the mining companies and the Mine Safety and Health Administration (MSHA). The NIOSH 7400 method was used to estimate total cumulative EMP exposure. Using the measured data with regression model estimates for those times where measurements were not present, exposures were reconstructed for each SEG by mine for each year between 1955 and 2010 (Hwang *et al.*, 2014; Appendix 2). Results of this approach showed sizeable slope, indicating significant time dependency.

The third major component of the exposure assessment involved the measures of exposures to respirable dust (RD) and respirable silica (RS) (Appendix 3). Personal samples (n=679) were collected to assess the present-day exposure levels of workers to RD and RS at the six active taconite mines. RD and RS concentrations were measured using NIOSH 0600 and NIOSH 7500 methods, respectively. The concentrations of RD in all mines fell below the ACGIH TLV. The concentrations of RS in crushing and concentrating processes were higher than those measured in the other mining processes, and some were higher than the ACGIH TLV for RS. The highest concentrations of RS were generally found in the crushing departments for all mines. The concentrating department may have reduced the levels of RS significantly, as well as lowered the percentage of quartz in RD in the pelletizing department. There was little to no variability between the six mines for either RD or RS exposures because the taconite mining and milling processes are similar across all mines. Reconstruction of historical exposures to respirable dust and silica was carried out in a manner similar to that for EMPs. As in the case of EMPs, the historical measurements made by the companies were fewer compared to the onsite comprehensive exposure assessment carried out as part of this study.

In these surveys, we also evaluated the efficacy of existing exposure control measures including primary engineering controls (enclosures, ventilation, and particle collectors), work practice and administrative controls, and personal protective equipment. We toured the control systems of all the mines. We measured air velocity into selected enclosures and in selected ducts in four mines, and have compared our findings to the American Conference of Government Industrial Hygienists (ACGIH) ventilation guidelines. In general, the types of installed controls match ACGIH guidelines, although the velocity into some enclosures is lower than recommended. We have arrived at the following conclusions: (a) Engineering controls are appropriate for normal operations; (b) Miners may be exposed to elevated dust levels when making repairs or performing maintenance; (c) Atypical conditions may lead to significant exposures, and respiratory protection should be used under atypical conditions that contribute to excessive exposures whenever feasible.

Figure 1. Box plot of total EMP for each SEG in mines A–F (the horizontal line indicates the NIOSH REL for EMP = 0.1 particles cm−3).

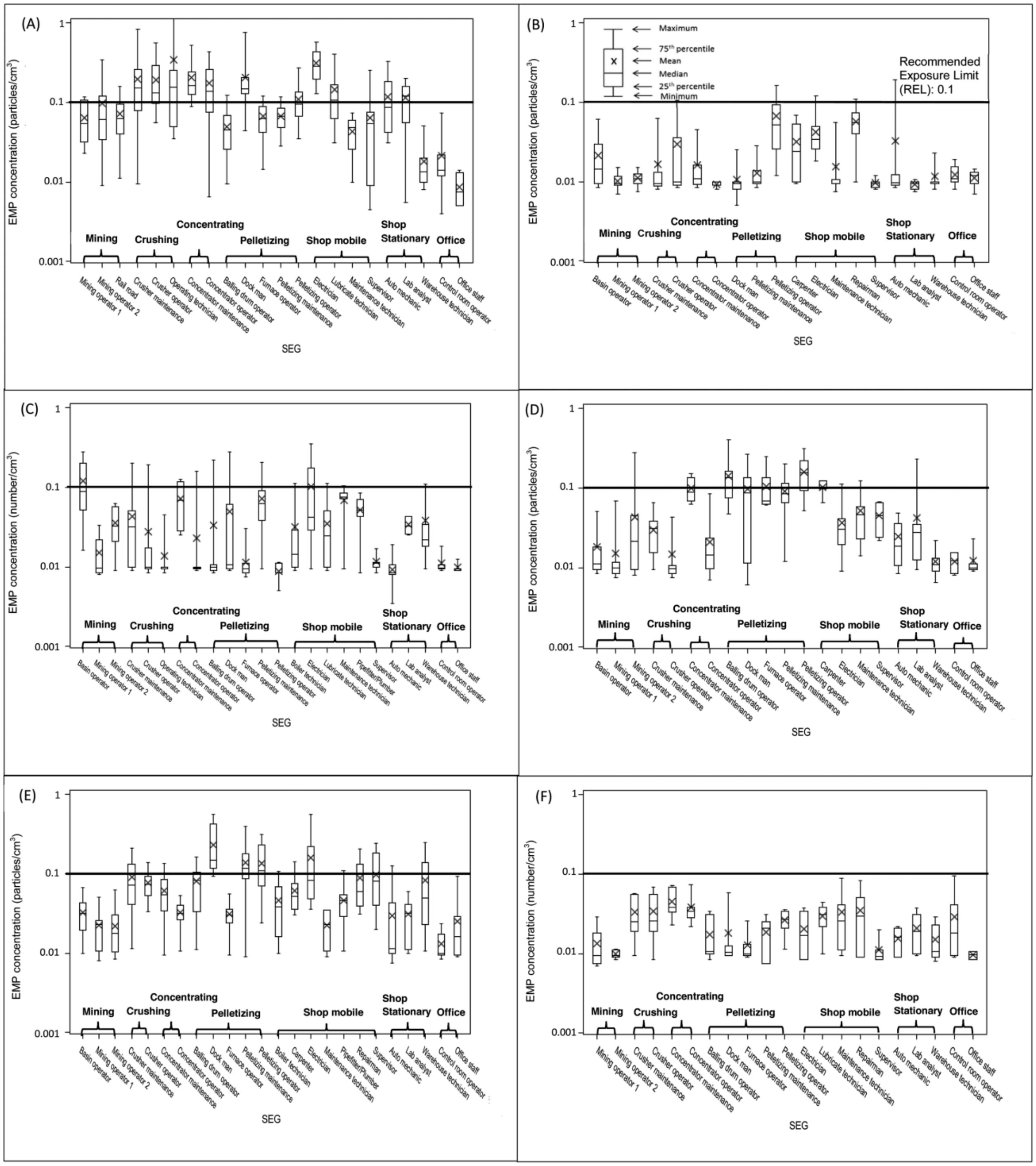
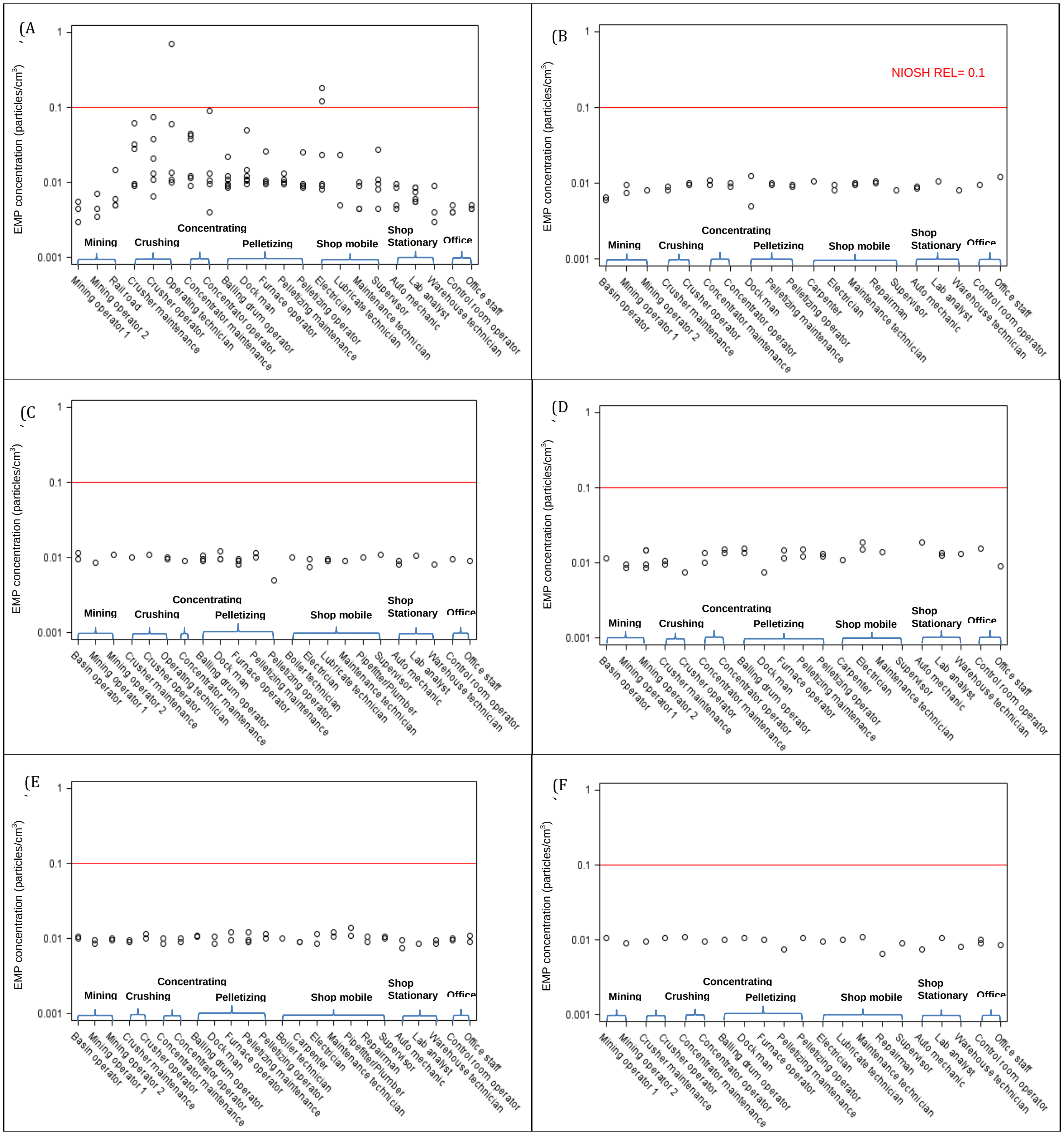


Figure 2. Scatter plot of amphibole EMP concentrations for each SEG in mines A-F (the horizontal line indicates the NIOSH REL for EMP = 0.1 particles/cm^3



IV. Taconite Workers Health Study
Mortality Study (component summary)

The goal of the mortality study was to determine the causes of death among the taconite mining cohort. This provided a measure of which diseases miners died from and the relative frequencies of these causes of death. Mortality studies are generally useful types of investigations to get a perspective of a group's mortality experience and to see if people in the group are dying from any disease category more often than those in a comparison group. This study did not use specific exposure measurements nor did it have smoking information available.

The detailed report for this study is included in the appendices (Allen *et al.*, 2014; Appendix 4). This study first determined the vital status of each member of the cohort. For those who died, death certificates were obtained from the state health departments where the death occurred. Once the death certificate was obtained, the causes of death were categorized in a standardized way. The standardized mortality ratio (SMR) was determined, based on the observed number of deaths within a disease category compared to the age, sex and disease specific expected numbers of death in the general population of Minnesota. An SMR greater than 1.0 implies more deaths in the cohort than expected. An SMR less than 1.0 implies fewer deaths in the cohort than expected. If the 95% confidence interval excludes one, the finding is statistically significant.

Mortality was evaluated between the years 1960 and 2010 for all miners employed by one of the existing mining companies in 1983. The cohort included 31,067 workers with at least one year of employment. Among this group, there were 9094 deaths in total, 949 of which were from lung cancer and 30 were from mesothelioma. The "all-cause" mortality was higher than expected, with an SMR of 1.04 (95% CI=1.02-1.04). Mortality was also higher than expected for mesothelioma, which had an SMR of 2.77 (95% CI=1.87-3.96). The SMR for trachea/bronchus/lung cancer in this cohort of miners was 1.16 (95% CI=1.09-1.24). The death rate for cardiovascular disease was 1.10 (95% CI=1.06-1.14), including hypertensive heart disease (SMR=1.81, 95% CI=1.39-2.33) and ischemic heart disease (SMR=1.11, 95% CI=1.07-1.16). These findings did not vary by duration of employment in this analysis. The frequency of mesothelioma deaths was low in comparison to other disease frequencies. The vast majority of remaining disease categories occurred as expected (Table IV-1).

This study provides evidence that taconite workers may be at increased risk for mortality overall and more specifically from lung cancer, mesothelioma, and cardiovascular disease. Occupational exposures during taconite mining operations may be associated with these increased risks, but non-occupational exposures may also be important contributors. Additional investigation of the cardiovascular disease findings appears warranted and risk factor reduction strategies for cardiovascular diseases should be considered further.

Table IV-1. Selected SMRs for Minnesota Taconite Workers with ≥ 1 year employment*

Underlying Cause of Death	Observed	Expected	SMR	95% CI
All Causes	9,094	8,764.69	1.04	1.02-1.06
All Cancers	2,710	2,609.86	1.04	1.00-1.08
Respiratory	981	846.74	1.16	1.09-1.23
Larynx	26	23.84	1.09	0.71-1.60
Trachea, bronchus, lung	949	815.67	1.16	1.09-1.24
Pleura	1	1.81	0.55	0.01-3.08
Mesothelioma	30	10.82	2.77	1.87-3.96
Heart diseases	2,676	2,435.81	1.10	1.06-1.14
Hypertensive heart disease	62	34.17	1.81	1.39-2.33
Ischemic heart disease	2,185	1,964.93	1.11	1.07-1.16
Cerebrovascular disease	391	384.30	1.02	0.92-1.12
Hypertension w/o heart disease	35	52.80	0.66	0.46-0.92
Respiratory Diseases	582	621.19	0.94	0.86-1.02
COPD	363	369.89	0.98	0.88-1.09
Asbestosis	1	2.90	0.35	0.01-1.92
Silicosis	1	1.09	0.91	0.02-5.09
Transportation injuries	339	329.15	1.03	0.92-1.15
Other injury	239	221.75	1.08	0.95-1.22
Violence	289	258.41	1.12	0.99-1.26

*adjusted for age, calendar period, and sex

V. Taconite Workers Health Study
Cancer Incidence Study (component summary)

The purpose of this investigation was to evaluate cancer morbidity among Minnesota Taconite mining industry workers. This assessment is designed to evaluate all cancers, including those which may be successfully treated. The full report is contained in Appendix 5.

Cancer morbidity between 1988 and 2010 was evaluated in a cohort of 40,720 Minnesota taconite mining workers employed between 1930 and 1983 and who were alive at the beginning of the state's cancer surveillance system in 1988. Standardized incidence ratios (SIRs) with 95% confidence intervals (CI) were determined by comparing observed numbers of incident cancers with frequencies in the Minnesota Cancer Surveillance System. SIRs for lung cancer by histological subtypes were also estimated. SIRs were adjusted to account for out-of-state migration and a bias factor was estimated to adjust smoking related cancers. An SIR greater than 1.0 implies more disease than expected; an SIR less than 1.0 implies less disease than expected. If the 95% confidence interval excludes 1.0, the finding is statistically significant.

A total of 5,700 cancers were identified in the study cohort including 51 mesotheliomas and 973 lung cancers. After adjusting for out-of-state migration, the SIR for lung cancer and mesothelioma was 1.3 (95% CI: 1.2-1.4) and 2.4 (95% CI: 1.8-3.2) respectively. Other elevated cancers included stomach (SIR = 1.4, 95% CI: 1.1-1.6), laryngeal (SIR = 1.4, 95% CI: 1.1-1.7), and bladder (SIR = 1.1, 95% CI: 1.0-1.2) (Table V-1). Among the lung cancers, SIRs for adenocarcinoma (SIR = 1.2, 95% CI: 1.1-1.4), squamous cell (SIR = 1.3, 95% CI: 1.2-1.5) non-specified (SIR = 1.6, 95% CI: 1.4-1.8), and other (SIR = 1.4, 95% CI: 1.1-1.8) were elevated. This study did not have information available for smoking. Instead, an adjustment was made with a bias factor for smoking. This attenuated the lung cancer SIR (SIR = 1.1, 95% CI: 1.0-1.1).

Taconite workers have an increased cancer incidence for mesothelioma, lung, laryngeal, stomach and bladder cancer. Adjustment for smoking attenuates but does not completely eliminate the lung cancer risk in this population. Bladder cancer may be occupational in origin and has been linked to certain dyes as well as smoking. Asbestos has a weak link to bladder cancer and is questionably related causally. Stomach cancer studies have shown the strongest risk factor to be from *H. pylori* infection with smoking also playing a role. Asbestos has been shown to be a risk factor in some studies although a strong occupational basis for stomach cancer has not been demonstrated. Other than these disease categories, with the likely explanations above, the cohort did not have higher observed numbers of other cancers compared to a Minnesota population of the same age and gender. The extent to which mining-related exposures contribute to disease burden for mesothelioma and lung cancer was further investigated in the case-control study.

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Table V-1. Selected SIRs for Minnesota Taconite Workers

Cancer	Observed	Expected	SIR*	95% CI
Mesothelioma	51	21.1	2.4	1.8-3.2
Lung	973	750.9	1.3	1.2-1.4
Esophagus	87	76.9	1.1	0.9-1.4
Kidney	170	178.2	1.0	0.8-1.1
Larynx	94	68.6	1.4	1.1-1.7
Liver & bile duct	52	49.4	1.1	0.8-1.4
Oral	172	162.5	1.1	0.9-1.2
Pancreas	120	105.9	1.1	0.9-1.4
Stomach	105	77.7	1.4	1.1-1.6
Bladder	363	338.5	1.1	1.0-1.2

*Adjusted for age, gender, calendar period, and out-of-state migration

VI. Taconite Workers Health Study
Mesothelioma Case-Control Study (component summary)

A detailed evaluation of mesothelioma cases and exposures was performed, the full report for which is in Appendix 6. The goals for this component included the following:

1. To examine the association between length of work in the taconite mines and the risk of mesothelioma.
2. To examine the association between exposure to EMPs in taconite mining and the risk of mesothelioma, looking at overall EMP exposure and EMP exposure within each geological zone to see if geological differences along the Mesabi Range impact mesothelioma risk.

This initial part of this evaluation required the identification of all cases in the mortality study and combining these with cases identified in the Minnesota Cancer Surveillance System from 1988 onward. From these sources, 80 cases were identified. Four controls were selected from the taconite cohort for each case, matched on age and without evidence of mesothelioma at the time of the case diagnosis or death. A detailed assessment of exposure to elongate mineral particles (EMP) was made in cases and controls, using the exposure approach described in Hwang *et al.*, 2013. In short, data from exposure monitoring and work histories were combined to estimate the cumulative EMP exposures in case and control groups. Work history information was available from the 1950s through 1982 and was originally abstracted by University of Minnesota investigators in the 1980s. This information was used in the current investigation after records were reassessed. In the current investigation, attempts were made to exclude time worked in the hematite mining industry, which preceded the taconite industry and for which no exposure information was available. This study did not have information available on smoking, but smoking is not associated with mesothelioma.

Results indicated that the rate for mesothelioma was related to years of employment in the industry (Table VI-1). For each year worked the risk for mesothelioma increased by 3%. For workers who worked 20 years, their rate for mesothelioma would equate to a 60% increase.

An analysis of mesothelioma risk by EMP concentration was undertaken. The EMPs in this analysis were measured by the NIOSH 7400 method, which counts all EMP over 5 microns (µm) in length, 0.25 µm or more in diameter, with an aspect ratio (ratio of length to width) of 3:1 or greater. Exposures were estimated across all sites and by specific mineralogical zone (Table VI-2). Results suggested higher EMP exposures in the eastern-most mineralogical zone.

The rate ratio (RR) for mesothelioma across all sites was increased about 10% for each (EMP/cc/year of exposure (Table VI-3). With this metric, an individual exposed to 1 EMP/cc/year has a 10% increase in the RR. This could be a workplace average of 1.0 EMP for one year or 0.1 EMP for 10 years. This finding was of borderline statistical significance. When assessed by high EMP exposure category (greater than or equal to the median exposure) vs. low exposure category (less than the median), the risk nearly doubled. Because mesothelioma is a rare disease it is helpful to consider these results in the context of lifetime risk of mesothelioma. An average person who lives to be 80 years old has on average a 0.144 percent chance of developing mesothelioma in their lifetime, or about 1.4 cases per 1,000 individuals. A taconite miner who worked for 30 years in the taconite industry has on average a 0.333 percent chance of getting mesothelioma in their lifetime or about 3.33 cases per 1,000 taconite miners working for 30 years and living to be 80 years old.

Analysis by zone indicated a higher RR in the western-most zones. However, the west was measured to have had the lowest exposure, bringing into question the possibility of uncontrolled confounding in this assessment. These RRs were adjusted for age, employment in hematite, potential for commercial asbestos exposure, and exposures in other zones.

Table VI-1. Overall and zone-specific rate ratio estimates for mesothelioma by years of employment in taconite

	Cases	Controls	RR[1]	95% CI[2]
Taconite Years	57	184	1.03	1.00-1.06
Any hematite	48	212	0.99	0.94-1.04
High[3] vs. low				
Low employment	28	97	1.00	--
High employment	29	87	1.15	0.62-2.11
Years employment (tertiles)				
≤ 2 years (REF)	16	66	1.00	--
>2 to < 12 years	17	55	1.45	0.64-3.27
12+ years	25	63	1.78	0.84-3.75
Zone 1 Taconite years	18[4]	74[4]	1.05	1.00-1.11
Zone 2 Taconite years	31[4]	58[4]	1.06	1.02-1.09
Zone 4 Taconite years	12[4]	66[4]	0.97	0.92-1.02

[1] The rate ratio is interpreted as the relative increase in the frequency of mesothelioma associated with a one unit increase in the exposure for continuous measures of exposure, e.g. years of employment, or compared to the reference category (designated as 1.0). The rate ratio was adjusted for age, and years of employment in hematite.
[2] 95% CI= 95% confidence interval
[3] The high group represents workers with employment duration greater than that of the case median duration
[4] Cases and controls may have worked in more than one zone

In this analysis, attempts were made to assess other exposure definitions, since the most common exposure was to shorter EMPs. It was found that the other definitions, which included the Suzuki definition, the Chatfield and the cleavage fragment were all highly correlated, which limited further understanding of the role these size-specific EMPs may have played. Also in question was the role of asbestiform vs. non-asbestiform EMP. The former, although more pathogenic, cannot be identified with the NIOSH 7400 measurement method. No asbestiform EMP was found in the onsite occupational exposure assessment (above). Another limitation of this analysis was the lack of measured data on exposure to commercial asbestos, which would also be measured by the NIOSH 7400 method, is not distinguishable from the other EMP types using that method, and may have played a role in the elevated RR in this investigation.

In summary the results from this case-control study suggested an association between duration of employment in the taconite industry and risk of mesothelioma. There was also an association with mesothelioma and exposure to cumulative EMPs, as measured by the NIOSH 7400 method. Due to high correlations between the different EMP definitions, the specific details of size and type of EMP exposure (asbestiform, non-asbestiform) could not be further ascertained. The potential for residual effects from exposure to commercial asbestos in the taconite industry or elsewhere could not be entirely ruled out.

Table VI-2. Overall and zone specific cumulative exposure estimates (EMP/cc-year) for mesothelioma cases and controls who ever worked in taconite operations[1,2]

	Cases			Controls		
	N	Median[3]	75th Percentile[3]	N	Median[3]	75th Percentile[3]
Overall	57	1.15	2.95	184	0.24	2.63
Zone 1	18	0.22	0.73	74	0.12	0.18
Zone 2	31	1.88	2.95	58	0.58	2.61
Zone 4	12	1.10	3.23	66	2.09	5.97

[1] Measured by NIOSH 7400 method
[2] Cases and controls may have worked in more than one zone.
[3] Cumulative exposures for the median and 75th percentile were expressed as EMP/cc/year.

Table VI-3. Rate Ratios for cumulative EMP exposure and mesothelioma

Exposure	Cases	Controls	RR[1]	95% CI
EMP/cc/yr[2]	57	184	1.10	0.97-1.24
Low:<1.15 EMP/cc/yr	29	124	1.00	--
High: ≥ 1.15 EMP/cc/yr	28	60	1.93	1.00-3.72
Tertiles[2,3]				
0 to<0.25 (REF)	16	77	1.00	--
0.25 to <2.0	19	57	1.66	0.75-3.68
2.0+	22	50	1.84	0.80-4.23
EMP/cc/yr[4] Zone 1	18	74	1.96	1.15-3.34
EMP/cc/yr[4] Zone 2	31	58	1.31	1.12-1.54
EMP/cc/yr[4] Zone 4	12	66	0.88	0.71-1.09
Hematite	48	212	0.99	0.94-1.04

[1] Exposure measured by NIOSH 7400 method (NIOSH EMP definition: > 5 µm length, aspect ratio ≥ 3). The rate ratio is interpreted as the relative increase in the frequency of mesothelioma associated with a one unit increase in the exposure for continuous measures of exposure, e.g. years of employment, or compared to the reference category (designated as 1.0). The rate ratio was adjusted for age, and years of employment in hematite.
[2] Results adjusted for age, employment in hematite, and potential for commercial asbestos exposure
[3] Based on the lower, middle and upper one-third of the case exposure distribution
[4] Results adjusted for age, employment in hematite, potential for commercial asbestos, and exposures in other zones. Cases and controls may have worked in more than one zone.

VII. Taconite Workers Health Study
Lung Cancer Case-Control Study (component summary)

A case-control study of lung cancer was performed to further examine the association between employment duration, elongate mineral particle (EMP) exposure and silica exposure in the taconite mining industry. The full report for this study is in Appendix 7. The study of lung cancer was nested within a cohort of Minnesota taconite iron mining workers employed by any of the seven mining companies in operation in 1983. Lung cancer cases were identified by vital records and cancer registry data through 2010. Two age-matched controls were selected from risk sets of cohort members alive and lung cancer free at the time of case diagnosis. Calendar time specific exposure estimates were made for each similarly exposed job group (SEG) and used to estimate workers cumulative exposures. Odds ratios (OR) and 95% confidence intervals (CI) were estimated using logistic regression. Lung cancer risk was evaluated by total time worked, and cumulative EMP and silica exposure modeled continuously and by quartile.

A total of 1,706 cases, each matched to approximately two controls, were included in the analysis (Table VII-1). After adjusting for work in hematite mining, asbestos exposure, silica exposure and sex, the OR for total duration of employment was 0.99 (95% CI: 0.96-1.01) (Table VII-2). The ORs for total exposure were 0.94 (95% CI: 0.89-1.01) for EMPs and 1.22 (95% CI: 0.81-1.83) for silica. The risk of lung cancer did not appear to change with increasing exposure when examined by quartiles (Table VII-2).

This study suggests that taconite mining exposures do not increase the risk for the development of lung cancer.

Table VII-1. Characteristics of cases and controls

	CASES (N=1706)	CONTROLS (N=3381)
	N (%)	**N (%)**
Sex		
Male	1637 (95.96)	3183 (94.14)
Female	69 (4.04)	198 (5.86)
Ore type		
Taconite only	668 (39.16)	1239 (36.67)
Hematite only	738 (43.26)	1530 (45.28)
Taconite & hematite	300 (17.58)	610 (18.05)
Ever worked by zone		
Zone 1	347 (20.34)	642 (18.99)
Zone 2	366 (21.45)	618 (18.28)
Zone 4	327 (19.17)	699 (20.67)
	Mean	**Mean**
Years of employment		
Taconite	7.67	8.52
Hematite	3.57	3.67
Years of taconite employment by zone		
Zone 1	7.38	7.60
Zone 2	5.41	7.11
Zone 4	8.81	9.27
(EMP/cc)-years		
Total	1.48	1.68
Zone 1	0.52	0.52
Zone 2	1.17	1.54
Zone 4	2.51	2.60
Silica (mg/m^3)-years		
Total	0.2809	0.3070
Years of employment by department		
Mining	1.28	1.36
Crushing	0.16	0.20
Concentrating	0.19	0.22
Pelletizing	0.25	0.23
Shop mobile	2.59	2.98
Shop stationary	0.68	0.71
Office	0.30	0.65
Missing/unknown	0.48	0.46
General mine	0.69	0.47
General plant	0.38	0.44
General shop	0.68	0.79

Table VII- 2. Risk of lung cancer by employment duration, cumulative EMP, and cumulative silica exposure

	OR	95% CI
Employment duration		
Taconite years[a]	0.99	0.96-1.01
Hematite years[b]	0.99	0.98-1.01
Duration by Department[c]		
Mining	0.99	0.97-1.01
Crushing	0.96	0.88-1.05
Concentrating	0.99	0.93-1.06
Pelletizing	1.02	0.97-1.07
Shop Mobile	0.99	0.98-1.01
Shop Stationary	1.01	0.98-1.05
Office	0.95	0.92-0.99
Total Exposure		
EMP/cc/years[a]	0.95	0.89-1.01
Silica mg/m^3/years[d]	1.22	0.81-1.83
EMP/cc/years quartiles[e]		
Q1	1	
Q2	1.00	0.79-1.25
Q3	0.98	0.77-1.24
Q4	0.82	0.57-1.19
Unexposed[f]	0.81	0.67-0.98
Silica mg/m^3/years quartiles[g]		
Q1	1	
Q2	1.04	0.84-1.29
Q3	0.95	0.74-1.22
Q4	0.97	0.70-1.35
Unexposed[f]	0.81	0.68-0.98

a Adjusted for hematite exposure, silica exposure, asbestos exposure, and gender
b Adjusted for taconite exposure, silica exposure, asbestos exposure, and gender
c Adjusted for years in unknown SEGs, hematite, general mine, general plant, general shop, gender, and asbestos
d Adjusted for taconite exposure, hematite exposure, asbestos exposure, and gender
e Lower cut point for Q1-4 = 0, 0.1298, 0.4527, and 2.353 EMP/cc/years
f Worked only in hematite production and did not have taconite exposure
g Lower cut point for Q1-4 = 0, 0.0373, 0.2064, 0.5189 mg/m^3/years

VIII. Taconite Workers Health Study
Respiratory Health Survey (component summary)

The goal of the Respiratory Health Survey (RHS) was to assess non-malignant respiratory disease (NMRD) by the degree of lung function impairment (spirometry) and anatomical abnormality (chest x-ray) that existed within taconite workers and spouses. In general, the results from this investigation are useful for assessing the prevalence of lung abnormalities and functional impairment in workers and spouses, who could have "take home" exposures. The full report for the RHS is contained in Appendix 8.

This study assessed a common lung ailment, NMRD, also known as pneumoconiosis, determined on the basis of chest x-ray and spirometry findings. Measured exposure information to elongate mineral particles (EMPs), silica and respirable dust was available from the prior exposure assessment (Hwang *et al.*, 2013, 2014; Appendix1, 2, 3). Since NMRD is not contained in any of the public data bases collected by the Minnesota Department of Health, this approach required the collection of information by the study research team. A cross-sectional screening of current and former workers and their spouses was undertaken in Virginia, MN in 2010-11. Spouses were included because of reports in the medical literature concerning spousal risk and occupational dust exposure through take home exposure. Each participant filled out a detailed occupational and health questionnaire which included information on where they worked, when they worked and which job they had. The type of work prior to the taconite industry job was also included in the questionnaire, as was a smoking history. Based on the work history, calendar time specific exposure estimates were made for every job and used to estimate workers' cumulative exposures. Rate ratios (RR) and 95% confidence intervals were estimated using Poisson regression for duration worked and cumulative exposure for all exposure types.

There were 1188 workers and 496 spouses who participated in the complete screening (medical history, pulmonary function testing and chest x-ray). There were another 134 individuals who filled out the medical questionnaire but who did not participate in the medical testing. The total number of participants was 1818. A random sample of 3310 workers was invited to participate. Non-response is being investigated further but it is known that those individuals who were younger and who lived further than 2 hours away participated at lower frequencies than older workers who lived closer. This is likely because of work responsibilities of younger workers as well as distances required to get to the testing facility, which in some cases could have been over three hours by car.

Within the workers, restrictive lung function on spirometry, the type of abnormality associated with dust exposure, occurred in 4.5 % of those screened. Obstructive lung function occurred in 16.8% with another 2.9% having mixed (obstructive and restrictive) function. Chest x-ray abnormalities, defined by a consensus of two B-readers, suggested that parenchymal abnormalities ($\geq$ 1/0), as seen in dust-exposure, occurred in 5.4% of those screened with another 16.7% with pleural abnormalities. Spousal chest x-rays showed 0.6% parenchymal findings, and 4.5% pleural abnormalities. Spousal findings compare to other descriptions of pleural abnormalities in the non-working population of western countries, which have been described to be in the range of 1-6.8%[3].

Cumulative silica and cumulative respirable dust exposures, determined with onsite and historical exposure estimates, were not associated with spirometry or chest x-ray abnormalities. Exposure to EMP was associated with pleural abnormalities, suggesting the likely exposure to asbestiform EMPs in the past. For workers who were employed in the industry over 21 years the rate of pleural abnormalities increased by 60%, compared to those working less than 21 years. Pleural abnormalities had a graded response to years employed in the industry, with the rate ratio increasing to 1.84 (95% CI=1.11-3.07) for working 35 or more years (Table VIII-1). For workers with cumulative EMP exposure greater than the median, the rate of pleural abnormalities nearly doubled (RR=1.93, 95% CI=1.32-2.83) (Appendix 8).

In summary, this survey of taconite workers and spouses demonstrated increased findings of both pleural and parenchymal abnormalities in workers compared to spouses. Spousal risk for lung disease appeared to be comparable to what would be expected in the general population. Despite the lack of association with estimated cumulative silica and respirable dust, the parenchymal findings on chest x-ray are consistent with exposure to a mixed mineral dust. Worker abnormalities for pleural disease were related to length of employment in the taconite industry and to EMP exposure. The specific type of EMP exposure could not be determined in this evaluation. The pleural findings were not specific to mineralogical zone.

(3) Hillerdal G. Pleural plaques: incidence and epidemiology, exposed workers and the general population: a review. Indoor and Built Environment 1997, 6:86-95.

Table VIII-1. Pleural abnormality associated with duration of taconite employment (years) and duration of taconite employment in each Iron Range Zone

Exposure	Abnormalities Yes/No	Pleural RR[d]	Pleural 95%CI
Overall Employment[b]			
Employment duration	198/980	1.02	1.00-1.04
Hematite	15/43	1.01	0.95-1.07
Duration Quartile[b]			
0 < years < 21	40/342	1.00	---
21 to < 30	50/248	1.39	0.86-2.26
30 to < 35	57/218	1.65	1.02-2.65
35+ years	51/172	1.84	1.11-3.07
Zone Analysis[c]			
Employment duration-Zone 1	116/606	1.02	1.0-1.04
Employment duration-Zone 2	73/339	1.03	1.01-1.05
Employment duration-Zone 4	45/248	1.01	0.99-1.03

a Pleural abnormality defined as abnormality consistent with pneumoconiosis.
b Results adjusted for age, gender, BMI, smoking status, hematite years, and outside occupation with high probability of asbestos exposure
c Results adjusted for age, gender, BMI, smoking status, hematite years, outside occupation with high probability of asbestos exposure, and duration in other zones
d Rate ratio is interpreted as the relative increase in the frequency of abnormality associated with a one unit increase in the exposure for continuous measures of exposure, e.g.) years of employment, or compared to the reference category (designated as 1.0).

Appendices

The following manuscripts are included in the Legislative Report. They are in various stages of publication, as indicated below. The papers to be submitted will have additional editing before publication, but are not expected to differ substantively. At the time of this report, first authors are listed as the graduate students working on the respective studies.

Appendix 1. Published paper: Comprehensive Assessment of Exposures to Elongate Mineral Particles in the Taconite Mining Industry (Hwang *et al.,* 2013)

Appendix 2. Published paper: The Relationship between Various Exposure Metrics for Elongate Mineral Particles (EMP) in the Taconite Mining and Processing Industry (Hwang *et al.*, 2014)

Appendix 3. To be submitted: A Comprehensive Assessment of Present-Day Exposures to Respirable Dust and Silica in the Taconite Mining Industry (Hwang *et al.*)

Appendix 4. Published paper: Mortality Experience among Minnesota Taconite Mining Industry Workers (Allen *et al.*, 2014)

Appendix 5. To be submitted: Cancer Incidence among Minnesota Taconite Mining Industry Workers (Allen *et al.*)

Appendix 6. To be submitted: A Case-Control Study of Mesothelioma in Taconite Miners Exposed to Elongate Mineral Particles (EMPs) (Lambert *et al.*)

Appendix 7. To be submitted: Lung Cancer Risk among Minnesota Taconite Mining Workers (Allen *et al.*)

Appendix 8. To be submitted: Medical Screening and Exposure Assessment of Current and Former Workers in the Taconite Industry of Minnesota and Spouses (Odo *et al.*)

Appendix 1

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Comprehensive Assessment of Exposures to Elongate Mineral Particles in the Taconite Mining Industry

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Since the 1970s, concerns have been raised about elevated rates of mesothelioma in the vicinity of the taconite mines in the Mesabi Iron Range. However, insufficient quantitative exposure data have hampered investigations of the relationship between cumulative exposures to elongate mineral particles (EMP) in taconite dust and adverse health effects. Specifically, no research on exposure to taconite dust, which includes EMP, has been conducted since 1990. This article describes a comprehensive assessment of present-day exposures to total and amphibole EMP in the taconite mining industry. Similar exposure groups (SEGs) were established to assess present-day exposure levels and buttress the sparse historical data. Personal samples were collected to assess the present-day levels of worker exposures to EMP at six mines in the Mesabi Iron Range. The samples were analyzed using National Institute for Occupational Safety and Health (NIOSH) methods 7400 and 7402. For many SEGs in several mines, the exposure levels of total EMP were higher than the NIOSH Recommended Exposure Limit (REL). However, the total EMP classification includes not only the asbestiform EMP and their non-asbestiform mineral analogs but also other minerals because the NIOSH 7400 cannot differentiate between these. The concentrations of amphibole EMP were well controlled across all mines and were much lower than the concentrations of total EMP, indicating that amphibole EMP are not major components of taconite EMP. The levels are also well below the NIOSH REL of 0.1 EMP cc^{-1}. Two different approaches were used to evaluate the variability of exposure between SEGs, between workers, and within workers. The related constructs of contrast and homogeneity were calculated to characterize the SEGs. Contrast, which is a ratio of between-SEG variability to the sum of between-SEG and between-worker variability, provides an overall measure of whether there are distinctions between the SEGs. Homogeneity, which is the ratio of the within-worker variance component to the sum of the between-worker and within-worker variance components, provides an overall measure of how similar exposures are for workers within an SEG. Using these constructs, it was determined that the SEGs are formed well enough when grouped by mine for both total and amphibole EMP to be used for epidemiological analysis.

Keywords: elongate mineral particles; exposure assessment; exposure variability; fiber measurement; similar exposure groups; taconite

INTRODUCTION

Since the 1970s, concerns about occupational health have intensified in both the taconite mining industry and the communities adjacent to the mines in the Mesabi Iron Range in north-eastern Minnesota (Axten and Foster, 2008; Wilson *et al.*, 2008). Minnesota counties in the vicinity of taconite mining operations have been found to have elevated age-adjusted rates for mesothelioma (Case *et al.*, 2011). The elevated rates challenge conventional understanding because mineralogical data

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suggest that the ore body comprised primarily non-asbestiform cleavage fragments which have not been thought to have high potential for disease (Berry and Gibbs, 2008; Gamble and Gibbs, 2008; Mossman, 2008). For the last three decades, ongoing and unresolved concerns about health risks from taconite mining have been driven, in part, by limited epidemiological assessments and insufficient quantitative exposure data. Concerns about the elevated rates of mesothelioma in the Mesabi mining cohort led to epidemiological investigations evaluating the relationship between cumulative exposures to components of taconite dust and mesothelioma, lung cancer, and non-malignant respiratory disease. However, no research on exposure to taconite dust, which includes elongate mineral particles (EMP), has been conducted since 1990 (Sheehy and McJilton, 1990).

The results presented here are part of a larger epidemiological study assessing the respiratory health effects of exposure to components of taconite dust. This article describes our approach to comprehensively assess present-day exposure levels to total and amphibole EMP in the taconite mining industry. The term 'total EMP' refers to any mineral particle with a minimum aspect ratio of 3:1 that is of inhalable, thoracic, or respirable size, while the term 'amphibole EMP' refers to a subset of double chain silicate minerals (crocidolite, amosite, anthophyllite, tremolite, and actinolite) that can be asbestiform or non-asbestiform (NIOSH, 2011). Asbestiform EMP are likely to be thinner, longer, and more flexible than non-asbestiform EMP, with layers parallel to those from 'native (unprocessed) samples' (Addison and McConnell, 2008). Although the chemical composition of asbestiform and non-asbestiform EMP can be the same, they differ in their 'habit' or morphology (Langer *et al.*, 1979).

The first and most critical step of our exposure assessment involves the classification of workers into similar exposure groups (SEGs). SEGs can be used to efficiently assess exposure levels based on job titles, locations, tasks, and procedures rather than individual workers (Bullock and Ignacio, 2006). Workers who have similar exposure profiles and whose tasks involve similar procedures and materials are grouped together in a single SEG. The success of a grouping strategy depends on the between-group variability, between-worker variability, and within-worker variability. To reduce exposure misclassification errors in subsequent epidemiological studies, it is important that the exposure distributions of SEGs be distinct from each other and homogeneous within (Kromhout and Heederik, 1995). This requires a detailed characterization of between-SEG and within-SEG exposure variability. However, the sparseness of the available historical exposure data precludes such an analysis for taconite workers. A detailed assessment of present-day exposure levels was carried out to understand exposure variability, which enabled the development of better-formed SEGs.

The mineralogy of the Mesabi Iron Range changes from east to west, with the three taconite mining companies owning five operating mines in the western and one in the eastern zone. Amphiboles are mainly detected in the east. Phyllosilicates such as minnesotaite, greenalite, and stilpnomelane, which are not regulated as asbestiform or amphibole EMP, dominate the west (McSwiggen and Morey, 2008; Zanko *et al.*, 2008). The amphiboles in the east are principally of the cummingtonite–grunerite series and include some actinolite (ferroactinolite). Amphiboles and phyllosilicates form two distinct groups of minerals, defined by fundamental differences in their internal crystalline structure. The structure of phyllosilicates is based on sheets of linked silicon tetrahedra. Fibers of phyllosilicate minerals are created when these sheets curl to form tubes. The crystalline structure of amphiboles is based on chains of silicon tetrahedra. The silicate minerals that form EMP have different morphologies in the east; however, the vast majority of the amphiboles are non-asbestiform EMP (Wilson *et al.*, 2008; Zanko *et al.*, 2008). Due to the distinct metamorphic mineralogical characteristics of the eastern versus the western zones, workers in the two zones may potentially be exposed to different types of EMP.

The goals of this article are (i) to assess the present-day levels of exposure to EMP in the taconite industry across the two mineralogical zones, (ii) to estimate the between-SEG, between-worker, and within-worker components of variability in EMP exposures, (iii) to use the components of variability to assess whether the SEG are distinct from each other and relatively homogeneous within, and (iv) to evaluate the impact of variability on the exposure estimates for the SEGs that will be used in the epidemiological studies. We also examined whether SEGs developed for total EMP are valid for amphibole EMP and if the same set of SEGs can be used for workers in the mineralogically distinct eastern and western zones of the Mesabi Iron Range.

METHODS

Formation of SEGs

For this study, we derived job titles from four sources: (i) records maintained by the Mine Safety and Health Administration that listed approximately 190 job titles; (ii) information from a previous University of Minnesota study by Sheehy (1986) that listed 140 job titles; (iii) industrial hygiene and human resources databases maintained by the three companies currently operating mines in the Mesabi Iron Range (U.S. Steel, Cliffs Natural Resources, Arcelor Mittal), which listed approximately 150 job titles; and (iv) *Job Descriptions and Classifications* published by the Reserve Mining Company (1974), which contained 142 job titles. Using information on the tasks and processes related to these job titles, we created a set of 60 SEGs. This list was further condensed to 28 SEGs using the subjective professional judgments of the lead industrial hygienists at the three mining companies. The number of job titles represented in each SEG ranged from 1 to 19. The final list contained 181 job titles, forming 28 SEGs that we further grouped into 7 departments. Due to the distinct mineralogical characteristics of the eastern versus the western zones, the SEGs for the eastern and western zones were considered separately.

Sampling design and data handing

Personal exposure assessment was conducted across all operating mines in both zones of the Mesabi Iron Range, beginning in January 2010 and ending in May 2011. The purpose of the personal sampling was to assess the present-day levels of worker exposures to EMP in the taconite mining industry. The researchers and representatives from each of the three mining companies discussed workers' schedules to identify potential participants prior to the day of sampling. At the beginning of the work shift on each sampling day, the researchers explained the purpose of the study to the potential participants and presented them with the consent form approved by the University of Minnesota Institutional Review Board (IRB code: 0901M58041).

To perform a baseline exposure profile for a job title, the American Industrial Hygiene Association sampling strategy by Bullock and Ignacio (2006) recommends a minimum of six data points per SEG and recommends 8–10. Two workers per SEG were selected for personal EMP sampling in the eastern zone and each worker was sampled during three different shifts. In the western zone, approximately eight workers per SEG were chosen, with each worker being sampled on three different shifts. For the SEGs in the western zone, the eight workers were drawn from five different mines. This design allows the estimation of between- and within-SEG, between- and within-mine, between- and within-zone, and within-worker variance components.

Each consenting participant wore a personal air-sampling pump (Apex Pro pump, Casella Inc., Amherst, NH, USA) on his or her waist, with the sampler located in the breathing zone, for approximately 6 h during the work shift. Six hours accounts for at least 70% of a daily work shift. Personal sampling for each worker was completed during three different work shifts, though not necessarily on consecutive days.

EMP sampling was conducted using a mixed cellulose ester membrane filter, 25 mm in diameter with 0.8 μm pores. The filter was placed in a polycarbonate membrane cassette with a conductive extension cowl of 50 mm. The flow rate for the EMP sampling pump was set at the lowest available flow rate per pump to avoid overloading the filter (range 0.65–0.95 l min^{-1}). As a further precaution against overloading, the polycarbonate membrane cassettes usually were changed at the end of about the first 3 h of sampling. Overall, 18 samples were excluded because they either were overloaded particles or had damaged filter. Exceptions were made if the participants had a conflict in their work schedule or the researchers decided not to change the cassettes due to lower expected particle exposure levels for some samples (e.g. warehouse technician, office staff).

Analytical methods and limitations

The personal filter samples were analyzed by phase contrast microscopy (PCM) using National Institute for Occupational Safety and Health (NIOSH) method 7400 (NIOSH, 1994a), which identifies all EMP longer than 5 μm with an aspect ratio ≥3.0 (Counting Rules A). While this method can be used to count the number of EMP, it cannot differentiate between asbestiform and non-asbestiform EMP. While it is commonly stated that NIOSH 7400 cannot identify EMP with a width less than 0.25 μm (NIOSH, 1994a), this depends on the refractive index of the EMP (NIOSH, 2011). If the refractive index does not differ from the substrate material or the counting medium, the resolution is low, and vice versa (Kenny and Rood, 1987). Rooker *et al.* (1982) have shown that under proper calibration and use of appropriate mounting media, EMP with widths of 0.15 µm were measured using PCM. Kenny and Rood (1987) measured widths of 0.125 µm under PCM.

In contrast, the NIOSH method 7402 by transmission electron microscopy (TEM; NIOSH, 1994b) is used to identify EMP that meet the PCM counting criteria. This method includes expanded characterization of elemental composition with energy dispersive X-ray analysis and crystalline structure by selected area electron diffraction. Therefore, it can identify EMP that are amphiboles or chrysotile. While laboratories typically claim to distinguish between asbestiform and non-asbestiform EMP using TEM, a more conservative assessment is that this method can identify amphibole versus non-amphibole EMP (in addition to chrysotile EMP), especially in the heterogeneous mixture of particles found in the taconite industry in Minnesota.

As indicated previously, two samples per work shift were collected for most participants on three different days. The results from the two samples were combined to calculate a single time-weighted average concentration for the shift for each participant. While all personal EMP samples were analyzed using NIOSH 7400, at least one sample per worker was randomly chosen to be analyzed using NIOSH 7402. Thus, while all of the filter samples underwent analysis using NIOSH 7400, ~18% of the samples underwent additional analysis using NIOSH 7402. For the NIOSH 7402 analysis, samples were analyzed by indirect preparation, which included suspension in solution, sonication, and re-filtration. For all personal samples, we used only one-fourth or half of the filter depending on the analysis methods chosen, and the remaining three-forth or half has been archived at the University of Minnesota.

Table 1 lists the number of personal samples analyzed using both NIOSH 7400 and NIOSH 7402 for each mine and zone. In addition, one blank sample per sampling day was obtained for NIOSH 7400 quality control for a total of 243. Further, one blank sample per NIOSH 7402 sampling day was obtained for quality control for a total of 66. Table 1 also shows the percentage of samples with EMP levels that fell below the limit of detection (LOD), as measured by NIOSH 7400 and NIOSH 7402. Overall, many of the samples had levels less than the LOD, especially the NIOSH 7402 samples in the western zone. If all the measurements for a given SEG were below the LOD, summary statistics such as the arithmetic and geometric means (GM) and geometric standard deviations (GSD) were not reported. If at least one sample for an SEG in a particular mine was above the LOD, then summary statistics were calculated by assuming that censored data were represented by one half of the LOD.

Only three chrysotile asbestiform EMP (0.24% of all EMP samples) were identified by the NIOSH 7402 analysis. These were excluded from our analyses, leaving only amphibole—specifically cummingtonite–grunerite and actinolite—and non-amphibole EMP in our data set. Using the NIOSH 7400 and 7402 results, average concentrations of EMP identified as total and amphibole for each SEG in each mine were calculated. This estimate was then applied to all of the NIOSH 7400 samples for that SEG in that mine to obtain personal exposure levels to NIOSH 7402 amphibole EMP when the samples had at least one value above LOD for that SEG.

Table 1. Number of personal samples and percent of samples less than LOD by mine and mineralogical zone.

Zone	Mine	Workers	Samples analyzed by PCM[a]	% <LOD by PCM	Samples analyzed by TEM[b]	% <LOD by TEM
Eastern	A	56	266	7.1	102	68.6
Western	B	34	197	68.5	34	100.0
	C	38	218	53.2	36	100.0
	D	34	203	37.0	34	100.0
	E	48	267	20.6	47	100.0
	F	22	129	48.8	22	100.0
Total		232	1298	—	275	—

[a]Personal samples analyzed by NIOSH 7400 PCM, counting all EMP with length >5 µm and aspect ratio >3.0.
[b]Personal samples analyzed by NIOSH 7402 TEM, counting only amosite, non-amosite and chrysotile EMP with length >5 µm and aspect ratio >3.0.

$$C_{ij}(\text{NIOSH 7402, amphibole EMP}) = C_{ij}(\text{NIOSH 7400, total EMP}) \times \frac{\overline{C_i}(\text{NIOSH 7402, amphibole EMP})}{\overline{C_i}(\text{NIOSH 7400, total EMP})} \quad (1)$$

for C, concentration (particles per cubic centimeter); $\overline{C}$, average concentration (particles per cubic centimeter); i, SEG in a mine; j, observation.

Statistical analysis methods

Of the 28 SEGs, 27 SEGs were monitored. We were not able to monitor the Janitor SEG because all janitors in the current taconite mining industry are independent contractors and not employed by the mining companies. A *t*-test was used to determine which SEGs differed between the two zones for each EMP classification (Table 2). Of the 27 SEGs, 21 were present in both zones for statistical evaluations. To ensure that at least one of the 27 SEGs is different from the others and that the exposures within each SEG are homogeneous, two different approaches were used to evaluate the variability of exposure between SEGs, between workers, and within workers.

One-way analysis of variation. We used a simple one-way analysis of variation (ANOVA) model to compare the log-transformed estimated exposures Y_{ij} of each SEG.

$$Y_{ij} = \log(X_{ij}) = \mu_y + \alpha_i + \varepsilon_{ij} \text{ for } i = 1, 2, \ldots, 27, \text{ and } j = 1, 2, \ldots, 24 \quad (2)$$

where X_{ij} = exposure concentration of the ith SEG at the jth observation for each SEG, μ_y = overall mean of Y_{ij}, α_i = random deviation of the ith SEG's true exposure from μ_y, and ε_{ij} = random deviation of the jth observation from the ith SEG's true exposure. Equation (2) assumes that the ε_{ij} is independently and identically distributed with a normal distribution. This model was used to determine if the differences between the SEGs were statistically significant. A pairwise comparison of the SEGs was used to identify which SEGs were significantly different from each other.

Contrast and homogeneity. Kromhout and Heederik (1995) proposed a two-way nested random-effects ANOVA model for estimating between-SEG, between-worker, and within-worker variance components using the log-transformed exposure concentrations. The variance components were constructed using PROC NESTED with a nested structure of data set as follows:

$$Y_{ikn} = \log(X_{ikn}) = \mu_y + \alpha_{ik} + \beta_{ikn} + \varepsilon_{ikn} \text{ for the observations } i = 1, 2, \ldots, 27, k = 1, 2, \ldots, 4; \text{ and } n = 1, 2, \ldots, 6 \quad (3)$$

where X_{ikn}, nth observation of exposure concentration for the kth worker of the ith SEG; μ_y, overall mean of Y_{ikn}; α_i, random deviations of the ith SEG's true exposure from μ_y; β_{ik}, random deviations of the ith SEG's kth worker's true exposure from $\mu_{y,i}$ (mean exposure of the ith SEG); and ε_{ikn}, random deviations of the nth observation for the ith SEG's kth worker from $\mu_{y,ik}$ (mean exposure of the kth worker in the ith SEG). The random deviations (α_i, β_{ik}, and ε_{ikn}) are assumed to be normally distributed with zero means and variances (σ^2_α, σ^2_β, and σ^2_ε, respectively). These variances are mutually uncorrelated and estimated as variance components ($S^2_{y\text{BG}}$, $S^2_{y\text{BW}}$, and $S^2_{y\text{WW}}$, respectively).

According to Kromhout and Heederik (1995), contrast (ε) is a ratio of between-SEG variability to the sum of between-SEG and between-worker (i.e. within SEG) variability and provides an overall measure of whether there are distinctions between the SEGs and is given as follows:

$$\text{Contrast}(\varepsilon) = \frac{S^2_{y\text{BG}}}{S^2_{y\text{BG}} + S^2_{y\text{BW}}} \quad (4)$$

When the between-SEG variance component ($S^2_{y\text{BG}}$) approaches 0, the contrast value approaches 0, indicating that the SEGs are similar and not distinct from each other. When the between-worker variance component within the SEG ($S^2_{y\text{BW}}$) approaches 0, the contrast value approaches 1, indicating that between-SEG variability are dominant and implying that at least one SEG is distinct from the others.

Analogously, we can define homogeneity (η) to provide an overall measure of how similar the exposures are for workers within an SEG. It is defined as the ratio of the within-worker variance component to the sum of the between-worker and within-worker variance components, and is given as follows:

Table 2. Arithmetic mean (particles per cubic centimeter) in each zone and *t*-test results (*P* value) by EMP classification for each SEG.

Department	SEG	Total EMP (particles cm^{-3})			Amphibole EMP (particles cm^{-3})		
		East	West	*P* value	East	West	*P* value
Mining	Basin operator	—	0.053	—	—	<LOD	—
	Mining operator 1	**0.065**	**0.015**	**<0.0001**	<LOD	<LOD	NA
	Mining operator 2	**0.097**	**0.031**	**0.0016**	0.004	<LOD	NA
	Rail road	0.072	—	—	<LOD	—	—
Crushing	Crusher maintenance	**0.194**	**0.044**	**<0.0001**	0.026	<LOD	NA
	Crusher operator	**0.193**	**0.038**	**<0.0001**	0.030	<LOD	NA
	Operating technician	**0.341**	**0.014**	**<0.0001**	0.110	<LOD	NA
Concentrating	Concentrator maintenance	**0.207**	**0.058**	**<0.0001**	0.030	<LOD	NA
	Concentrator operator	**0.176**	**0.023**	**<0.0001**	0.024	<LOD	NA
Pelletizing	Balling drum operator	0.050	0.077	0.9371	0.010	<LOD	NA
	Dock man	**0.206**	**0.085**	**0.0014**	0.020	<LOD	NA
	Furnace operator	**0.066**	**0.040**	**0.0141**	0.015	<LOD	NA
	Pelletizing maintenance	0.067	0.073	0.0852	<LOD	<LOD	NA
	Pelletizing operator	0.109	0.095	0.1739	0.014	<LOD	NA
Shop (mobile)[a]	Boiler technician	—	0.041	—	—	<LOD	—
	Carpenter	—	0.064	—	—	<LOD	—
	Electrician	**0.309**	**0.077**	**<0.0001**	0.063	<LOD	NA
	Lubricate technician	**0.145**	**0.033**	**0.0006**	0.016	<LOD	NA
	Maintenance technician	0.043	0.031	0.0919	<LOD	<LOD	NA
	Pipefitter/Plumber	—	0.048	—	—	<LOD	—
	Repairman	—	0.064	—	—	<LOD	—
	Supervisor	0.064	0.045	0.3246	0.012	<LOD	NA
Shop (stationary)[b]	Auto mechanic	**0.118**	**0.023**	**<0.0001**	<LOD	<LOD	NA
	Lab analyst	**0.114**	**0.030**	**<0.0001**	<LOD	<LOD	NA
	Warehouse technician	0.018	0.041	0.3243	0.004	<LOD	NA
Office/control room	Control room operator	0.021	0.017	0.5269	<LOD	<LOD	NA
	Office staff	0.009	0.016	0.0546	<LOD	<LOD	NA

Numbers in **boldface** indicate statistically significant differences between eastern and western zone ($P < 0.05$).
<LOD, samples containing LOD; NA, data containing LOD in either one of two zones.
[a]Shop (mobile) refers to those SEGs whose work is more likely done in multiple places in the plants.
[b]Shop (stationary) refers to those SEGs whose work is more likely done in a single workplace.

$$\text{Homogeneity } (\eta) = \frac{S^2_{y\text{WW}}}{S^2_{y\text{BW}} + S^2_{y\text{WW}}} \tag{5}$$

When the within-worker variance component ($S^2_{y\text{WW}}$) is small compared with the between-worker variability, homogeneity approaches 0, indicating that the exposures of the workers within each SEG are heterogeneous. When the between-worker variance component ($S^2_{y\text{BW}}$) is small, homogeneity approaches 1.

The statistical analyses were conducted for total and amphibole EMP. Significance was defined by *P* values of 0.05 or lower. All analyses reported here were conducted using SAS version 9.3 (SAS Institute, Cary, NC, USA).

RESULTS

The results of *t*-tests used to determine the differences between the zones by SEG are shown in Table 2. When a SEG was not present in both zones, the *P* value could not be calculated. Sixty-two percent (13 of 21) of the SEGs were significantly different between the zones for total EMP. For the amphibole EMP exposures in the western zone, all the data were less than the LOD. Additionally, eight SEGs in the eastern zone contained all data less than the LOD. Therefore, we did not test for differences between two zones for amphibole EMP. Both the total and amphibole EMP classifications had substantially different arithmetic mean exposures between the two zones. Only four SEGs (balling drum operator, pelletizing maintenance, warehouse technician, and office staff) were found to have higher total EMP exposures in the western zone, but none of these four were significantly different between the two zones ($P > 0.05$).

Total and amphibole EMP concentrations

The box plots in Fig. 1 show the total EMP concentrations by SEG across all mines. The concentration of total EMP in mine A tended to be higher than in the mines in the western zone. For most of the SEGs in the various mines, the arithmetic mean (the *X* in the box plot) was greater than the median (the middle line in the box plot), indicating a non-normal, skewed distribution.

Table 3 shows the GM and GSD of total EMP concentration by SEG in all mines. Table 4 summarizes the amphibole EMP concentration by SEG in the eastern zone (mine A). Since all amphibole EMP concentrations are less than the LOD in the western zone, we do not present the GM and GSD estimates. The GM for each SEG in mine A was markedly less for amphibole EMP than for total EMP.

The measured amphibole EMP concentrations by SEG across all mines are illustrated using scatter plots in Fig. 2. Figure 2 shows that, with a few exceptions in mine A, the concentrations of amphibole EMP were lower than the NIOSH Recommended Exposure Limit (REL) of 0.1 particles cm^{-3} for EMP by roughly an order of magnitude.

Comparison of EMP exposure differences

To explore the EMP exposure differences between the SEGs, a pairwise comparison of the SEGs within each mine was performed. The logarithms of the estimated EMP exposures were used in a simple one-way ANOVA model. In each mine, at least two of the SEG means were significantly different for total EMP ($P < 0.0005$).

Comparison of SEG variance components

Table 5 shows the between-SEG (S^2_{BG}), between-worker (S^2_{BW}), and within-worker (S^2_{WW}) variance components as absolute values and as percentage of total variance (sum of the three components), as well as the contrast (ε) and homogeneity (η) values for total EMP by mine in both geologic zones.

DISCUSSION

The available historical data on exposure of workers to taconite EMP are sparse and typically based on NIOSH 7400. They are insufficient for assessing exposure variability in any detail. Our detailed measurements allow for a study of the components of variance of exposure, that in turn, allows the creation of well-formed SEGs and reducing the likelihood of exposure misclassification (Nieuwenhuijsen, 1997; Ramachandran, 2005). Moreover, this analysis identifies notable heterogeneity of exposure to total EMP in the taconite mining industry.

Levels of total and amphibole EMP

This is the first study to report on the concentrations of total and amphibole EMP in the taconite mining industry. Overall, higher concentrations of total EMP were found in mine A, including the highest exposure of 2.2 particles cm^{-3}, ~ 22 times greater than the REL (0.1 particles cm^{-3}) for EMP. The lowest concentration of total EMP was found in mine F, and the total EMP exposure concentrations for all SEGs in this mine were lower than the NIOSH REL. The concentrations of amphibole EMP were much less than the concentrations of total EMP, indicating that amphibole EMP are not major components of taconite EMP. In general, the amphibole EMP concentrations were lower than the NIOSH REL, except for a few SEGs in mine A. Three individual measurements exceeded the NIOSH REL of the amphibole EMP.

Comparison of eastern and western zones

Overall, the exposure levels were higher in the eastern zone than in the western zone. The differences in the exposure levels support the idea of considering the SEGs in the eastern and western zones separately for the larger epidemiology study, and are consistent with the geological differences between the zones. For both total and amphibole EMP categories, the SEG with the highest exposure level in the eastern zone was operating technician (Table 2). In the western zone, the pelletizing operator was the SEG with the highest exposure levels for total EMP (Table 2). More than half of the SEGs had significantly different levels of total EMP exposures between the eastern and western

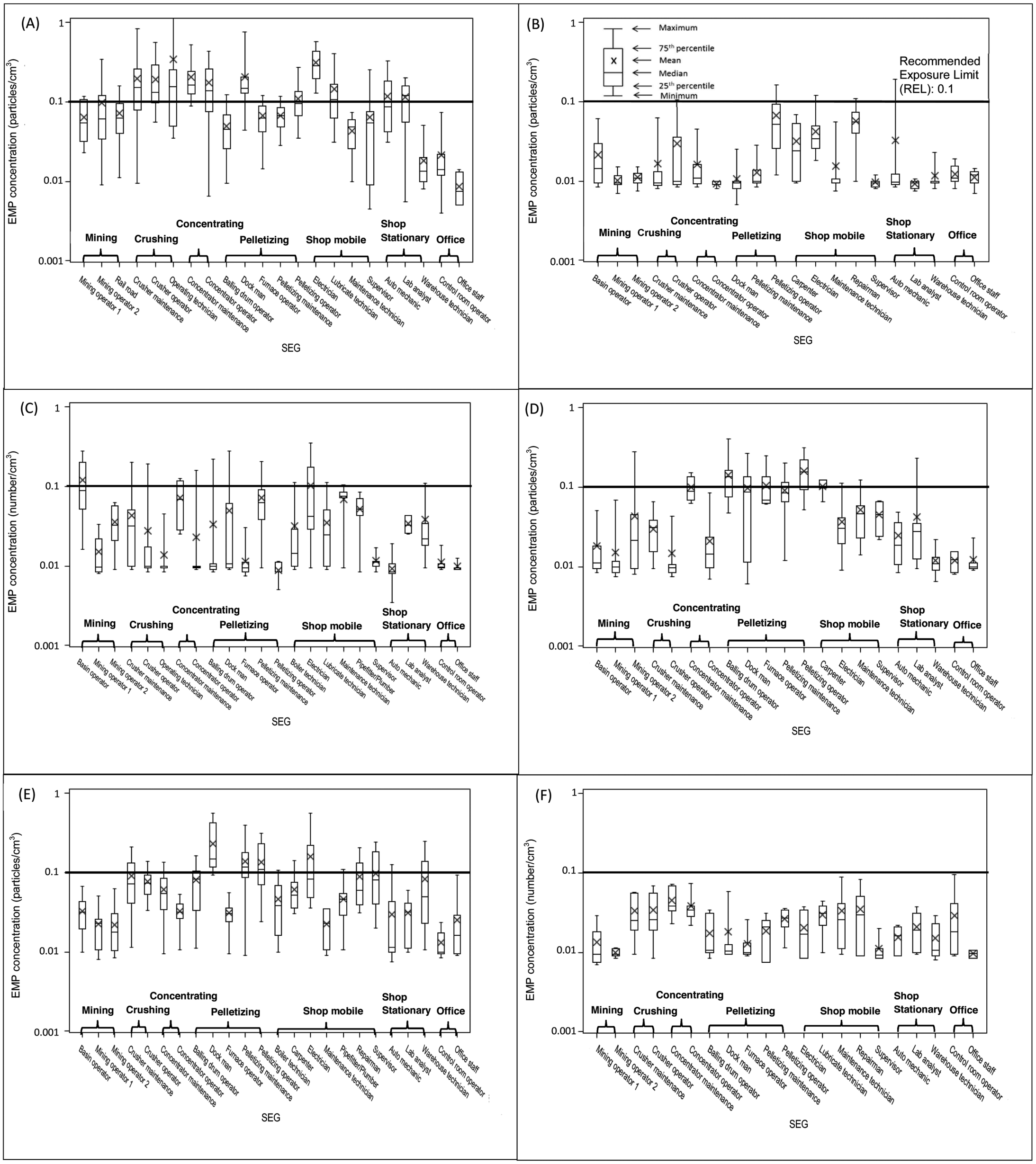

Fig. 1. Box plot of total EMP for each SEG in mines A–F (the horizontal line indicates the NIOSH REL for EMP = 0.1 particles cm^{-3}).

zones. This analysis provides empirical evidence that the geological differences between the two zones are reflected in EMP exposures.

The highest concentration in each mine was observed not only in departments directly involved in the mining process (mining, crushing, concentrating, and pelletizing departments) but also in the Shop (mobile) department, suggesting that the non-mining process may be similarly affected. The employees in the Shop (mobile) department work at various places in the mine, rather than at specific workstations. Therefore, the characteristics of the exposure levels for this department can be similar to those found in the mining process, and these SEGs potentially can have high exposure levels.

When the amphibole EMP concentrations are subtracted from the total EMP concentrations in the eastern zone, there remains a substantial excess

Table 3. Summary statistics of total EMP for each SEG measured in A–F mines (GM unit: particles per cubic centimeter).

Department	SEG	A		B		C		D		E		F	
		GM	GSD	GM	GSD	GM	GSD	GM	GSD	GM	GSD	GM	GSD
Mining	Basin operator	—	—	0.017	1.96	0.089	2.40	0.014	1.94	0.028	1.88	—	—
	Mining operator 1	0.054	1.96	0.010	1.25	0.013	1.80	0.012	1.81	0.019	1.78	0.012	1.76
	Mining operator 2	0.057	3.14	0.011	1.27	0.030	2.04	0.025	2.73	0.018	1.95	0.010	1.14
	Rail road	0.054	2.53	—	—	—	—	—	—	—	—	—	—
Crushing	Crusher maintenance	0.131	2.70	0.013	1.95	0.026	2.68	0.025	1.85	0.068	2.29	0.027	2.13
	Crusher operator	0.157	1.95	0.018	2.66	0.015	2.43	0.012	1.91	0.071	1.51	0.027	2.13
	Operating technician	0.140	3.53	—	—	0.012	1.67	—	—	—	—	—	—
Concentrating	Concentrator maintenance	0.180	1.71	0.013	1.77	0.060	2.01	0.093	1.42	0.048	2.16	0.042	1.57
	Concentrator operator	0.116	3.06	0.009	1.08	0.013	2.27	0.016	2.07	0.029	1.69	0.035	1.50
Pelletizing	Balling drum operator	0.042	1.90	—	—	0.015	2.79	0.119	1.77	0.063	2.23	0.015	1.86
	Dock man	0.155	2.12	0.010	1.48	0.024	3.28	0.049	4.48	0.187	1.88	0.014	2.04
	Furnace operator	0.056	1.94	—	—	0.010	1.45	0.091	1.65	0.028	1.64	0.012	1.49
	Pelletizing maintenance	0.061	1.56	0.012	1.45	0.057	2.14	0.077	2.00	0.103	2.57	0.016	1.98
	Pelletizing operator	0.094	1.77	0.050	2.32	0.009	1.39	0.140	1.72	0.104	2.21	0.024	1.52
Shop (mobile)[a]	Boiler technician	—	—	—	—	0.020	2.63	—	—	0.034	2.39	—	—
	Carpenter	—	—	0.023	2.50	—	—	0.100	1.26	0.054	1.65	—	—
	Electrician	0.279	1.62	0.036	1.71	0.057	3.06	0.029	2.04	0.104	2.51	0.017	2.06
	Lubricate technician	0.104	2.43	—	—	0.025	2.40	—	—	—	—	0.026	1.72
	Maintenance technician	0.036	2.04	0.012	1.80	0.054	2.66	0.041	2.15	0.019	1.85	0.025	2.32
	Pipefitter/Plumber	—	—	—	—	0.042	2.28	—	—	0.039	1.91	—	—
	Repairman	—	—	0.050	1.85	—	—	—	—	0.070	2.07	0.023	2.81
	Supervisor	0.034	3.70	0.010	1.17	0.011	1.29	0.041	1.64	0.073	2.22	0.011	1.39
Shop (stationary)[b]	Auto mechanic	0.086	2.34	0.015	2.85	0.009	1.48	0.020	2.12	0.019	2.49	0.015	1.49
	Lab analyst	0.093	2.23	0.009	1.14	0.033	1.28	0.026	2.41	0.025	2.06	0.018	1.91
	Warehouse technician	0.015	1.82	0.011	1.46	0.027	2.48	0.011	1.51	0.053	2.86	0.013	1.71
Office/control room	Control room operator	0.008	1.65	0.011	1.34	0.010	1.13	0.011	1.42	0.018	2.15	0.010	1.10
	Office staff	0.016	2.18	0.012	1.37	0.011	1.29	0.012	1.36	0.012	1.45	0.021	2.35

[a]Shop (mobile) refers to those SEGs whose work is more likely done in multiple places in the plants.
[b]Shop (stationary) refers to those SEGs whose work is more likely done in a single workplace.

of non-amphibole EMP concentration. This is significantly higher than the non-amphibole EMP concentration in the western zone for most SEGs. It is possible that this difference in non-amphibole oncentrations between the zones is related to the mineralogy. As described earlier, there are distinct metamorphic mineralogical differences between the zones. Phyllosilicates are prevalent in the western zone, while amphiboles are prevalent in the eastern zone. However, an analysis of how mineralogy affects the non-amphibole EMP concentration is beyond scope of this study.

Analysis of between-SEG and between-worker variabilities

The SEGs formed for this analysis identify workers with similar exposures; however, the exposures to EMP do not vary across all SEGs an only certain SEGs contribute significantly to variance. The between-SEG variance component was higher than the between-worker variance component in the eastern zone. Therefore, at least one of the SEGs is significantly different from the other SEGs in the eastern zone. However, the others may still not be distinguishable. Within the western zone, the between-SEG variance component was highest in mine D and the between-worker variance component was highest in mine F for total EMP.

Much higher contrast was observed in the eastern zone (0.740) than in the western zone (0.130). Since the western zone included five different mines, each SEG included exposures from five different mines, leading to higher between-worker (or within-SEG) variability, which in turn led to lower contrast. In particular, the between-SEG variance component was low in

Table 4. Summary statistics of amphibole EMP for each SEG measured in eastern zone (GM unit: particles per cubic centimeter).

Department	SEG	GM	GSD
Mining	Basin operator	—	—
	Mining operator 1	<LOD	<LOD
	Mining operator 2	0.003	2.62
	Rail road	<LOD	<LOD
Crushing	Crusher maintenance	0.019	2.11
	Crusher operator	0.023	2.07
	Operating technician	0.037	4.02
Concentrating	Concentrator maintenance	0.025	1.96
	Concentrator operator	0.015	3.11
Pelletizing	Balling drum operator	0.009	1.71
	Dock man	0.014	2.18
	Furnace operator	0.013	2.01
	Pelletizing maintenance	<LOD	<LOD
	Pelletizing operator	0.012	1.66
Shop (mobile)[a]	Boiler technician	—	—
	Carpenter	—	—
	Electrician	0.041	2.95
	Lubricate technician	0.012	2.27
	Maintenance technician	<LOD	<LOD
	Pipefitter/Plumber	—	—
	Repairman	—	—
	Supervisor	0.007	3.26
Shop (stationary)[b]	Auto mechanic	<LOD	<LOD
	Lab analyst	<LOD	<LOD
	Warehouse technician	0.004	1.60
Office/ Control room	Control room operator	<LOD	<LOD
	Office staff	<LOD	<LOD

[a]Shop (mobile) refers to those SEGs whose work is more likely done in multiple places in the plants.
[b]Shop (stationary) refers to those SEGs whose work is more likely done in a single workplace.

the western zone except mine D for total EMP. Across the five mines in the western zone, there was a wide range of contrast values (0.000–0.865 for total EMP). Contrast was zero in mine F for total EMP (Table 5). However, the smallest number of subjects was monitored and the fewest number of samples were taken at mine F. The variability for each SEG in mine F was also the least (GSD range: 1.10–2.81 for total EMP), as shown in Table 3. Interestingly, the percentage of the between-worker variance component was ~8% in mine D in the western zone, which led to high contrast regardless of the value of the between-SEG variance component.

The between-worker variance is the only component that affects both contrast and homogeneity. A smaller value for the between-worker variance component leads to higher contrast and homogeneity of the SEG and thus increases the ability to identify exposure differences between the SEGs. The between-worker variance component was lower in the eastern than in the western zone, a finding consistent with the lower contrast in the western zone.

The pattern of total EMP concentrations between-SEGs in each mine and the range of total EMP concentrations between-workers as displayed in the individual box plots were consistent with S^2_{BG} and S^2_{BW}, respectively (Fig. 1). For example, for total EMP, the pronounced fluctuation in the pattern of EMP concentrations between-SEGs in mine D is reflected in the highest S^2_{BG}, as shown in Fig. 1 and Table 5. Likewise, the stable pattern of EMP concentrations between-SEGs found in the mine F is reflected in the lowest S^2_{BG} for that mine.

Analysis of within-worker variability

Within-worker variability was higher in the eastern zone than the western. Although taconite

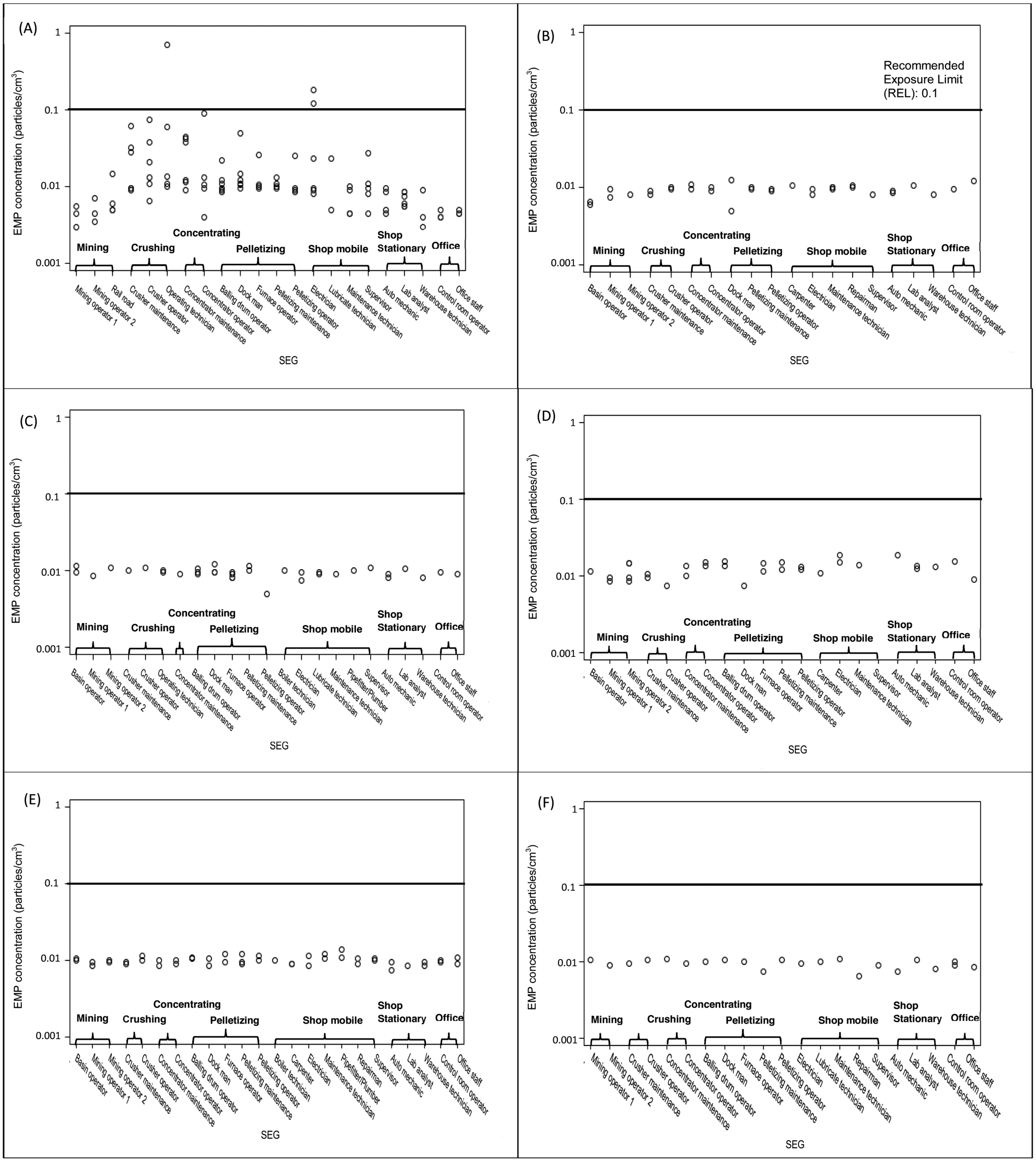

Fig. 2. Scatter plot of amphibole EMP for each SEG in mines A–F (the horizontal line indicates the NIOSH REL for EMP = 0.1 particles cm^{-3}).

processes are similar across all mines currently, the responsibilities for similar job classifications varied slightly between the mines due to the presence or absence of unionization, number of employees, and management. For instance, the workers at mine A, the sole mine in the eastern zone, are non-unionized, and the tasks performed by workers with the same job titles vary more depending on the work shift. Censored data, or values less than the LOD, also impact estimated within-worker variability. A higher percentage of values below the LOD were observed in the western zone, which led to the lower estimated within-worker variability.

The highest S^2_{WW} was observed in mine D and the lowest in mine B for total EMP. Overall, S^2_{WW} was

Table 5. Between-SEGs, between-worker, and within-worker variance components by mine and zone for total EMP.

Zone	Mine	Subject	Sample	BG		BW		WW		ε	η
				S^2_{BG}	%	S^2_{BW}	%	S^2_{WW}	%		
East	A	56	266	0.097	39.65	0.034	13.91	0.113	46.44	0.740	0.77
West	All	176	1014	0.021	8.69	0.142	58.24	0.081	33.07	0.130	0.36
	B	34	197	0.041	33.85	0.020	16.70	0.060	49.45	0.670	0.75
	C	38	218	0.038	19.17	0.076	37.76	0.086	43.07	0.337	0.53
	D	34	203	0.120	53.24	0.019	8.30	0.087	38.46	0.865	0.82
	E	48	267	0.054	28.85	0.069	36.80	0.065	34.36	0.439	0.48
	F	22	129	0.000[a]	0.00	0.204	76.39	0.063	23.61	0.000[a]	0.24

ε, contrast; η, homogeneity.
[a]Assuming that the use of the PROC NESTED model is appropriate, the negative variance components were treated as zero.

the dominant variance component compared to S^2_{BG} and S^2_{BW}, for total EMP for all mines except mines D and F. This finding indicates that the workers' daily tasks are the main source of variability rather than environmental influences. Higher homogeneity was found in the eastern zone than in the western.

Optimality of SEGs

Our results suggest that, in the eastern zone, the SEGs that we defined are formed well enough for total EMP. The pairwise comparison of SEGs between the two zones indicates that 62% of the SEGs had significantly different levels for total EMP. However, for the amphibole EMP, the *P* value for each SEG was not comparable due to LOD presented in either one or both zones. Specifically, the western zone had lower values for contrast and homogeneity than the eastern zone. The primary reason we have low contrast between-SEGs in the western zone is that all amphibole EMP exposure levels in the western zone were below the LOD.

As described earlier, department is a grouping variable that can be used as an alternative to SEG. Therefore, we also evaluated the variance components at the departmental level. However, the contrast and homogeneity values were lower than those calculated for the original SEGs. This finding reconfirmed that the original SEGs were as good as, if not better than, other possible grouping schemes that we considered and represent an appropriate level of analysis.

CONCLUSIONS

For many SEGs in several mines, the exposure levels of total EMP were higher than the REL for EMP. However, the total EMP classification does not necessarily refer to regulated asbestiform EMP because the NIOSH 7400 cannot differentiate between asbestiform and non-asbestiform EMP. The concentrations of amphibole EMP were well controlled across all mines and were much lower than the concentrations of total EMP, indicating that amphibole EMP are not major components of taconite EMP. Overall, we found that the variability of each SEG across mines was small for both total and amphibole EMP. Theoretically, the variability in the eastern zone should have been lower than the western as it consists of only one mine as opposed to five. However, due to the low concentration of EMP (often below LOD), we found lower variability in the western zone. When we compared zones, higher values for contrast and homogeneity were observed in the eastern zone. While low contrast and homogeneity was observed for the western zone taken as a whole, higher values were observed when these parameters were calculated for each mine. We conclude that the SEGs that we defined are appropriate for use in an epidemiological study when grouped by mine for total EMP.

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REFERENCES

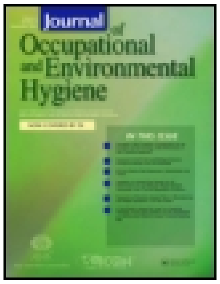
Addison J, McConnell EE. (2008) A review of carcinogenicity studies of asbestos and non-asbestos tremolite and other amphiboles. Regul Toxicol Pharmacol; 52(1 Suppl.): S187–99.

Axten CW, Foster D. (2008) Analysis of airborne and waterborne particles around a taconite ore processing facility. Regul Toxicol Pharmacol; 52(1 Suppl.): S66–72.

Berry G, Gibbs GW. (2008) An overview of the risk of lung cancer in relation to exposure to asbestos and of taconite miners. Regul Toxicol Pharmacol; 52(1 Suppl.): S218–22.

Bullock W, Ignacio J. (2006) A strategy for assessing and managing occupational exposures. Fairfax, VA: AIHA. ISBN: 1-931504-69-5.
Case BW, Abraham JL, Meeker G *et al.* (2011) Applying definitions of "asbestos" to environmental and "low-dose" exposure levels and health effects, particularly malignant mesothelioma. J Toxicol Environ Health B Crit Rev; 14: 3–39.
Gamble JF, Gibbs GW. (2008) An evaluation of the risks of lung cancer and mesothelioma from exposure to amphibole cleavage fragments. Regul Toxicol Pharmacol; 52(1 Suppl.): S154–86.
Kenny L, Rood A. (1987) A direct measurement of the visibility of amosite asbestos fibres by phase contrast optical microscopy. Ann Occup Hyg; 31: 261–4.
Kromhout H, Heederik D. (1995) Occupational epidemiology in the rubber industry: implications of exposure variability. Am J Ind Med; 27: 171–85.
Langer AM, Maggiore CM, Nicholson WJ *et al.* (1979) The contamination of Lake Superior with amphibole gangue minerals. Ann N Y Acad Sci; 330: 549–72.
McSwiggen PL, Morey GB. (2008) Overview of the mineralogy of the Biwabik Iron Formation, Mesabi Iron Range, northern Minnesota. Regul Toxicol Pharmacol; 52(1 Suppl.): S11–25.
Mossman BT. (2008) Assessment of the pathogenic potential of asbestiform vs. nonasbestiform particulates (cleavage fragments) in in vitro (cell or organ culture) models and bioassays. Regul Toxicol Pharmacol; 52(1 Suppl.): S200–3.
Nieuwenhuijsen MJ. (1997) Exposure assessment in occupational epidemiology: measuring present exposures with an example of a study of occupational asthma. Int Arch Occup Environ Health; 70: 295–308.
NIOSH. (1994a) NIOSH manual of analytical methods (NMAM) 7400, fourth edition: ASBESTOS and OTHER FIBERS by PCM, issue 2. NIOSH.
NIOSH. (1994b) NIOSH manual of analytical methods (NMAM) 7402, fourth edition: ASBESTOS by TEM, issue 2. NIOSH.
NIOSH. (2011) Asbestos fibers and other elongate mineral particles: state of the science and roadmap for research. Current intelligence bulletin 62. Cincinnati, OH: NIOSH.
Ramachandran G. (2005) Occupational exposure assessment for air contaminants. Boca Raton, FL: CRC Press. ISBN: 1-56670-609-2.
Reserve mining company. (1974) Job descriptions and classifications: united steelworkers of America and Reserve mining company. Minneapolis, MN: Reserve mining company.
Rooker SJ, Vaughan NP, Guen, JM. (1982) On the visibility of fibers by phase contrast microscopy. Am Ind Hyg Assoc; 43: 505–15.
Sheehy J. (1986) Reconstruction of occupational exposures to silica containing dusts in the taconite industry. Doctoral dissertation. Minneapolis, MN: University of Minnesota.
Sheehy J, McJilton C. (1990) Reconstruction of thirty years of free silica dust exposure in the taconite industry. VIIth International Pneumoconiosis Conference, Part II. Sampling and control of mineral dust, Pittsburgh, pp. 1001–06.
Wilson R, McConnell EE, Ross M *et al.* (2008) Risk assessment due to environmental exposures to fibrous particulates associated with taconite ore. Regul Toxicol Pharmacol; 52(1 Suppl.): S232–45.
Zanko LM, Niles HB, Oreskovich JA. (2008) Mineralogical and microscopic evaluation of coarse taconite tailings from Minnesota taconite operations. Regul Toxicol Pharmacol; 52(1 Suppl.): S51–65.

[Appendix 2]



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The Relationship between Various Exposure Metrics for Elongate Mineral Particles (EMP) in the Taconite Mining and Processing Industry

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Keywords: elongate mineral particles (EMP), taconite, size-based definitions for EMP exposures, NIOSH 7400

Word Count: 5,061

ABSTRACT

Different dimensions of elongate mineral particles (EMP) have been proposed as being relevant to respiratory health end-points such as mesothelioma and lung cancer. In this article, a methodology for converting personal EMP exposures measured using the NIOSH 7400/7402 methods to exposures based on other size-based definitions has been proposed and illustrated. Area monitoring for EMP in the taconite mines in Minnesota's Mesabi Iron Range was conducted using a Micro Orifice Uniform Deposit Impactor (MOUDI) size-fractionating sampler. EMP on stages of the MOUDI were counted and sized according to each EMP definition using an indirect-transfer transmission electron microscopy (ISO Method 13794). EMP were identified using energy-dispersive x-ray and electron diffraction analysis. Conversion factors between the

EMP counts based on different definitions were estimated using (1) a linear regression model across all locations and (2) a location-specific ratio of the count based on each EMP definition to the NIOSH 7400/7402 count. The highest fractions of EMP concentrations were found for EMP that were 1–3 µm in length and 0.2 – 0.5 µm in width. Therefore, the current standard NIOSH method 7400, which only counts EMP > 5 µm in length and ≥ 3 in aspect ratio, may underestimate amphibole EMP exposures. At the same time, there was a high degree of correlation between the exposures estimated according to the different size-based metrics. Therefore, the various dimensional definitions probably do not result in different dose-response relationships in epidemiological analyses. Given the high degree of correlation between the various metrics, a result consistent with prior research, a more reasonable metric might be the measurement of all EMP irrespective of size.

INTRODUCTION

A number of studies have been published on the relationship between exposure to asbestiform "fibers" and health effects such as lung cancer and mesothelioma. Since the term "fiber" has been controversial in the context of asbestos [(1)], the National Institute for Occupational Safety and Health (NIOSH) has recently proposed the use of the term "elongate mineral particles" or EMP to refer to mineral particles with a minimum aspect ratio of 3:1 that are of inhalable, thoracic, or respirable size [(2)].

The current regulations for asbestiform EMP are based on length (≥ 5 µm) and aspect ratio (> 3:1) measured using the NIOSH Method 7400, a counting protocol that has been criticized as lacking a scientific basis [3, 4]. EMP dimensions are important because: (1) the different sizes of EMP penetrate to and deposit in different regions of the lung, (2) the macrophages cannot remove EMP from the lung when they are longer than the macrophage diameter, and (3) the lung cannot function properly when thinner EMP deposit in the alveolar region of the lung [5]. Other EMP characteristics related to toxic health effects include the morphological habit, chemical composition, and activity [5, 6, 7].

Minnesota counties in the vicinity of taconite mining operations have been found to have elevated age-adjusted rates for mesothelioma [8], a disease thought to be associated with exposure to asbestiform EMP. Studies measuring EMP dimensions have been relatively scarce [9]. However, due to the characteristics of the ore body, non-asbestiform EMP are a potentially major source of exposure and therefore, adverse health effects may be linked also to non-asbestiform EMP. To date, no study has conducted an extensive assessment of the relationship between non-asbestiform EMP and adverse health effects in taconite mining industry. In general, non-asbestiform cleavage fragments have not been thought to have high potential for disease [7, 10, 11].

In the taconite mining industry, cleavage fragments refer to the fractured mineral EMP created during the crushing and fracturing process [2]. Because no standard definition exists, distinguishing cleavage fragments from asbestiform EMP is challenging [12]. Even if a given EMP counting criterion is met, standard methods such as phase contrast microscopy (NIOSH method 7400) [13] or transmission electron microscopy (NIOSH method 7402) [14] cannot distinguish between non-asbestiform cleavage fragments and asbestiform EMP. Researchers have found that non-asbestiform cleavage fragments are inactive in *in vitro* bioassays and that they have less strength and flexibility in morphologic analyses [6, 7]. A linear relationship has been found to exist between the width and length of cleavage fragments, while no such relation exists in asbestiform EMP [15]. The term "amphibole EMP" refers to a subset of double chain silicate minerals that can be asbestiform or non-asbestiform [2, 15]. Cleavage fragments are likely thicker than asbestiform EMP, while asbestiform EMP are likely to be longer and more flexible [4].

Because of the difficulty in distinguishing between asbestiform and non-asbestiform EMP, the relationship between the size of non-asbestiform EMP and carcinogenic lung disease is still not well understood [2]. Although the chemical composition of asbestiform and non-asbestiform EMP can be the same, they differ in their habit or morphology [16, 17]. Asbestiform EMP are "polyfilamentous" whereas non-asbestiform EMP display a "multidirectional" pattern [15].

No consensus exists regarding the most health-relevant, dimension-based exposure metric for EMP. Stanton et al. [18] ascribed carcinogenicity to EMP with a length greater than 8 µm and a diameter less than 0.25 µm. Berman et al. [19] suggested that asbestos EMP greater than 5 µm in length contributed to lung tumor risk, while those less than 5 µm did not contribute to the risk. A panel of experts convened by the Agency for Toxic Substances and Disease Registry [1] concluded that asbestos and synthetic vitreous fibers shorter than 5 µm are unlikely to cause cancer in humans. Chatfield [20] proposed a protocol that defined asbestiform EMP as those with widths between 0.04 µm and 1.5 µm in width and aspect ratio between 20 and 1000; EMP that

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did not fall in these ranges are considered non-asbestiform EMP including cleavage fragments. The Occupational Safety and Health Administration [21] also defined the cleavage fragments as those with aspect ratio less than 20.

Other researchers have argued against ruling out the effect of short fibers. Suzuki et al. [22] concluded that shorter (≤ 5 μm) and thinner EMP (≤ 0.25 μm) were more strongly associated with malignant mesothelioma through analysis of lung and mesothelial tissues in human patients. Dement et al. [23] showed that exposures to EMPS with all combinations of dimensions (lengths ranging from < 1.5 μm to > 40 μm and widths ranging from < 0.25 μm to > 3.0 μm) were highly associated with lung cancer and asbestosis. This result led them to conclude that the traditional method, which only counts EMP longer than 5 μm, may be deficient. In fact, shorter EMP also contribute to health-relevant work exposures, a contribution that may be important [24].

Table 1 summarizes the dimension-based EMP definitions that will be used in this paper. In Figure 1, the same four size-based EMP definitions are compared using a typical sample collected for this study. Each graph shows the same particle counts from five stages of a Micro Orifice Uniform Deposit Impactor (MOUDI) cascade impactor (Model 125R MOUDI-II, MSP Co., Shoreview, MN), overlaid by a polygon that indicates one of the size-based definitions. There are no overlapping areas between the NIOSH and Suzuki et al. definitions or the Chatfield EMP and Cleavage Fragment definitions. Typically, few EMP were identified by the NIOSH and Chatfield definitions, while many were identified by the Suzuki and Cleavage fragment

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definitions. A lack of consensus on the appropriate exposure metric can partially explain the different exposure-response relationships obtained in an epidemiological study [25].

The aims of this study were to: 1) determine the size distribution by length and width of EMP as measured using the MOUDI in different representative locations in each of the six taconite mines currently operating in the Mesabi Iron Range; 2) develop a methodology to determine the relationships between the standard NIOSH Methods 7400/7402-based EMP exposure metric to the other dimension-based EMP exposure metrics.

The current research was carried out as part of an epidemiological study investigating the relationship between exposures to EMP during the mining and processing of taconite ore and respiratory diseases.

METHODS

Sampling sites

The mineralogy of the Mesabi Iron Range in northeastern Minnesota changes from east to west with distinct metamorphic mineralogical zones. In the eastern zone, the iron ore contains amphibole, whereas the ore in the western zone contains predominantly phyllosilicates that are not regulated as asbestiform or amphibole EMP [26, 27].

Based on the mineralogical characteristics of the two zones, taconite mining may potentially lead to exposures to different types of EMP. Our exposure assessment strategy attempted to capture this difference. Currently, one mine operates in the eastern zone (mine A) and five mines in the western zone (mines B, C, D, E, and F). The first criterion for the sampling design was to determine locations for area sampling representing the eastern and western zones that generally corresponded to the similar exposure groups (SEGs), the basis for personal sampling [(28)]. The term location is used to refer to physical places where the area measurements were obtained for each SEG. Table 2 lists the number of area MOUDI samples taken and the number of locations sampled by mine.

Sampling design

Area samples, taken during normal operating conditions at locations representative of each SEG, were collected in up to two samples per location. The samples were obtained using a MOUDI impactor. The cut sizes of the 13 impactor stages ranged from 0.010 µm to 10 µm. Based on observations of stage loading and to be able to assess a broad range of aerodynamic particle size intervals within a budget that limited the number of samples, we chose stages 3, 5, 7, 9 and 11 – corresponding to size intervals of 3.2-5.6 µm, 1.0-1.8 µm, 0.32-0.56 µm, 0.10-0.18 µm, and 0.032-0.056 µm, respectively – for further microscopic analysis. The inlet flow rate from the attached vacuum pump (Model R 5, Busch USA, Virginia Beach, VA, USA) was ~10 L/min and the duration of each sample was 4 hours. The impaction plate used a hydrophilic polycarbonate membrane filter (Isopore Co., Billerica, MA, USA) suitable for analyzing the chrysotile,

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amphibole, and non-amphibole EMP on each stage. The after-filter for the impactor used polytetrafluoroethylene (PTFE) filters with laminated PTFE supports (SKC Inc., Eighty Four, PA, USA).

Analytical methods

The ISO 13794 method, adopted to analyze the impactor samples, provides details of EMP dimension, structure type, and mineral type for each EMP regardless of the EMP dimension [29]. ISO 13794 immerses the whole filter in water and re-filters the particles suspended in the water through a secondary filter. Thus, the particles are indirectly but evenly distributed across the surface of the secondary filter. Eypert_Blaison et al. [33] compared previous studies in which the direct versus the indirect methods of measuring EMP were used. They found that the indirect method resulted in higher measurements of EMP than the direct, suggesting several reasons for the difference. With the indirect method, large structures can be separated by calcinations, ultrasonic dispersion, and re-dispersion procedures during TEM preparation [32]. Conversely, with the direct method, organic debris can hide EMP because the filters are not ashed [34]. Eypert_Blaison et al. [33] also compared studies in which the direct versus the indirect methods of measuring chrysotile were used, finding that the direct method resulted in higher measurements than the polycarbonate indirect method although the majority of EMP in this study were amphibole. They pointed out that EMP can be lost during evaporation using indirect method, while the EMP density for an overloaded filter is underestimated using the direct method.

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However, they did not identify any differences between the two methods due to EMP size distribution.

The resolution limit of ISO 13794 is 0.3 µm in length and 0.1 µm in width, and we counted all fibers > 0.3 µm in length with an aspect ratio > 3. Therefore, our data have both counts and sizes of each EMP for each of the MOUDI stages analyzed in each location. All analyses were carried out at an American Industrial Hygiene Association-accredited laboratory (EMSL Analytical Inc., Minneapolis, MN, USA).

ISO 13794 classifies EMP into three distinct categories: chrysotile, amphibole, and non-amphibole EMP. The non-amphibole EMP do not include the chrysotile EMP. The amphibole EMP were further classified into five types: amosite/cummingtonite-grunerite, crocidolite/riebeckite, tremolite asbestiform/tremolite, anthophyllite asbestiform/ anthophyllite, and actinolite asbestiform/actinolite. The transmission electron microscopy (TEM) method for identifying each EMP using ISO 13794 was the same as that used for NIOSH Method 7402 [(14)], based on the diffraction pattern and chemical spectrum for each EMP. Each type of amphibole EMP has a certain ratio of Na, Mg, Si, Ca, and Fe. EMP that did not fit in either the chrysotile or amphibole category were classified as non-amphibole.

Data management

The impactor data were used to determine the distribution of EMP sizes and derive the relationships between various dimension-based EMP exposure metrics. The assessment of cumulative exposure according to these metrics will enable epidemiological testing of various hypotheses regarding the health-relevance of different sizes of EMP.

Since only five chrysotile EMP (also known as a common commercial asbestiform EMP) were found from a total of 2931 identified EMP, we excluded these particles from further analysis. While EMP analysis using TEM can distinguish between amphibole and non-amphibole EMP, it cannot distinguish between asbestiform and non-asbestiform EMP. Therefore, in this paper, “total EMP” refers to both amphibole and non-amphibole/non-chrysotile EMP and “amphibole EMP” refers to amosite/cummingtonite-grunerite and actinolite asbestiform/actinolite EMP (which were the only types of amphiboles found in our samples).

For each sample, grid openings were analyzed for EMP until either the 100th particle was counted or the required analytical sensitivity was achieved, whichever occurred first [29]. The EMP count was normalized by the number of grid openings analyzed in each substrate for each location by zone. If more than one sample was obtained at a location in a mine, we tallied the EMP for all samples and then divided by the corresponding number of samples to obtain the average EMP count for that location. If a sampled location was representative of more than one SEG, we assigned the data from the sampled location to all the relevant SEGs.

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Because we analyzed only selected stages, the non-analyzed stages were estimated as an arithmetic average of the two adjacent stages. As we show later, this interpolation was justifiable because the counts of EMP on alternate MOUDI stages were not significantly different. Only the data from stages 3 to 11 were considered because EMP were not analyzed on stages 1, 2, 12, and 13. Size-integrated EMP counts for an impactor sample were the sum of the counts for all stages between 3 and 11. Total (or amphibole) EMP were counted for each stage using dimension-based metrics. We converted the normalized EMP count from number of particles to concentration (particles/cm^3) by dividing the number of EMP per sample by the product of the grid opening area and the number of grid openings observed, multiplying by the effective area of the secondary filter, and then dividing by the sampled air volume.

Statistical analyses

All analyses reported here were conducted using SAS version 9.3 (SAS Institute, Cary, NC, USA). Statistical significance was defined by levels of 0.05 or lower.

A two-way ANOVA was used to examine whether concentration differences between stages of the MOUDI are significant for each location. We started with two main effects (impactor stage and location) and then included the interaction of impactor stage and location to see if the interaction term was significant. In addition, Tukey's studentized range was used for pair-wise comparisons of the log of the number concentration of EMP collected on each stage.

The associations between NIOSH 7400 and various total EMP concentration metrics such as Suzuki, Chatfield, and Cleavage Fragments were assessed (a) using a simple linear regression based on the log-transformed exposure concentrations across all locations in the eastern zone (Equation 1) and (b) the ratio of the log-transformed exposure concentrations according to each alternative metric and the NIOSH 7400 metric across all locations in the western zone (Equation 2). Since no amphibole EMP were counted by the NIOSH metrics in the western zone, the regression approach characterizes an overall conversion factor for total EMP across locations in each zone:

$C_{Definition}=a_1 (C_{NIOSH\ EMP})^b$ for total and amphibole EMP in the eastern zone

(Equation 1)

$C_{Definition}=a_2 (C_{NIOSH\ EMP})$ for total EMP in the western zone

(Equation 2)

where $C_{Definition}$ = concentration of total EMP that meet a specific size definition, $C_{NIOSH\ EMP}$ = concentration of total EMP that meet the NIOSH 7400 definition, a_1= intercept based on linear regression between the log-transformed concentrations $C_{Definition}$ and $C_{NIOSH\ EMP}$, b = slope based on the linear regression, and a_2 = ratio of concentration of each size EMP definition to NIOSH 7400 definition based on linear regression.

The second approach characterizes the ratio of each size-based EMP definition to NIOSH 7400 and 7402 by location (Equation 3). In this way there is a separate conversion factor for each location for both total and amphibole EMP in both zones.

$C_{Definition} = a_i C_{NIOSH\ EMP}$ for the i^{th} location (Equation 3)

RESULTS

To assess the relationship between the EMP size distribution and stages, we performed pair-wise comparisons of the counts on the various stages. Ten stage comparisons (combinations of stages 3, 5, 7, 9, and 11) were carried out for both the total and amphibole EMP concentration. Only two pair-wise stage comparisons (stages 5 vs. 9, and 5 vs. 11) out of 10 in the eastern zone and one pair-wise stage (stages 3 vs. 11) out of 10 in the western zone were significantly different at $\alpha = 0.05$. The interaction of location and stage was not a significant variable in either geologic zone (p-value: 0.9980 in the east, 0.3967 in the west). When the model was run without the interaction term, the two main effects (stage and location) were significant variables in both zones.

Considerable differences between the two geological zones were found for total and amphibole EMP. Figure 2 shows the combined EMP concentration of stages 3 through 11 by location in the eastern zone, with a reference line indicating the NIOSH recommended exposure limit (REL) of

0.1 particles/cm^3 for EMP. The reference line is shown only as a benchmark, and not to show compliance as the MOUDI measurements are area samples obtained over 4 hours. However, the total EMP classification does not necessarily refer to regulated asbestiform EMP, because the NIOSH 7400 cannot differentiate between asbestiform and non-asbestiform EMP and also refers to a very specific range of lengths and widths. We only present EMP results in the eastern zone because the concentrations of EMP in the eastern zone are markedly higher than that in the western zone. The highest exposure location per department was selected in Figures 2 – 3 (all locations are available in the online supplement). Pair-wise comparisons using a t-test indicated that average total and amphibole EMP concentrations at similar locations were significantly different between the two zones (p-value < 0.0001).

When a location had a high concentration of total EMP, there was also a high concentration of amphibole EMP (e.g., location corresponding to *Railroad* SEG). In the eastern zone, the highest concentration for total and amphibole EMP was found in the location corresponding to *Operating technician* SEG, which was at least 2.4 times higher than the second highest concentration found in the *Railroad* location. In the western zone, the location corresponding to the *Boiler technician* SEG was the only location in which the concentration of total EMP exceeded the NIOSH recommended exposure limit (REL) of 0.1 EMP/cm^3, while none of the locations had amphibole EMP concentrations exceeding the REL.

The total and amphibole EMP concentrations for the four different size-based definitions in the eastern zone are shown in Figure 3. Again, the reference line indicates the REL for EMP and the

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y-axis scale for amphibole EMP is different than for total EMP. Much lower concentrations were observed for the NIOSH and Chatfield definitions than the Suzuki, in which shorter EMP are counted. The highest concentrations for total and amphibole EMP were observed for the Cleavage Fragment definition. Again, the location corresponding to *Operating technician* SEG had the highest EMP concentration for all size-based definitions. In the western zone, we observed substantially lower concentrations of both total and amphibole EMP for all definitions. For total EMP, the concentration levels for most of the locations in the eastern zone were above the REL, while all but one location in the western zone had concentration levels below the REL. Figure 3 indicates that the relative magnitudes of the concentrations of total and amphibole EMP at selected locations were similar using the different exposure definitions. It is emphasized that the EMP concentrations in this paper are not personal exposure samples; therefore, the values do not necessarily mean that workers are exposed above the REL.

Figure 4 provides the coefficients of determination (R^2) between various dimension-based EMP definitions for total and amphibole EMP in the eastern zone for log-transformed concentration data. High R^2 were found for total and amphibole EMP (R^2 ranges: 0.90 - 0.98 and 0.84 - 0.99, respectively), consistent with the pattern of concentrations across locations according to the different EMP definitions in the eastern zone displayed in Figure 3. The slightly lower correlation among definitions for amphibole EMP might be taken as an indication that the concentrations based on these definitions are more independent, the low amphibole EMP concentration in the western zone support such an interpretation. The coefficients of determination for total EMP concentration in the western zone with log-transformed concentration data are shown in Figure 5. Except for one coefficient of determination between the Suzuki and Cleavage Fragment definitions ($R^2 = 0.88$), the coefficients of determination for total EMP in the western zone were low ($R^2 = 0.14 - 0.58$).

A regression model (Equation 1) was derived to relate EMP log-concentrations based on NIOSH 7400 to the log-concentrations based on each of the other size-based EMP definitions for total and amphibole EMP (Table 3). This regression equation is applicable across all locations for total EMP in the eastern zone. However, the regression coefficients for both the intercept and slope were not significant for total EMP in the western zone. Therefore, we used a different regression model (Equation 2) to determine a ratio of concentration based on each size-based definition to NIOSH 7400 EMP concentration across all locations in the western zone.
The regression coefficients for both total and amphibole EMP in the eastern zone were calculated for uncertainty estimates. The 95% confidence intervals are only shown for the slope. The largest range for the slope estimates was found for the amphibole Chatfield EMP (95% CI= 0.296, 1.707). The concentrations of amphibole EMP in the western zone identified by NIOSH 7400 were zero, except at the location corresponding to the *Concentrator operator* SEG (0.0002 particles/cm^3). Therefore, no regression parameters were estimated for amphibole EMP in the western zone.

Table 4 shows the ratios of EMP concentrations based on the Suzuki, Chatfield, and Cleavage fragment definitions to EMP concentration based on the NIOSH 7400 and 7402 definitions, by location for total and amphibole EMP in both zones. Many of these ratios for amphibole EMP are not available in the western zone because amphibole EMP were not observed in the MOUDI measurements in this zone. For both total and amphibole EMP, the ratios for the Cleavage Fragment definition generally have the largest values, followed by those for the Suzuki and Chatfield definitions. Also, the ratios for total EMP tend to be larger than those for amphibole EMP.

Figure 6 presents the size distribution by length and width of total EMP for six representative locations (one in each department except office/control room) in the eastern zone. For each location, the fraction of the total EMP in each of 25 categories (5 lengths x 5 widths) was calculated. The sum of the fractions of amosite/cummingtonite-grunerite (black) and non-amphibole/non-chrysotile EMP (gray) over all the categories is equal to one. Interestingly, the size distribution category 1- 3 μm in length and 0.2 - 0.5 μm in width contained the highest fraction of total EMP for all locations in the eastern zone.

DISCUSSION

This study is the first comprehensive assessment of the size distributions of EMP in the six currently operating mines in the Mesabi Iron Range. In addition, this is the first attempt to understand the relationships between exposures based on different EMP exposure metrics.

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Comparison between total and amphibole EMP by zones

The concentrations of both total and amphibole EMP were much higher in the eastern zone than in the western, which is consistent with the geological differences between the zones. Higher amphibole EMP concentrations are found in the mining processes than in the shop areas. Both total and amphibole Cleavage Fragment concentrations are clearly higher in the mining processes, consistent with the generation of cleavage fragments in the mining and processing of ore. Some of these EMP may conform to the regulatory fiber definition of length greater than 5 μm and aspect ratio of at least 3:1 even if they are not asbestiform in habit.

Comparison between various dimension-based EMP exposure metrics

We found that relative magnitudes of concentrations across locations were similar for the different dimension-based EMP definitions in the eastern zone, a similarity that was more obvious in the mining processes (e.g., mining, crushing, concentration, and pelletizing) than in the shop area. Even though the measured levels of total and amphibole EMP concentrations using each size-based definition were different, the metrics themselves were highly correlated in our study. The high correlation among these EMP concentration metrics will limit the ability of epidemiological analyses in determining relative differences in health effect due to exposure to different EMP metrics. In other words, the effects of correlated relationships are not identifiable. Quinn et al. [(25)] showed that the ranges of the R^2 for different size-based EMP definitions were 0.02-0.89. They explained the impact of relationships among the alternative definitions in epidemiologic analysis. If one EMP definition is more closely related to the health effects, there would be a loss of power using another EMP definition. Dement et al. [23] showed that exposures to various combinations of EMP dimensions (lengths ranging from < 1.5 µm to > 40 µm and widths ranging from < 0.25 µm to > 3.0 µm) were all highly associated with lung cancer and asbestosis. This could be because of correlation between the exposures based on various length and width combinations in that study. Stayner et al. [30] also conceded that the main limitation of their study about the fiber dimension in an asbestos textile plant was the high degree of correlation between size-specific cumulative exposure measures.

Relationship between NIOSH and other definitions

We assessed both the concentration and size distribution of EMP using different size-based definitions to understand the relationships among these exposure metrics. The various size-based definitions resulted in different EMP counts, implying that the specific definition used had a significant effect on the EMP exposure levels. The relationships developed from this analysis will be used to convert historical personal exposure data measured by NIOSH 7400 to the alternative exposure metrics for use in epidemiological analyses.

Quinn et al. [25] and Dement et al. [23] presented an “adjustment factor” or a simple ratio of PCM to TEM for the EMP dimension categories. In our study, the relationship between each EMP dimension index and the NIOSH 7400 definition was created by 1) a location-specific ratio, and 2) a regression model based on data across all locations. The regression equation led to ratios that were in the same range as the location-specific ratios.

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The ratios varied by zone. The high ratios and wide range for total EMP using the Cleavage Fragment definition in the western zone indicate that cleavage fragments are a greater percentage of what is in the western zone. On the other hand, ratios for amphibole EMP detected using the Chatfield definition in the eastern zone had a narrow range, indicating that relatively few Chatfield EMP in this zone. We also found that the short EMP metrics (Suzuki and Cleavage fragments) were more likely to have high ratios. Thus, exposures based on these metrics are likely to be greater than those measured by the standard analytical methods that do not count short EMP.

Taconite EMP size distribution

The highest count fractions of EMP concentration were found for particles with 1 - 3 µm in length and 0.2 - 0.5 µm across locations. This refers to short EMP and is a subset of the Suzuki and Cleavage Fragment definitions. Dodson et al. [(31)] concluded that asbestos EMP of all lengths induce pathological responses and cautioned against ignoring EMP shorter than 5 µm in length, as they constitute most of the contributions of EMP to exposure. In our measurements, most of the EMP are shorter than 5 µm in length and 1 µm in width. The NIOSH methods only count EMP greater than 5 µm in length; thus, shorter EMP are not counted. No significant differences existed in the EMP length and width distributions across locations.

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Limitations of this study

This study was conducted using area measurements with limited number of samples for each location in each mine to understand the relationship between the various exposure metrics that can then be applied to personal exposure measurements based on NIOSH 7400. Ideally, each personal sample would have been analyzed using ISO 13794 to obtain EMP counts according to each exposure metric. However, this approach was not feasible due to budgetary constraints. Furthermore, the area samples from stages 1, 2, 12, 13 were not analyzed, and the potential impact of this might underestimate the EMP exposures. However, the area measurements provided useful insights, chief among them that the exposures based on various metrics were significantly correlated with each other. Since asbestiform and non-asbestiform amphibole EMP are chemically identical, our data based on TEM analysis cannot distinguish between them. This method includes expanded characterization of elemental composition with energy dispersive X-ray analysis and crystalline structure by selected area electron diffraction. While laboratories typically claim to distinguish between asbestiform and non-asbestiform EMP using TEM, a more conservative assessment is that this method can identify amphibole versus non-amphibole EMP (in addition to chrysotile EMP). For instance, although the contracted laboratory used the terms "amosite" and "actinolite", common in asbestos terminology, "amosite" can mean either amosite (asbestiform) or cummingtonite-grunerite (non-asbestiform). The Chatfield definition can classify each amphibole EMP into asbestiform and non-asbestiform categories using TEM. It is important to note, however, that asbestiform amphibole EMP can typically be identified using scanning electron microscopy. However, these methods have not been extensively validated.

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While we expect that most of amphibole EMP are likely non-asbestiform in the Iron Range, this is based on past studies [9, 27].

CONCLUSIONS

Many size-based definitions have been proposed for assessing concentrations of EMP. We chose four different EMP dimensional definitions, including the NIOSH standard method to understand the relationships between these metrics. These four have been proposed as being relevant to respiratory diseases such as mesothelioma and lung cancer. Conversion factors were calculated using both simple linear regressions across all locations and the ratio of the exposure according to each definition to the NIOSH 7400 definition for each location, and these two approaches yielded similar results.

Both the total and amphibole EMP concentrations were much higher in the eastern zone than in the western zone. The highest fractions of EMP concentrations were found for EMP that were 1-3 μm in length and 0.2 - 0.5 μm in width, which is a subset of Suzuki and Cleavage Fragment definitions. Therefore, the EMP counts based on the current standard NIOSH 7400 method are much lower than counts based on shorter EMP.

Similar exposure patterns were observed based on different EMP size definitions, consistent with the high degree of correlation between these EMP exposures. Therefore, the independent effects of the EMP of these various sizes will not be identifiable in epidemiological analysis. Given the high degree of correlation between the various metrics, consistent with previous work by other researchers, a more reasonable metric might be to measure all EMP irrespective of size.

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REFERENCES

1. Eastern Research Group. (2003). Report on the Expert Panel on Health Effects of Asbestos and Synthetic Vitreous Fibers: The Influence of Fiber Length, Lexington, MA

2. NIOSH. (2011). Asbestos fibers and other elongate mineral particles: State of the science and roadmap for research, Current intelligence bulletin 62, DHHS(NIOSH) Publication No. 2011-159. Intelligence. Cincinnati, Ohio.

3. Wylie, A., Bailey, K., Kelse, J., & Lee, R. (1993). The importance of width in asbestos fiber carcinogenicity and its implications for public policy. American Industrial Hygiene Association Journal, 54(5), 239 –252.

4. Addison, J., & McConnell, E. E. (2008). A review of carcinogenicity studies of asbestos and non-asbestos tremolite and other amphiboles. Regulatory Toxicology and Pharmacology: 52(1 Suppl), pp.S187-99, 2008.

5. Baron, P. A. (2003). Measurement of Fibers. NIOSH Manual of Analytical Methods, (NIOSH/DART), 143–166.

6. Wylie AG. (1990). Discriminating amphibole cleavage fragments from asbestos: Rationale and methodology. Proceedings VII pneumoconiosis conference (Pittsburgh, Pennsylvania, USA, 23–26 August1988), DHHS (NIOSH), Cincinnati, OH, USA, Publication no. 90-108, part II.

7. Mossman, B. T. (2008). Assessment of the pathogenic potential of asbestiform vs. nonasbestiform particulates (cleavage fragments) in in vitro (cell or organ culture) models and bioassays. Regulatory Toxicology and Pharmacology : RTP, 52(1 Suppl), S200–3.

8. Case, B. W., Abraham, J. L., Meeker, G., Pooley, F. D., & Pinkerton, K. E. (2011). Applying definitions of “asbestos” to environmental and “low-dose” exposure levels and health effects, particularly malignant mesothelioma. J of Toxicol and Environ Health, Part B, 14: 3-39, 2011.

9. Wilson, R., McConnell, E. E., Ross, M., Axten, C. W., & Nolan, R. P. (2008). Risk assessment due to environmental exposures to fibrous particulates associated with taconite ore. Regulatory Toxicology and Pharmacology : RTP, 52(1 Suppl), S232–45.

10. Berry, G., & Gibbs, G. W. (2008). An overview of the risk of lung cancer in relation to exposure to asbestos and of taconite miners. Regulatory Toxicology and Pharmacology : RTP, 52(1 Suppl), S218–22.

11. Gamble, J. F., & Gibbs, G. W. (2008). An evaluation of the risks of lung cancer and mesothelioma from exposure to amphibole cleavage fragments. Regulatory Toxicology and Pharmacology : RTP, 52(1 Suppl), S154–86.

12. Axten, C. W., & Foster, D. (2008). Analysis of airborne and waterborne particles around a taconite ore processing facility. Regulatory Toxicology and Pharmacology : RTP, 52(1 Suppl), S66–72.

13. NIOSH. (1994a). NIOSH manual of analytical methods (NMAM) 7400, fourth edition: ASBESTOS and OTHER FIBERS by PCM, issue 2.

14. NIOSH. (1994b). NIOSH manual of analytical methods (NMAM) 7402, fourth edition: ASBESTOS by TEM, issue 2.

15. Bailey, K., Kelse, J., Wylie, A., & Lee, R. (2003). The asbestiform and nonasbestiform mineral growth habit and their relationship to cancer studies a pictorial presentation.

16. Langer, a M., Maggiore, C. M., Nicholson, W. J., Rohl, a N., Rubin, I. B., & Selikoff, I. J. (1979). The contamination of Lake Superior with amphibole gangue minerals. Annals of the New York Academy of Sciences, 330, 549–72.

17. Berndt, M. E., & Brice, W. C. (2008). The origins of public concern with taconite and human health: Reserve Mining and the asbestos case. Regulatory Toxicology and Pharmacology : RTP, 52(1 Suppl), S31–9.

18. Stanton, M., Layard, M., Tegerls, A., Miller, E., May, M., Morgan, E., & Smith, A. (1981). Relation of particle dimension to carcinogenicity in amphibole asbestoses and other fibrous minerals. Journal of National Cancer Institute, 67(5), 965–975.

19. Berman, W., Crump, K., Chatfield, E., Davis, J., & Jones, A. (1995). The sizes, shapes, and mineralogy of asbestos structures that induce lung tumors or mesothelioma in AF/HAN rats following inhalation. Risk Analysis, 15(No. 2).

20. Chatfield, E. (2009). A procedure for quantitative description of fibrosity in amphibole minerals, Oral presentation, ASTM Michael E. Beard Asbestos Conference, January 28-29, 20120, San Antonio, Texas.

21. OSHA. (1998). OSHA method ID-160. Occupational Safety and Health Administration.

22. Suzuki, Y., Yuen, S., & Ashley, R. (2005). Short, thin asbestos fibers contribute to the development of human malignant mesothelioma: pathological evidence. International Journal of Hygiene and Environmental Health, 208(3), 201–210.

23. Dement, J. M., Kuempel, E. D., Zumwalde, R. D., Smith, R. J., Stayner, L. T., & Loomis, D. (2008). Development of a fibre size-specific job-exposure matrix for airborne asbestos fibres. Occupational and environmental medicine, 65(9), 605–12.

24. Dement, J., Harris, R., Symons, M., & Shy, C. (1983). Exposures and mortality among chrysotile asbestos workers. Part II: Mortality. Am J Ind Med., (4(3)), 421–33.

25. Quinn, M. M., Smith, T. J., Eisen, E. a, Wegman, D. H., & Ellenbecker, M. J. (2000). Implications of different fiber measures for epidemiologic studies of man-made vitreous fibers. American journal of industrial medicine, 38(2), 132–9.

26. McSwiggen, P.L., and Morey, G.B. (2008) Overview of the mineralogy of the Biwabik Iron Formation, Mesabi Iron Range, northern Minnesota: Regulatory Toxicology and Pharmacology : RTP; 52(1 Suppl), S11-25.

27. Zanko, L. M., Niles, H. B., & Oreskovich, J. A. (2008). Mineralogical and microscopic evaluation of coarse taconite tailings from Minnesota taconite operations. Regulatory toxicology and pharmacology : RTP, 52(1 Suppl), S51–65.

28. Hwang, J., Ramachandran, G., Raynor, P. C., Alexander, B. H., & Mandel, J. H. (2013). A Comprehensive Assessment of Exposures to Elongate Mineral Particles (EMP) in the Taconite Mining Industry. Ann Occup Hyg, doi: 10.1093/annhyg/met026.

29. ISO. (1999). Ambient Air-Determination of Asbestos Fibres-Indirect-Transfer Transmission Electron Microscopy Method (ISO 13794). Geneva, Switzerland.

30. Stayner, L., Kuempel, E., Gilbert, S., Hein, M., & Dement, J. (2008). An epidemiological study of the role of chrysotile asbestos fibre dimensions in determining respiratory disease risk in exposed workers. Occupational and environmental medicine, 65(9), 613–9.

31. Dodson, R. F., Atkinson, Ã. M. A. L., & Levin, J. L. (2003). Asbestos Fiber Length as Related to Potential Pathogenicity : A Critical Review. Online, 297, 291–297.

32. Chesson, J., & Hatfield, J. (1990). Comparison of airborne asbestos levels determined by transmission electron microscopy, using direct and indirect transfer techniques. United States Environmental Protection Agency Report 560/5-89-0004. Washington D.C: Office of Toxin substnaces, US EPA.

33. Eypert-Blaison, C., Veissiere, S., Rastoix, O., & Kauffer, E. (2010). Comparison of direct and indirect methods of measuring airborne chrysotile fibre concentration. The Annals of occupational hygiene, 54(1), 55–67.

34. Sebastien, P. (1985). Assessing asbestos exposure in buildings. In E. Chatfield (Ed.), Asbestos fibres measurement in building atmospheres (pp. 139–51). Ontario, Canada:

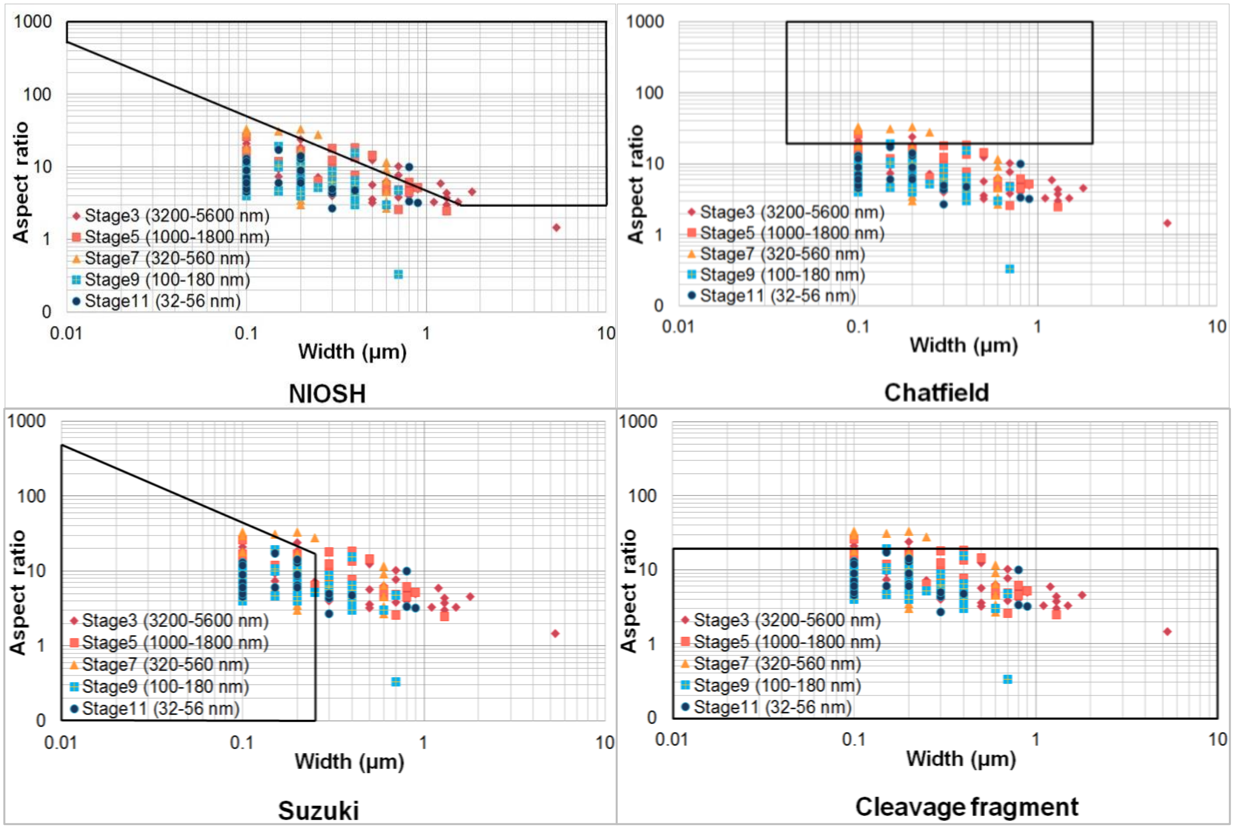

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Figure 1 Comparison of total EMP count for four dimension-based EMP exposure metrics by MOUDI impactor stage for the *Crusher Maintenance* location in mine A. The black boxes indicate the dimension-based EMP exposure metrics based on each definitions.

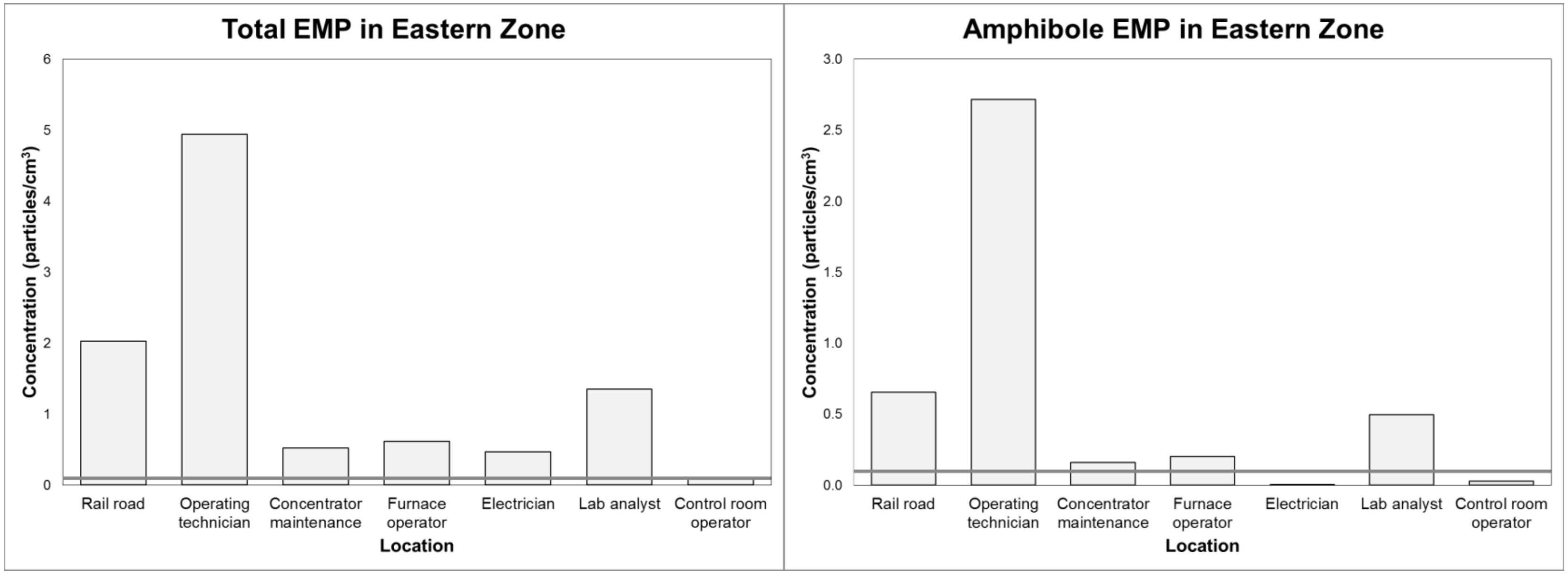

Figure 2 Total and amphibole EMP concentration by selected location in the eastern zone (line indicates the NIOSH REL for NIOSH 7400/7402 EMP= 0.1 particles/cm^3)

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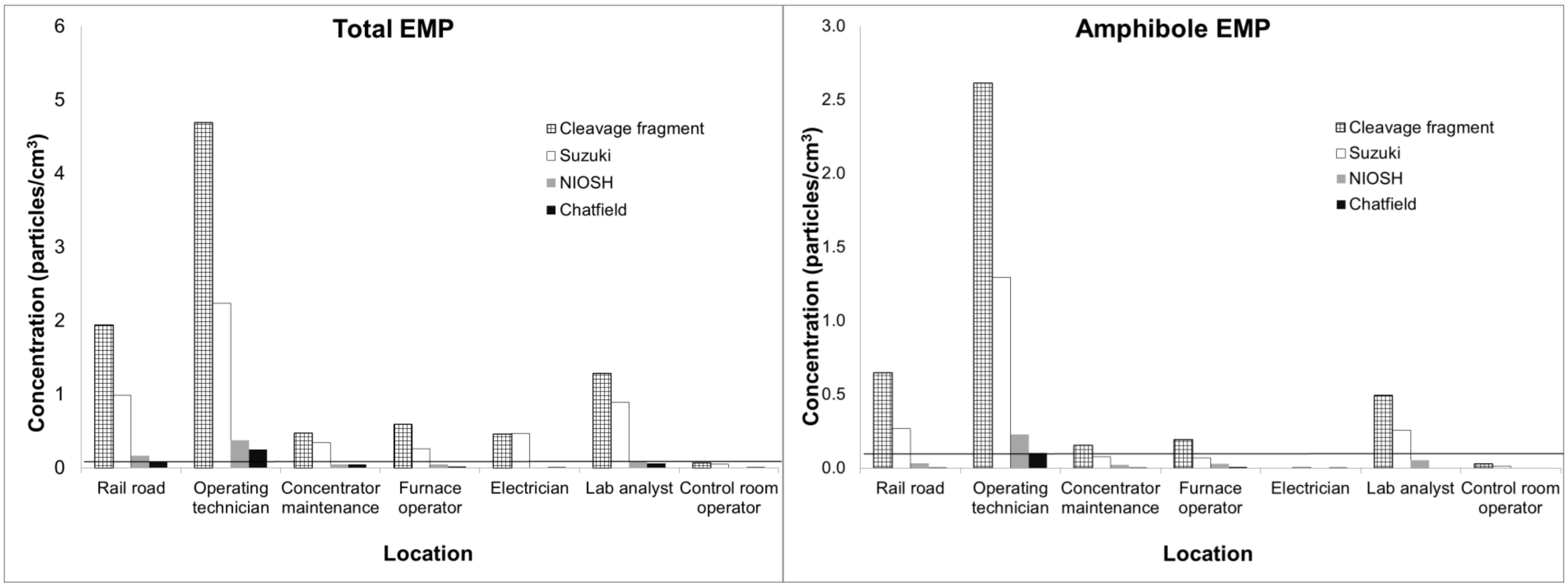

Figure 3 Total and amphibole EMP concentration by size-based definitions in eastern zone (line indicates the NIOSH REL for NIOSH 7400 EMP = 0.1 particles/cm^3)

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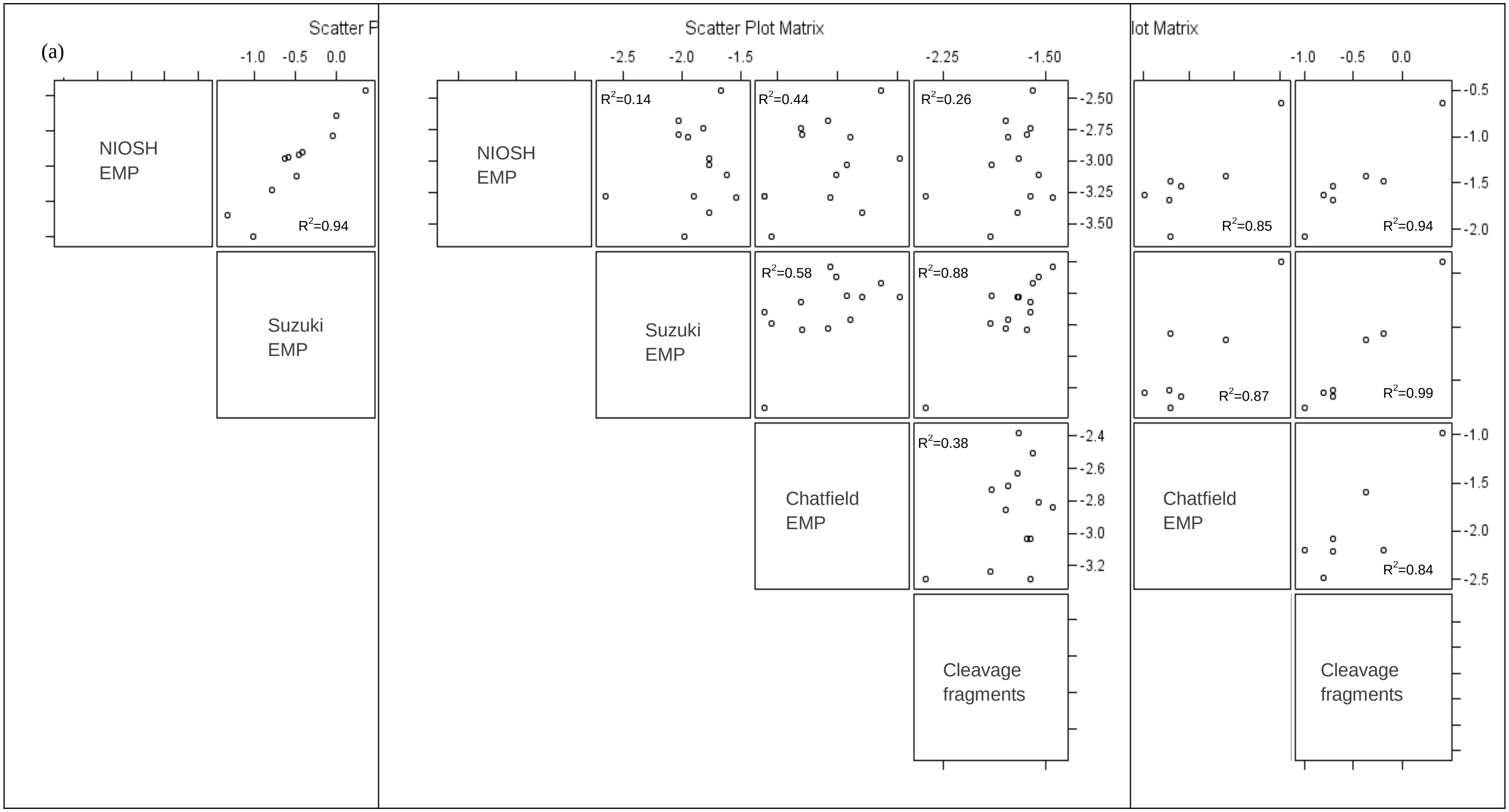

Figure 4 Coefficients of determination between (a) total and (b) amphibole EMP definitions in the eastern zone

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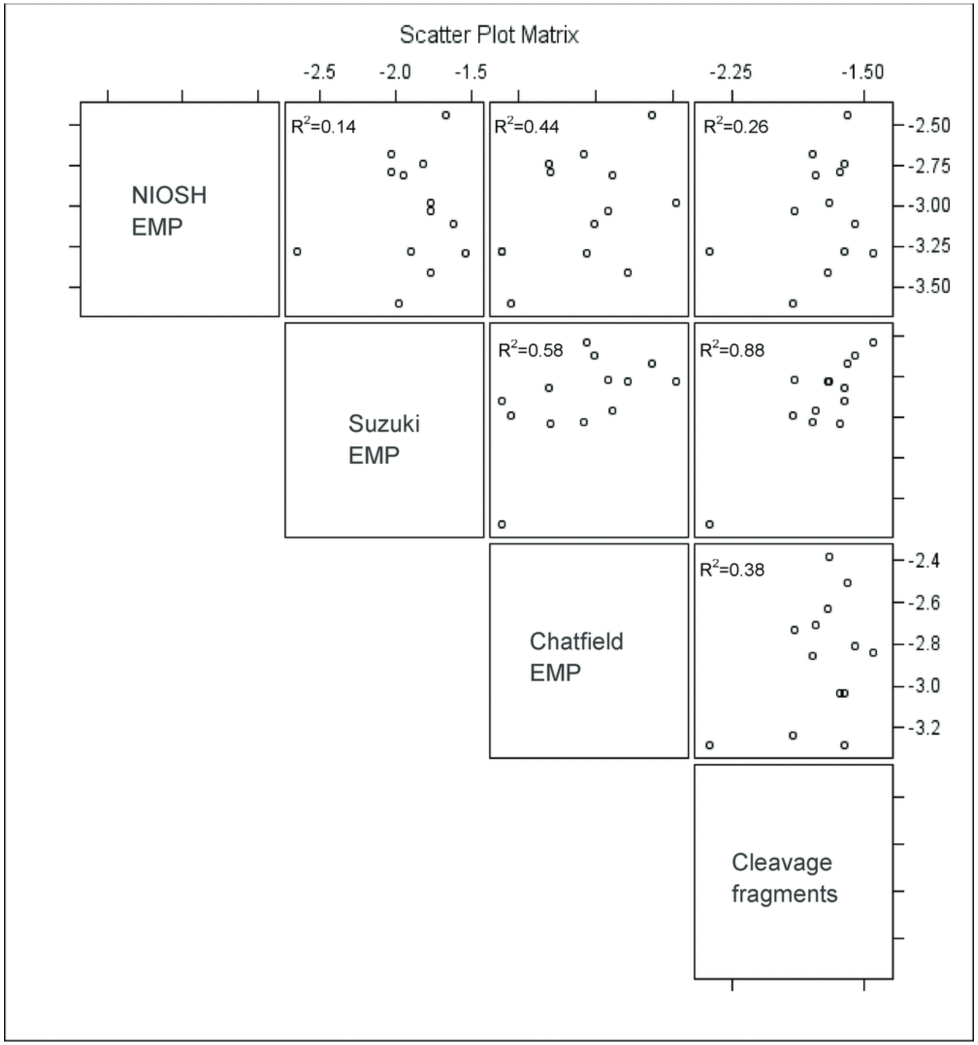

Figure 5. Coefficients of determination between total EMP definitions in the western zone

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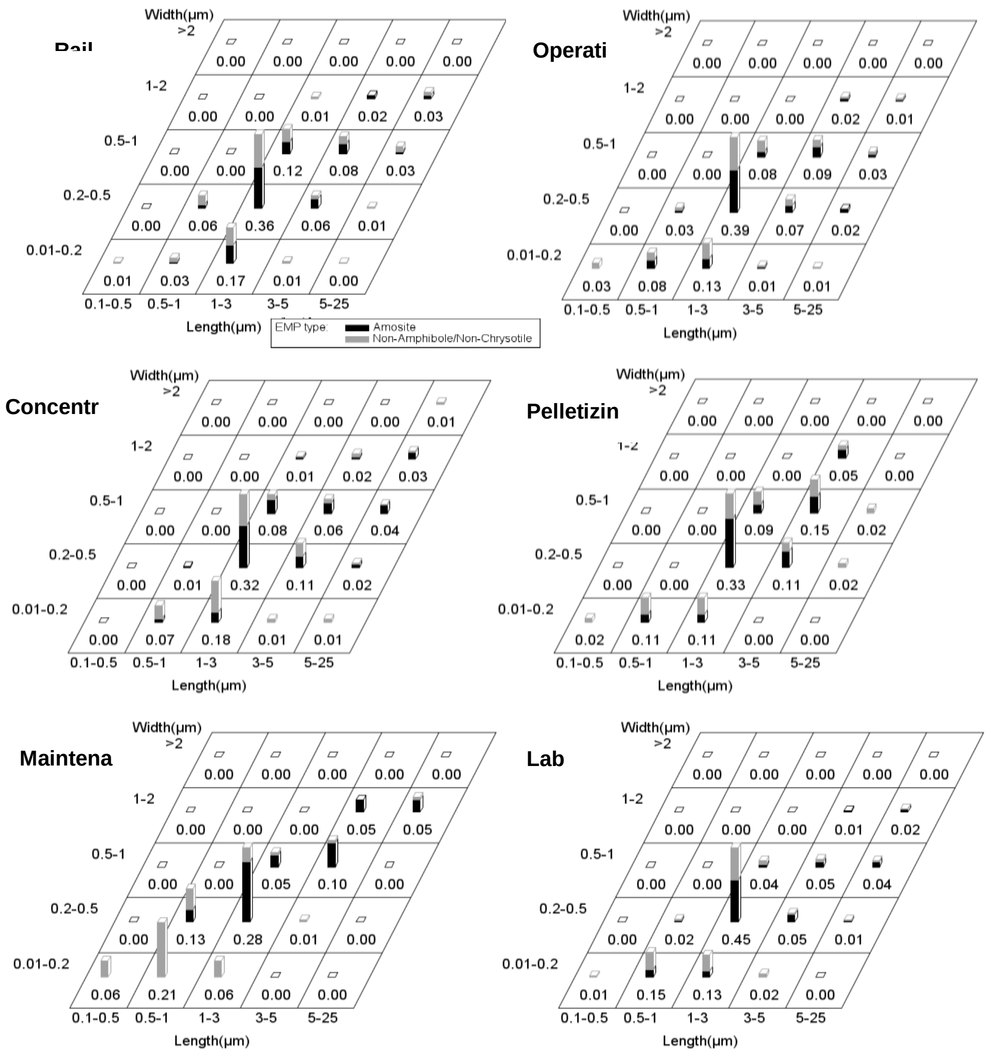

Figure 6. EMP size distribution by location in eastern zone. The height of the bar in each cell represents the fraction of the total EMP for that combination of length and width.

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Table 1 Characteristics of four dimension-based EMP metrics

Size-based definition	**Width (μm)**	**Length (μm)**	**Aspect ratio**	**Analysis methods** [a]
NIOSH EMP	-	> 5	≥ 3	PCM, TEM
Suzuki et al. EMP	W ≤ 0.25	≤ 5	-	PCM, TEM
Chatfield EMP	0.04 < W < 1.5	-	20 < AR < 1000	TEM
Cleavage fragment	-	-	AR ≤ 20	TEM

[a] PCM: Phase contrast microscopy

TEM: Transmission electron microscopy

Table 2 Number of MOUDI samples and locations by mine

Mine	# MOUDI samples	# Locations
A	23	17
B	14	14
C	20	16
D	12	11
E	15	15
F	8	8

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Table 3 Regression coefficient equations between NIOSH and other definitions for total EMP in eastern zone

$C_{Definition}$[a]	Total EMP		Amphibole EMP	
	East[e] (95% CI)	**West[b]**	**East (95% CI)**	**West[c]**
$C_{Suzuki\ EMP}$	$3.83C_{NIOSH\ EMP}^{0.744}$ (95% CI= 0.543, 0.945)	$13.0C_{NIOSH\ EMP}$	$6.40C_{NIOSH\ EMP}^{1.089}$ (95% CI= 0.829, 1.349)	NA[d]
$C_{Chatfield\ EMP}$	$0.501C_{NIOSH\ EMP}^{0.894}$ (95% CI= 0.600, 1.189)	$1.46C_{NIOSH\ EMP}$	$0.328C_{NIOSH\ EMP}^{1.011}$ (95% CI= 0.269, 1.707)	NA
$C_{Cleavage\ fragment}$	$8.28C_{NIOSH\ EMP}^{0.819}$ (95% CI= 0.662, 0.977)	$14.9C_{NIOSH\ EMP}$	$11.9C_{NIOSH\ EMP}^{1.062}$ (95% CI= 0.788, 1.335)	NA

[a] Concentration of all ISO 13794 EMP that meet a specific EMP size definition.

[b] Regression coefficients from both intercept and slope are not statistically significant at p-value = 0.5.

[c] Concentrations of amphibole by NIOSH are zero in the western zone except at the *Concentrator operator* location.

[d] Not applicable (NA) because no regression parameters are estimated for amphibole EMP in the western zone."

[e] The 95% confidence intervals are only shown for the slope (appearing as the exponent in this table).

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Table 4. Ratios of EMP concentrations based Suzuki, Chatfield, and Cleavage Fragment definitions to EMP concentrations based on NIOSH 7400 and 7402 definitions

Department	Location	Total EMP						Amphibole EMP					
		East			West			East			West		
		Suzuki	Chatfield	Cleavage	Suzuki	Chatfield	Cleavage	Suzuki	Chatfield	Cleavage	Suzuki	Chatfield	Cleavage
Mining	Basin operator	.	.	.	.	.	.	.	.[a]	.	.	.	.
	Mining operator 1	.	.	.	.	.	.	.	.	.	.	.	.
	Mining operator 2	.	.	.	.	.	.	.	.	.	.	.	.
	Rail road	6.0	0.48	12	.	.	.	8.2	0.19	20	.	.	.
Crushing	Crusher maintenance	7.6	0.60	12	8.4	0.51	14	6.5	0.68	11	.	.	.
	Crusher operator	6.0	0.69	12	4.5	0.67	7.7	3.9	0.30	9.5	—	—	—
	Operating technician	6.0	0.67	13	.	.	.	5.7	0.45	11	.	.	.
Concentrating	Concentrator maintenance	7.5	1.1	10	24	1.0	47	3.2	0.14	6.7	—	—	—
	Concentrator operator	.	.	.	57	2.8	71	.	.	.	2.0	0	3.8
Pelletizing	Balling drum operator	—	—	—	43	6.0	50	—	—[b]	—	—	—	—
	Dock man	—	—	—	0.0	0	1.0	—	—	—	—	—	—
	Furnace operator	6.2	0.35	14	7.1	1.3	11	2.4	0.29	6.7	—	—	—

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	Pelletizing maintenance	11	0.43	21	5.7	0.57	14	—	—	—	—	—	—
	Pelletizing operator	14	1.9	18	5.8	0.86	7.0	6.5	0.75	12	—	—	—
Shop mobile	Boiler technician	.	.	.	—	—	—	.	.	.	—	—	—
	Carpenter	.	.	.	4.8	0	5.8	.	.	.	—	—	—
	Electrician	—	—	—	—	—	—	—	—	—	—	—	—
	Lubricate technician	.	.	.	.	.	.	.	.	.	.	.	.
	Maintenance technician	31	1.0	39	31	2.0	36	3.3	0 [c]	12	—	—	—
	Pipefitter/Plumber	.	.	.	.	.	.	.	.	.	.	.	.
	Repairman	.	.	.	—	—	—	.	.	.	—	—	—
	Supervisor	.	.	.	.	.	.	.	.	.	.	.	.
Shop stationary	Auto mechanic	—	—	—	41	2.3	50	—	—	—	—	—	—
	Lab analyst	11	0.70	16	16	4.0	19	4.8	0	9.2	—	—	—
	Warehouse technician	—	—	—	18	2.0	14	—	—	—	—	—	—
Office/Control room	Control room operator	—	—	—	—	—	—	—	—	—	—	—	—
	Office staff	7. 7	0	13	4.3	1.0	8.0	0	0	3.7	—	—	—

[a] : No samples/ [b] : NIOSH is zero / [c] : Suzuki, Chatfield, or Cleavage fragment is zero.

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A Comprehensive Assessment of Present-Day Exposures to Respirable Dust and Silica in the Taconite Mining Industry

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ABSTRACT

This study assessed the present-day levels of exposure to respirable dust (RD) and respirable silica (RS) in taconite mines and evaluated how the mining process influences exposure concentrations. Personal samples (n=679) were collected to assess the present-day exposure levels of workers to RD and RS at six mines on the Mesabi Iron Range. The RD and RS concentrations were measured using NIOSH 0600 and NIOSH 7500, respectively. Between-mine, between-SEG, and within-SEG components of variability for RD and RS exposures were estimated using a one or two-way nested random-effects ANOVA model. The concentrations of RD in all mines fell below the ACGIH TLV for RD. With a few exceptions, the concentrations of RS in the crushing and concentrating processes were higher than those measured in the other mining processes, as well as higher than the ACGIH TLV for RS. The magnetic separation and flotation processes in the concentrating department may have reduced the levels of RS significantly, and lowered the percentage of quartz in RD in the pelletizing department. There was little variability among the six mines or between the two mineralogically distinct zones for either RD or RS exposures. The between-SEG variability for RD did not differ across mines

except that significantly smaller between-SEG variability for RS was observed in one of the mines. This finding could be the result of the characteristics of the taconite rock, seasonal effects during sampling, or the tasks assigned for each job in that mine.

INTRODUCTION

The potential relationship between taconite dust and health risks on northeastern Minnesota's Mesabi Iron Range has raised concerns in the taconite mining industry and surrounding communities. Respirable dust and silica are the most common dust components observed during the taconite mining processes – drilling, crushing, feeding, and transferring. Respirable dust is the fraction of inhaled dust that can penetrate into the alveolar region of the respiratory tract using a sampler following the respirable criterion curve (ACGIH, 2013) that has a 50% sampling efficiency for particles with an aerodynamic diameter of 4 µm. Respirable silica, which is a sub-fraction of respirable dust, consists of two mineral forms: crystalline (free silica) and amorphous. The crystalline form has three subgroups: quartz, tridymite, and cristobalite (Steenland & Stayner, 1997), the most common of which is quartz. In our study, we focused on crystalline quartz.

Exposure to the crystalline forms of silica in industrial settings has long been associated with the development of silicosis, a fibrotic pulmonary disease (Hayumbu *et al*., 2008; Pelucchi *et al*., 2006; Steenland & Sanderson, 2001; Archer *et al*., 2002; Chen *et al*., 2001; Collins *et al*., 2005). Although the United States Geological Survey (USGS, 2013) reported that quartz production in the U.S. dramatically increased between 1968 and 1988 (from 30 to 389 tons), production dropped (from 464 to 189 tons) between 1989 and 2000, and data were not available after 2001.

Although the National Institute for Occupational Safety and Health (NIOSH, 2012) found that the number of deaths from silicosis has decreased by a factor 10 between 1968 and 2007, several hundred deaths per year continue as does the non-lethal lung impairment related to silica exposure. A radiographic study of taconite miners in 1980 found several cases of silicosis but no other significant abnormalities or diseases (Clark *et al*., 1980). Higgins *et al*. (1981) studied the taconite workers in the Reserve Mining Company and found no association between mortality and lifetime exposure to either respirable dust or respirable silica and concluded that the taconite miners did not have an elevated risk of mortality. However, these were small studies with limitations in exposure assessment and disease latency.

Only a few studies have investigated measured exposure to respirable dust and respirable silica in the taconite mining industry. Sheehy (1986) found that respirable silica exposures in the taconite industry often exceeded 0.1 mg/m^3, which was the NIOSH REL at that time. Sheehy and McJilton (1990) reported that the concentrations of silica-containing dust were above acceptable limits in mines, crushers, and concentrators, but not in pellet plants. The limits referenced included the Recommended Exposure Limit (REL), set by NIOSH, and the Permissible Exposure Limit (PEL), set by the Mine Safety and Health Administration (MSHA). Quartz silica concentrations ranged from less than 0.04 to 0.11 mg/m^3, and no tridymite or cristobalite was found in any of the samples (McJilton, 1984). Since the 1990s, exposure levels to respirable dust and respirable silica have not been studied in the taconite mining industry.

Concentrations of respirable dust and respirable silica can vary across taconite processes. In this article, we focus on the taconite mining processes, sub-grouped by department (mining, crushing, concentrating, and pelletizing). In the mining step, the hard taconite rock is broken up by dynamite. Production trucks haul the taconite rocks directly to the crushing plant, where a large amount of dust is generated as the crushing step in processing begins. The ore is crushed to about 10 cm in diameter in the primary crusher and to smaller sizes in the secondary or tertiary crusher. The size of the crushed ore varies by the type of crusher and mine, The crushing process produces a noticeable amount of dust. Next, in the concentrating department, the rock is mixed with water and ground in rotating mills until it becomes a fine powder. A magnetic separator then removes the waste rock (called "tailings") from the iron-bearing grains of taconite powder (called "concentrate"). Flotation processes separate lighter silica-containing particles from heavier iron-containing particles that settle out. The last milling process, pelletizing, removes water from the concentrated iron slurry and then mixes the slurry with bentonite clay and/or limestone in large rotating cylinders to make pellets about 1 cm in diameter. The pellets are dried and hardened by heating to 1300 ºC. Although this last process is dry, silica is less likely to be present in the dust after the concentrating process.

The goals of this paper are (1) to assess the present-day exposures to respirable dust (RD) and respirable silica (RS) in all active mines within the Minnesota taconite mining industry; (2) to estimate the between-mine, between- SEG (similar exposure group), and within-SEG components of variability for RD and RS exposures; and (3) to evaluate the influence of the taconite mining and processing on exposures to RD and RS. To assess exposure concentrations of these dust components, we conducted personal air sampling across all the operating mines in the Mesabi Iron Range. Currently, one mine operates in the eastern zone (mine A) and five mines in the western zone (mines B, C, D, E, and F).

METHODS

Formation of SEGs

SEGs can be used to assess exposures more efficiently using job titles, locations, tasks, and procedures (Bullock & Ignacio 2006).We created a historical exposure database, which listed job titles and areas according to tasks and processes. The job titles were mainly derived from (i) records maintained by MSHA; (ii) information from a previous study (Sheehy, 1986) that listed 140 job titles; (iii) industrial hygiene and human resources databases maintained by the three companies currently operating mines on the Mesabi Iron Range (U.S. Steel, Cliffs Natural Resources, Arcelor Mittal) which listed approximately 150 job titles; and (iv) *Job Descriptions and Classifications*, published by the Reserve Mining Company (1974) which contained 142 job titles. Using information on the tasks and processes related to these job titles, we created a set of 60 SEGs. This list was further condensed to 28 SEGs using the subjective professional judgments of the lead industrial hygienists at the three mining companies. The number of job titles represented in each SEG ranged from 1 to 19. The final list contained 181 job titles, forming 28 SEGs that we further grouped into seven departments. The final list contained 181 job titles, forming 28 SEGs that we further grouped into seven departments (Hwang *et al*., 2013).

Sampling design and data handling

An assessment of personal exposures was conducted across six currently operational mines on the Mesabi Iron Range beginning in January 2010 and ending in May 2011. Prior to the day of sampling, the researchers and representatives from the mining companies discussed workers' schedules and identified potential participants. At the beginning of the work shift on each sampling day, the researchers explained the purpose of the study and presented the potential participants with the consent form approved by the University of Minnesota Institutional Review Board (IRB code: 0901M58041).

To perform a baseline exposure assessment for a job title, the American Industrial Hygiene Association (AIHA) sampling strategy (Bullock & Ignacio, 2006) recommends that a minimum of 6, but preferably 8 to 10, exposure samples be obtained per SEG. Two workers per SEG were selected for personal sampling in the eastern zone; approximately eight workers per SEG were chosen in the western zone. Each consenting participant wore a personal air-sampling pump (Apex Pro pump, Casella Inc., Amherst, NH, USA) on his or her waist, with the sampler located in the breathing zone, for approximately six hours, which accounts for at least 70% of a daily work shift. Personal sampling for each worker was completed during three different work shifts, though not necessarily on consecutive days. One blank sample per sampling day (approximately 14% of the samples) was collected for quality control.

Each sample for RD and RS was obtained using a single filter cassette. We used a 5-μm pore size, 37-mm diameter polyvinyl chloride (PVC) membrane filter and 3-piece filter cassettes with a 37-mm aluminum cyclone (SKC Inc., Eighty Four, PA, USA) for sampling. The flow rate for the sampling pump was calibrated at 2.5 liter/min.

Analytical methods and limitations

The RD concentration, based on the mass of the respirable dust fraction, was calculated using NIOSH 0600 *Respirable particulates not otherwise regulated gravimetric* (NIOSH, 1998). The RS analysis was performed using NIOSH 7500 *Crystalline silica X-ray diffraction* (NIOSH, 2003). These NIOSH methods stipulate that particles collected by the filter not exceed a mass of 2 mg because the collected particles could then block the filter, resulting in a lower airflow rate than that in the calibrated air sample. We excluded three samples that were overloaded with particles and six that exhibited a low sampling volume from further data analysis.

If all of the measurements for a given SEG fell below the limit of detection (LOD), summary statistics such as the arithmetic and geometric means and geometric standard deviations were reported as "<LOD". If at least one sample for an SEG in a particular mine had measurements above the LOD, then summary statistics were calculated under the assumption that censored data were represented by one half of the LOD.

Statistical analysis methods

Of the 28 SEGs, 27 were monitored. We were not able to monitor the *Janitor* SEG because all of the janitors currently working in the taconite mining industry are independent contractors.

Furthermore, not all 27 SEGs were represented in each mine. For instance, some mines have detailed job titles that correspond to an SEG (e.g., *Boiler technician*), but others have no corresponding jobs or tasks.

For each SEG, we used a simple one-way ANOVA model to determine if there were significant differences between mines for each SEG. The dependent variables were RD and RS, respectively. The log-transformed estimated exposures Y_{ij} of each mine were expressed as

$$Y_{ij} = \log(X_{ij}) = \mu_y + \alpha_i + \varepsilon_{ij} \text{ for } i = 1, 2, \ldots, 6, \text{ and } j = 1, 2, \ldots, 12$$

(Equation 1)

where X_{ij} = exposure concentration of the i^{th} mine at the j^{th} observation for each SEG, μ_y = overall mean of Y_{ij}, α_i = random deviation of the i^{th} mine's true exposure from μ_y, and ε_{ij} = random deviation of the j^{th} observation from the i^{th} mine's true exposure. Equation 1 assumes that the ε_{ij} are independently and identically distributed with a normal distribution. In addition to the one-way ANOVA, Tukey's Studentized Range test was used for pair-wise comparison of exposures within each mine by SEG to determine homogeneity.

A one-way nested random-effects ANOVA model was used for estimating between-SEG (BG) and within-SEG (WG) variance components using the log-transformed exposure concentrations.

$$Y_{kj} = \log(X_{kj}) = \mu_y + \alpha_k + \varepsilon_{kj} \text{ for the observations } k = 1, 2, \ldots, 27, \text{ and } j = 1, 2, \ldots, 12$$

(Equation 2)

where X_{kj} = j^{th} observation of exposure concentration for the k^{th} SEG, μ_y = overall mean of Y_{kj}, α_k = random deviations of the k^{th} SEG's true exposure from μ_y, and ε_{kj} = random deviations of the j^{th} observation for k^{th} SEG from $\mu_{y,\,k}$ (mean exposure of the k^{th} SEG). The random deviations α_k and ε_{kj} are assumed to be normally distributed with zero means and variances σ^2_α and σ^2_ε, respectively. These variances are mutually uncorrelated and estimated as variance components $S_y{}^2{}_{BG}$ and $S_y{}^2{}_{WG}$, respectively.

A two-way nested random-effects ANOVA model was used for estimating between-mine (BM), between-SEG (BG), and within-SEG (WG) variance components using the log-transformed exposure concentrations.

$Y_{ikj} = \log(X_{ikj}) = \mu_y + \alpha_i + \beta_{ik} + \varepsilon_{ikj}$ for the observations i =1, 2, ...6, k = 1, 2, …, 27, and j =1, 2,…, 12 (Equation 3)

where X_{ikj} = j^{th} observation of exposure concentration for the k^{th} SEG of the i^{th} mine, μ_y = overall mean of Y_{ikj}, α_i = random deviations of the i^{th} mine's true exposure from μ_y, β_{ik} = random deviations of the i^{th} mine's k^{th} SEG's true exposure from $\mu_{y,\,i}$ (mean exposure of the i^{th} mine), and ε_{ikj} = random deviations of the j^{th} observation for the i^{th} mine's k^{th} SEG from $\mu_{y,\,ik}$ (mean exposure of the k^{th} SEG in the i^{th} mine). The random deviations α_i, β_{ik}, and ε_{ikj} are assumed to be normally distributed with zero means and variances σ^2_α, σ^2_β, and σ^2_ε, respectively. These variances are mutually uncorrelated and estimated as variance components $S_y{}^2{}_{BM}$, $S_y{}^2{}_{BG}$, and $S_y{}^2{}_{WG}$, respectively.

All analyses reported here were conducted using SAS version 9.3 (SAS Institute, Cary, NC, USA). The variance components for each model (Equations 2 and 3) were determined using PROC NESTED. The statistical analyses were conducted for RD and RS. Significance was defined by p-values of 0.05 or lower.

RESULTS

Respirable dust (RD) and respirable silica (RS) concentrations

Table 1 lists the number of personal samples analyzed using both NIOSH 0600 and NIOSH 7500 for each mine. The total number of samples and the number of blanks were 679 and 132, respectively. The blanks did not show any dust or silica above limits of detection (LOD), so they were not used further in our analyses. Table 1 also shows the percentage of samples that had RD and RS levels below the limit of detection (LOD), as measured by NIOSH 0600 and NIOSH 7500, respectively. Overall, many of the RD samples had levels lower than the LOD across all mines (ranges: 39-74%), and most of the RS samples had levels lower than the LOD (ranges: 50-79%). Table 2 shows the geometric means (GM) and geometric standard deviations (GSD) of RD concentrations by SEG in all mines. The highest and lowest GMs were found in mine A (0.608 mg/m^3 for *Balling drum operator*, 0.059 mg/m^3 for *Supervisor*). Except for a few SEGs, most of the GSDs were less than 3, indicating moderate variability. The highest GSD was found for *Dock man* in mine D, which only had two measured values that differed widely (< 0.1 and 1.1 mg/m^3). In mine A, *Office staff* was the only SEG in which all samples had RD concentrations less than the LOD. The other five mines had multiple SEGs (~ 6–12) in which all measurements fell below the LOD.

Similarly, Table 3 summarizes the RS concentration by SEG in all mines. The highest GM (0.133 mg/m^3) was found for *Operating technician* in mine C, and the highest GSD (5.22) was found for *Mining operator 1* in mine A. Even if the RD concentration was less than the LOD for a given SEG, the RS concentration did not necessarily fall below the LOD for that same SEG, and vice versa. For instance, all samples for the *Crusher maintenance* SEG in mine D had RD concentrations less than the LOD, but not all RS concentrations were less than the LOD. For the *Pelletizing operator* SEG in mine A, all samples had RS concentrations less than the LOD, but not RD.

While mineralogical differences lead to different exposure levels for elongated mineral particles (EMP) (Hwang et al., 2013), respirable dust and respirable silica do not differ between the two zones. Although our sampling strategy took into account the two different mineralogical zones, we found no differences between them for most of the SEGs. Using Equation 1 to explore the differences in RD and RS exposure levels across mines, the p-values by SEG indicated groups for which there was a significant difference between at least two of the mines (see Table 2 and Table 3, respectively). Twelve SEGs had at least two mines with significantly different means for RD (p-values: <0.0005). Only seven SEGs had at least two mines with significantly different means for RS. We did not calculate p-values when no mines or only one mine had concentrations above the LOD.

The distribution of RD and RS concentrations is illustrated by box-plots in Figure 1 and Figure 2. The RD concentrations in all mines were below the ACGIH TLV of 3 mg/m^3 for RD (Figure 1 and Table 2). With a few exceptions, the RD concentrations in the milling processes (crushing, concentration, and pelletizing) tended to be higher than those in the non-milling processes (mining, shop (stationary), and office/control room). For many of the SEGs, the box-plot displays almost non-existent variability (e.g., *Basin operator* SEG in mine B) because the maximum and minimum values for the SEG were similar or equal because most of the samples had concentrations less than the LOD. The RS concentrations by mine across all SEGs are shown in Figure 2 and Table 3. Except for a few exceptions in mines B and D, the concentrations of RS in the crushing and/or concentration processes were higher than the ACGIH TLV for RS (0.025 mg/m^3), as well as higher than those measured in the rest of the taconite processes.

Comparison of SEG variance components

Table 4 shows the between-mine (S^2_{BM}), between-SEG (S^2_{BG}), and within-SEG (S^2_{WG}) variance components for RD and RS by mine, as well as the percentage of the total variance (the sum of the components) contributed by each component. Equation 2 was used to calculate the absolute values of S^2_{BG} and S^2_{WG} which were also expressed as percentages of the total variance (assuming that total variance was the sum of only the between- and within-SEG components).

Equation 3 was used to calculate the absolute values of S^2_{BM}, S^2_{BG}, and S^2_{WG}, which were also expressed as percentages of the total variance (assuming that total variance was the sum of all three components). The between-mine variance was a small portion of the total variance for both RD and RS (3.4% and 2.1 %, respectively). In other words, there was little variability among the six mines. Overall, mine A had the highest S^2_{TOTAL} (0.199) for RD, a finding that is consistent with the number of large GSDs (>3) for several SEGs (see Table 2). Mine B had the highest S^2_{TOTAL} (0.202) for RS, a similarly consistent finding given the number of SEGs with large GSDs (see Table 3).

Comparison of percent of quartz by department

The department, a grouping variable that can be utilized as an alternative to SEG, was used to compare the correlation of RD and RS as well as percent of quartz. After excluding all samples with values less than the LOD for both RD and RS, we calculated the coefficient of determination (R^2) between RD and RS concentrations by department across all mines (see Figure 3). The value of R^2 decreased substantially from 0.51 in *Crushing* department to 0.02 in *Concentrating* department. With the exception of the *Concentrating* department, the RD and RS concentrations in all departments have a significant positive relationship. The low correlation found in the *Concentrating* department may indicate that the RS concentrations are more independent from the RD as the concentrating processes remove the silica. To calculate the percentage of silica in the respirable dust in each department, we divided the RS concentration (mg/m^3) by the RD concentration (mg/m^3). Our results indicate that the mean percentage of quartz was approximately 14% across all departments except for the *Pelletizing* department, where the percentage dramatically dropped to 5% (see Figure 4). As mentioned earlier, the magnetic separator and flotation processes in the *Concentrating* department remove the silica including quartz. Therefore, the respirable dust in the *Pelletizing* department has a lower percentage of quartz.

DISCUSSION

Levels of RD and RS

Overall, the highest average concentrations of RD were found in mine A. Mine F had the lowest average concentration of RD, 0.116 mg/m^3, which is approximately 2 times lower than the average of 0.252 mg/m^3 in mine A. The differences in processes between these two mines were not significant. Mine F was the smallest in terms of production capacity (smaller by a factor of two than the next lowest mine). No single RD exposure concentration was higher than the TLV in any of the mines. The highest individual exposure level of 2.30 mg/m^3 was found in the *Maintainence technician* SEG in Mine E, a value lower than the ACGIH TLV for RD (3 mg/m^3) (see Figure 1). Overall, between-mine differences for the RD across all SEGs were almost nonexistent (S^2_{BM}=0.005).

All mines had some SEGs above the ACGIH TLV for RS (0.025 mg/m^3) (see Figure 2). Mine B had the highest average (across all SEGs) concentration of RS (0.025 mg/m^3) while mine D had the lowest (0.010 mg/m^3). As we can see in Figure 1, the highest concentrations of RD were often observed in either the *Pelletizing* or *Crushing* departments,which are inherently dusty operations. The highest concentrations of RS were consistently observed in the *Crushing* department (Figure 2) but not also in the *Pelletizing* department. The silica is a part of the ore during the crushing process but has been removed before the pelletizing step. For instance, the RS concentration in the *Crushing* department ranged from the minimum of 0.003 mg/m^3 for the *Crusher maintenance* SEG in mine A to the maximum of 0.280 mg/m^3 for the *Operating technician* SEG in mine C (Figure 2). The highest concentration of RS in mine D was found in the *Shop* (*mobile*) SEG; the *Crusher maintenance* SEG had a similar concentration. The RS concentrations were generally higher at the beginning of the taconite process, i.e., in the *Mining* and *Crushing* departments. The magnetic separator and flotation processes in the *Concentrating* department reduced the levels of RS significantly. This pattern was consistent across all mines. Sheehy (1986) found that the greatest potential for overexposure to respirable silica occurred in the mining (drill operator), crushing (crusher helper), and concentrating (primary attendant, concentrator laborer) departments; these departments correspond to the Mining operator 1, Crusher operator, and Concentrator operator SEGs respectively in the present work. However, it was unclear whether the specific job tasks performed by the concentrator laborer occurred before or after the magnetic separation processes.

Between-mine variability by process

The taconite mining and milling processes are very similar in all mines; thus, the levels of exposure to RD and RS during these processes display only a few significant differences across mines. Because most mining jobs in the pit are performed in a cab (e.g., driller, truck driver, shovel operator), the level of exposure to RD and RS depends primarily upon the ventilation system in the operating equipment. Although there are no major differences between mines for these jobs, there are differences between the equipment used for each job. For instance, the ventilation filters must be checked more often in some vehicles (e.g., bulldozer or grader) than others (e.g., truck or loader). Also, some small vehicles do not have a ventilation system.

Inside the taconite plants, the conveyance of rocks through the crushers is, in general, a dry process that generates significant RD and RS in all mines. A small fraction of the crushed rock is mixed with water and ground to a powder-like substance in the rod and ball mills. After this milling process, the amount of RD and RS is reduced because the process is wet.

Between-SEG vs. within-SEG variability

When only the between-SEG (S^2_{BG}) and within-SEG (S^2_{WG}) variance components were considered rather than S^2_{BG}, $S^2_{WG,}$ and the between-mine (S^2_{BM}) variance all together, the S^2_{BG} variance was slightly larger because it encompassed S^2_{BM} variance as well. The S^2_{BG} for RD did not differ much across mines. However, a significantly smaller S^2_{BG} for RS was observed in mine D (see Table 4). The S^2_{TOTAL} for mine D was 0.063, more than three times smaller than that for other mines (for example, 0.202 in mine B). Many of the SEGs had a relatively consistent level of RS exposure, especially between the departments in mine D (see box-plot in Figure 2). However, the RS levels in the *Crushing* department varied minimally in mine D, while the levels in the *Crushing* department in the other mines varied much more. In contrast, the levels of RS in all other departments varied less across mines. All of the RD concentrations for the *Crushing* department in mine D fell below the LOD because the crusher operator works in a relatively clean crusher control operating room at this mine. The work environment of the crusher operator is different in mine A, where the crusher operators are more exposed to the work done in the nearby crusher building.

Mine D is located at the end of the western zone of the Mesabi Iron Range and is the farthest mine from mine A. Therefore, the characteristics of the taconite rock in mine D and mine A are most different among the six mines. As one goes from mine D to mine A, the taconite rock changes from soft to hard. Thus, mine D only needs a primary crusher, because the taconite rock is much softer, whereas mine A has a primary and secondary crusher. Thus, differing taconite characteristics might contribute to lower RS concentrations in the mining process in mine D. In addition, sampling was conducted in mine D in June 2010, which had 21 rainy days (Minnesota Department of Natural Resources, 2013), a factor that may have contributed to lower RD and RS concentrations by droplet suppression and also the smaller S^2_{TOTAL}.

CONCLUSIONS

In Minnesota taconite mining operations, respirable dust (RD) and respirable silica (RS) levels vary little between the two mineralogically distinct zones. No single RD exposure concentration was higher than the ACGIH TLV in any of the mines, whereas the concentrations of RS were often greater than the TLV for RS. The highest concentrations of RS were generally found in the

Crushing departments for all mines. The processes in the *Concentrating* department may have reduced the levels of RS significantly, as well as lowered the percentage of quartz in RD in the *Pelletizing* department. There was little to no variability between the six mines for either RD or RS exposures because the taconite mining and milling processes are similar across all mines. The between-SEG variability for RD did not differ much among mines. However, significantly smaller between-SEG variability for RS was observed in mine D. This finding could result from the characteristics of the taconite rock, seasonal effects during sampling, or the tasks assigned for each job.

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REFERENCES

ACGIH (2013). Threshold Limit Values for Chemical Substances and Physical Agents and Biological Exposure Indices. ACGIH, Cincinnnaiti, OH.

Archer, J. D., Cooper, G. S., Reist, P. C., Storm, J. F., & Nylander-French, L. A. (2012). Exposure to respirable crystalline silica in eastern North Carolina farm workers. AIHA journal: a journal for the science of occupational and environmental health and safety, 63(6), 750–5. Retrieved from http://www.ncbi.nlm.nih.gov/pubmed/12570084

Bullock, W., & Ignacio, J. (2006). A strategy for assessing and managing occupational exposures. Fairfax, VA: AIHA.

Chen, W., Zhuang, Z., Attfield, M. D., Chen, B. T., Gao, P., Harrison, J. C., Fu, C., Chen, J, & Wallace, W. E. (2001). Exposure to silica and silicosis among tin miners in China: exposure-response analyses and risk assessment. Occupational and environmental medicine, 58(1), 31–7. Retrieved from http://www.pubmedcentral.nih.gov/articlerender.fcgi?artid=1740032&tool=pmcentrez&rendertype=abstract

Clark, T., Harrington, V., Asta, J., Morgan, W., & Sargent, E. (1980). Respiratory effects of exposure to dust in taconite mining and processing. Am Rev Respir Dis., 121(6), 959–966.

Collins, J. F., Salmon, A. G., Brown, J. P., Marty, M. a, & Alexeeff, G. V. (2005). Development of a chronic inhalation reference level for respirable crystalline silica. Regulatory toxicology and pharmacology: RTP, 43(3), 292–300. doi:10.1016/j.yrtph.2005.08.003

Hayumbu, P., Robins, T. G., & Key-Schwartz, R. (2008). Cross-sectional silica exposure measurements at two Zambian copper mines of Nkana and Mufulira. International journal of environmental research and public health, 5(2), 86–90. Retrieved from http://www.ncbi.nlm.nih.gov/pubmed/18678921

Higgins, I., Glassman, J., & Oh, M. (1981). The effect of taconite dust exposure on the health of employees of Reserve Mining Company: Mortality, respiratory symptoms and chest radiography. University of Michigan. Ann Arbor, MI.

Hinds, W. C. (1999). Aerosol Technology: Properties, Behavior, and Measurement of Airborne Particles. Hoboken, NJ: John Wiley & Sons, Inc.

McJilton, C. (1984). Mineral resources health assessment program, Chapter 3: Industrial hygiene assessment in Final report, 1981-1984. University of Minnesota.

Minnesota Department of Natural Resources. (2013). Climate Data Retrieval. Retrieved June 27, 2013, from http://climate.umn.edu/hidradius/radius.asp

NIOSH. (1998). NIOSH manual of analytical methods (NMAM) 0600, fourth edition: Respirable particulates not otherwise regulated gravimetric, Issue 3.

NIOSH. (2003). NIOSH manual of analytical methods (NMAM) 7500, fourth edition:Crystalline silica X-ray diffraction, Issue 4.

NIOSH. (2012). Work-Related Lung Disease Surveillance System (eWoRLD). Ref.No. 2012F03-01. U.S. Department of Health and Human Services, Public Health Service, Centers for Disease Control and Prevention, National Institute for Occupational Safety and Health, Division of. Retrieved from http://www2a.cdc.gov/drds/WorldReportData/FigureTableDetails.asp?FigureTableID=2595&GroupRefNumber=F03-01

Pelucchi, C., Pira, E., Piolatto, G., Coggiola, M., Carta, P., & La Vecchia, C. (2006). Occupational silica exposure and lung cancer risk: a review of epidemiological studies 1996-2005. Annals of oncology: official journal of the European Society for Medical Oncology / ESMO, 17(7), 1039–50. doi:10.1093/annonc/mdj125

Reserve mining company. (1974). Job descriptions and classifications: United steelworkers of America and Reserve mining company. MN.

Sheehy, J. (1986). Reconstruction of occupational exposures to silica containing dusts in the taconite industry. University of Minnesota.

Sheehy, J., & McJilton, C. (1990). Reconstruction of thirty years of free silica dust exposure in the taconite industry. VIIth International Pneumoconiosis Conference, Part II, DHHS (NIOSH) Publication No. 90-108 Part II, Sampling and control of mineral dust, 10(Pittsburgh), 1001–1006.

Steenland, K., & Sanderson, W. (2001). Lung cancer among industrial sand workers exposed to crystalline silica. American journal of epidemiology, 153(7), 695–703. Retrieved from http://www.ncbi.nlm.nih.gov/pubmed/11282798

Steenland, K., & Stayner, L. (1997). Silica, asbestos, man-made mineral fibers, and cancer. Cancer causes & control: CCC, 8(3), 491–503. Retrieved from http://www.ncbi.nlm.nih.gov/pubmed/9498906

United States Geological Survey (USGS). (2013). Historical Statistics for Mineral and Material Commodities in the United States. U.S. Geological Survey 140, Data Series 01-006, Supersedes Open-File Report. Retrieved from http://minerals.usgs.gov/ds/2005/140/index.html

Table 1 Number of personal samples and percent of samples < limit of detection (LOD) by mine and mineralogical zone

Zone	Mine	Workers	Number of RD/RS Samples	% <LOD of RD [a]	% <LOD of RS [b]
Eastern	A	56	161	39	50
Western	B	34	101	48	50
	C	38	113	47	56
	D	34	100	69	79
	E	48	139	68	65
	F	22	65	74	72
Total		232	679		

[a] Personal respirable dust (RD) samples analyzed by NIOSH 0600.
[b] Personal respirable silica (RS) samples analyzed by NIOSH 7500.

Table 2 Summary statistics of respirable dust for each SEG measured in all mines (GM unit: mg/m^3)

Department	SEG	A		B		C		D		E		F		P-values[e]
		GM	GSD	GM	GSD	GM	GSD	GM	GSD	GM	GSD	GM	GSD	
Mining	Basin operator	.[c]	.	<LOD[d]	<LOD	0.088	2.10	<LOD	<LOD	<LOD	<LOD	.	.	NA
	Mining operator 1	0.090	3.23	<LOD	<LOD	<LOD	<LOD	<LOD	<LOD	<LOD	<LOD	<LOD	<LOD	NA
	Mining operator 2	0.083	1.96	0.184	3.00	<LOD	<LOD	0.065	1.49	0.092	1.98	<LOD	<LOD	0.1380
	Rail road	0.095	4.14	.	.	.	.	.	.	.	.	.	.	NA
Crushing	Crusher maintenance	0.280	2.39	0.135	1.57	0.279	2.11	<LOD	<LOD	0.175	2.50	0.164	1.14	**0.0095**
	Crusher operator	0.225	2.53	0.355	2.42	0.099	1.66	<LOD	<LOD	0.186	2.78	0.201	1.19	**0.0387**
	Operating technician	0.225	1.21	.	.	0.563	1.73	.	.	.	.	.	.	**0.0064**
Concentrating	Concentrator maintenance	0.252	3.75	0.157	1.76	0.252	1.36	0.078	1.84	0.087	1.78	0.190	3.24	0.1206
	Concentrator operator	0.093	1.70	0.172	1.83	0.136	1.68	<LOD	<LOD	0.122	2.47	<LOD	<LOD	**0.0140**
Pelletizing	Balling drum operator	0.608	1.86			0.196	1.63	0.284	1.56	0.246	1.53	0.161	2.62	**0.0028**
	Dock man	0.258	2.39	0.172	2.81	<LOD	<LOD	0.235	8.90	0.092	2.07	<LOD	<LOD	**0.0377**
	Furnace operator	0.513	1.67			0.420	2.22	0.126	1.94	0.171	2.54	0.095	2.02	**0.0029**
	Pelletizing maintenance	0.593	1.83	0.155	1.82	0.243	1.36	0.186	2.81	0.134	2.04	0.086	1.54	**0.0031**
	Pelletizing operator	0.323	1.49	0.330	1.91	0.201	1.34	0.285	1.35	0.169	1.87	0.346	1.65	0.1678
Shop(mobile)[a]	Boiler technician	.	.	.	.	<LOD	<LOD	.	.	<LOD	<LOD	.	.	NA
	Carpenter	.	.	0.091	2.23	.	.	<LOD	<LOD	0.139	2.62	.	.	0.6130
	Electrician	0.097	1.92	<LOD	<LOD	0.102	2.17	0.157	2.12	0.069	1.41	<LOD	<LOD	**0.0469**
	Lubricate technician	0.068	1.57	.	.	0.163	1.89	.	.	.	.	<LOD	<LOD	**0.0065**
	Maintenance technician	0.152	2.52	0.125	2.84	<LOD	<LOD	0.159	2.34	0.180	5.26	0.212	2.99	0.7348
	Pipefitter/Plumber	.	.	.	.	0.103	1.72	.	.	<LOD	<LOD	.	.	NA
	Repairman	.	.	0.175	1.79	.	.	.	.	0.077	1.99	<LOD	<LOD	**0.0290**
	Supervisor	0.059	1.70	<LOD	<LOD	<LOD	<LOD	<LOD	<LOD	0.061	1.60	<LOD	<LOD	0.8962
Shop (stationary)[b]	Auto mechanic	0.113	2.24	0.111	2.12	0.075	1.62	0.103	1.79	0.062	1.40	0.075	1.72	0.4767
	Lab analyst	0.106	1.70	0.259	1.23	<LOD	<LOD	0.069	1.31	<LOD	<LOD	<LOD	<LOD	**0.0001**
	Warehouse technician	0.064	1.72	<LOD	<LOD	<LOD	<LOD	<LOD	<LOD	0.070	1.33	<LOD	<LOD	0.5491
Office/ Control room	Control room operator	0.080	1.99	<LOD	<LOD	<LOD	<LOD	<LOD	<LOD	<LOD	<LOD	<LOD	<LOD	NA
	Office staff	<LOD	<LOD	<LOD	<LOD	<LOD	<LOD	<LOD	<LOD	0.076	2.05	<LOD	<LOD	NA

[a] Shop (mobile) refers to those SEGs whose work is more likely done in multiple places in the plants.
[b] Shop (stationary) refers to those SEGs whose work is more likely done in a single workplace.
[c] . indicates no measurement.
[d] <LOD indicates all samples containing below LOD.
[e] Numbers in **boldface** indicate statistically significant differences among mines (P<0.05).

Table 3 Summary statistics of respirable silica for each SEG measured in all mines (GM unit: mg/m^3)

Department	**SEG**	**A**		**B**		**C**		**D**		**E**		**F**		**P-values**[e]
		GM	**GSD**	**GM**	**GSD**	**GM**	**GSD**	**GM**	**GSD**	**GM**	**GSD**	**GM**	**GSD**	
Mining	Basin operator	.[c]	.	<LOD[d]	<LOD	0.012	3.19	<LOD	<LOD	0.007	1.45	.	.	0.2853
	Mining operator 1	0.017	5.22	<LOD	<LOD	0.008	1.62	<LOD	<LOD	0.006	1.37	0.012	2.51	0.2005
	Mining operator 2	0.010	1.61	0.067	2.76	0.013	2.47	0.007	2.01	0.008	1.60	<LOD	<LOD	**0.0004**
	Rail road	0.010	4.84	.	.	.	.	.	.	.	.	.	.	NA
Crushing	Crusher maintenance	0.032	3.57	0.014	2.02	0.038	1.36	0.012	2.54	0.036	1.30	0.027	1.20	0.1014
	Crusher operator	0.061	2.40	0.066	2.21	0.028	1.44	<LOD	<LOD	0.033	2.02	0.052	1.09	**0.0003**
	Operating technician	0.045	1.22	.	.	0.133	1.56	.	.	.	.	.	.	**0.0007**
Concentrating	Concentrator maintenance	0.016	1.80	0.034	2.59	0.024	1.27	0.011	2.13	0.015	1.55	0.018	3.17	0.1979
	Concentrator operator	0.009	1.83	0.057	1.48	0.018	1.71	0.010	1.79	0.034	2.23	0.016	1.25	**<0.0001**
Pelletizing	Balling drum operator	0.009	1.76	.	.	0.008	1.57	0.009	1.65	0.007	1.47	<LOD	<LOD	0.6009
	Dock man	0.008	1.59	0.011	1.73	<LOD	<LOD	0.011	3.21	<LOD	<LOD	<LOD	<LOD	0.1260
	Furnace operator	0.007	1.59	.	.	0.010	2.50	<LOD	<LOD	<LOD	<LOD	<LOD	<LOD	0.4598
	Pelletizing maintenance	0.007	1.73	0.009	1.56	0.011	1.76	0.009	1.86	<LOD	<LOD	<LOD	<LOD	0.2500
	Pelletizing operator	<LOD	<LOD	0.010	1.69	<LOD	<LOD	0.008	1.65	0.008	1.72	<LOD	<LOD	0.2044
Shop(mobile)[a]	Boiler technician	.	.	.	.	<LOD	<LOD	.	.	0.006	1.39	.	.	NA
	Carpenter	.	.	<LOD	<LOD	.	.	<LOD	<LOD	0.019	3.48	.	.	NA
	Electrician	0.012	2.25	0.008	1.62	0.009	1.80	0.013	2.50	0.011	1.87	<LOD	<LOD	0.5163
	Lubricate technician	0.010	1.94	.	.	0.020	1.83	.	.	.	.	0.008	1.78	0.0534
	Maintenance technician	<LOD	<LOD	0.010	1.94	<LOD	<LOD	<LOD	<LOD	<LOD	<LOD	0.014	2.31	**0.0446**
	Pipefitter/Plumber	.	.	.	.	0.009	2.17	.	.	0.011	2.18	.	.	0.7187
	Repairman	.	.	0.048	1.36	.	.	.	.	0.010	1.88	0.010	1.61	**0.0002**
	Supervisor	0.011	2.59	<LOD	<LOD	<LOD	<LOD	<LOD	<LOD	0.008	2.05	<LOD	<LOD	0.5169
Shop (stationary)[b]	Auto mechanic	0.006	1.52	0.016	2.94	<LOD	<LOD	0.011	1.88	0.009	2.48	<LOD	<LOD	0.1216
	Lab analyst	0.012	1.75	0.032	2.42	<LOD	<LOD	0.007	1.46	<LOD	<LOD	<LOD	<LOD	**0.0006**
	Warehouse technician	0.008	1.80	<LOD	<LOD	<LOD	<LOD	<LOD	<LOD	0.008	1.56	<LOD	<LOD	0.4179
Office/ Control room	Control room operator	0.008	1.76	<LOD	<LOD	<LOD	<LOD	<LOD	<LOD	<LOD	<LOD	0.007	1.42	0.6488
	Office staff	<LOD	<LOD	<LOD	<LOD	<LOD	<LOD	<LOD	<LOD	0.008	2.37	<LOD	<LOD	NA

[a] Shop (mobile) refers to those SEGs whose work is more likely done in multiple places in the plants.
[b] Shop (stationary) refers to those SEGs whose work is more likely done in a single workplace.
[c] . indicates no measurement.
[d] <LOD indicates all samples containing below LOD.
[e] Numbers in **boldface** indicate statistically significant differences among mines ($P<0.05$).

Table 4 Between-mine, between-SEG, and within-SEG variance components across mine and by mine for respirable dust and respirable silica

Classification	Mine	Subject	Sample	Total [b]	BM		BG		WG	
				S^2_{TOTAL}	S^2_{BM}	%	S^2_{BG}	%	S^2_{WG}	%
RD	All [a]	232	679	0.144	0.005	3.4	0.063	43.5	0.077	53.1
	All	232	679	0.144			0.067	46.6	0.077	53.4
	A	56	161	0.199			0.093	46.7	0.106	53.3
	B	34	101	0.133			0.054	40.6	0.079	59.5
	C	38	113	0.149			0.097	65.0	0.052	35.0
	D	34	100	0.105			0.049	47.3	0.055	52.7
	E	48	139	0.115			0.028	24.5	0.087	75.5
	F	22	65	0.093			0.051	54.7	0.042	45.3
RS	All [a]	232	679	0.147	0.003	2.1	0.071	48.4	0.073	49.5
	All	232	679	0.147			0.074	50.3	0.073	49.7
	A	56	161	0.184			0.072	39.4	0.111	60.6
	B	34	101	0.202			0.135	66.7	0.067	33.3
	C	38	113	0.177			0.119	67.0	0.058	33.0
	D	34	100	0.063			0.001	1.4	0.062	98.6
	E	48	139	0.114			0.050	43.6	0.064	56.4
	F	22	65	0.090			0.056	61.5	0.035	38.5

[a] This variance components include between-mine.
[b] Total variance components (S^2_{TOTAL}) are sum of partitioned BM, BG, and WG variance components.

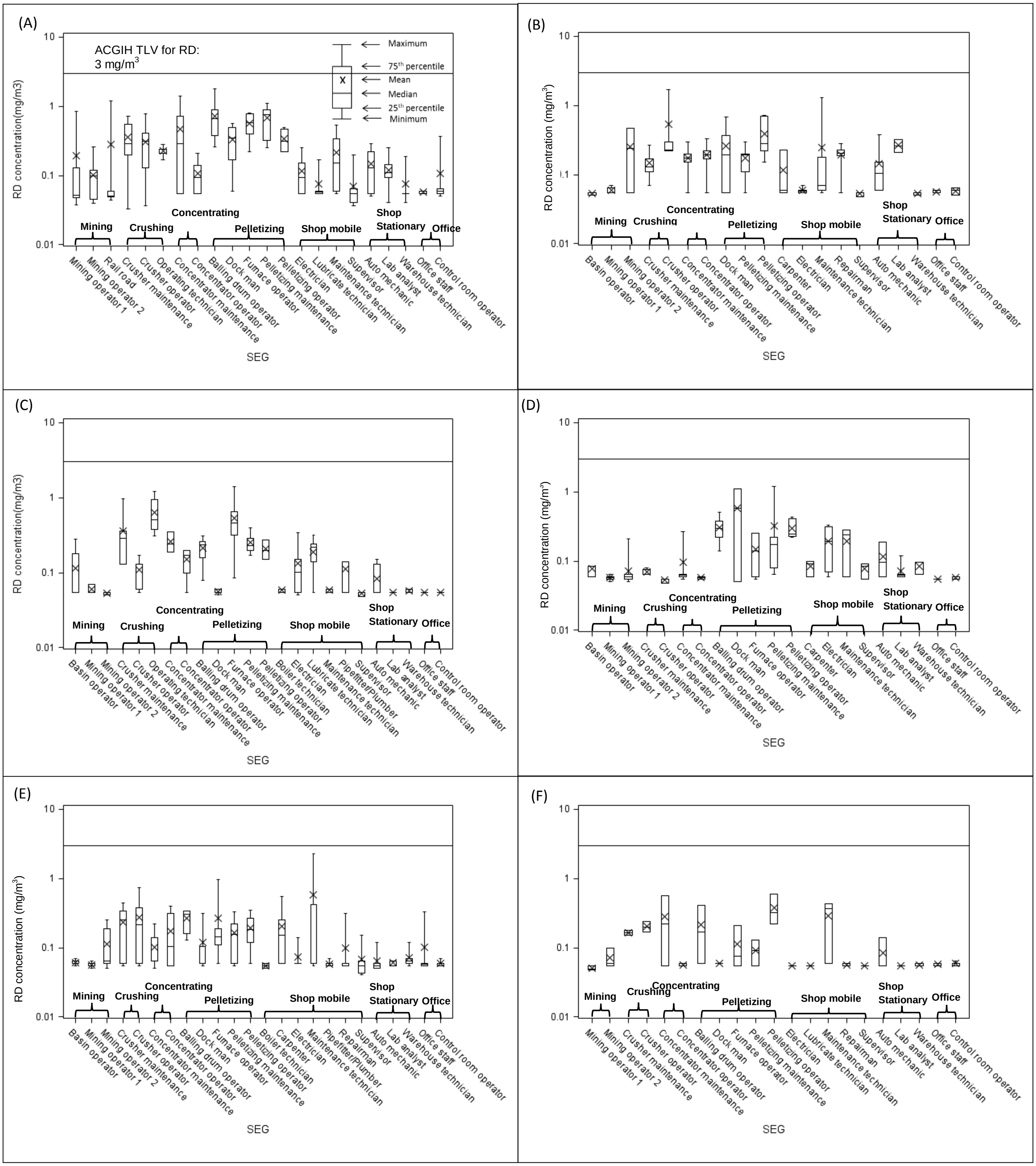

Figure 1 Box plots for respirable dust for each SEG in all mines (the horizontal line indicates the ACGIH TLV for RD = 3 mg/m^3)

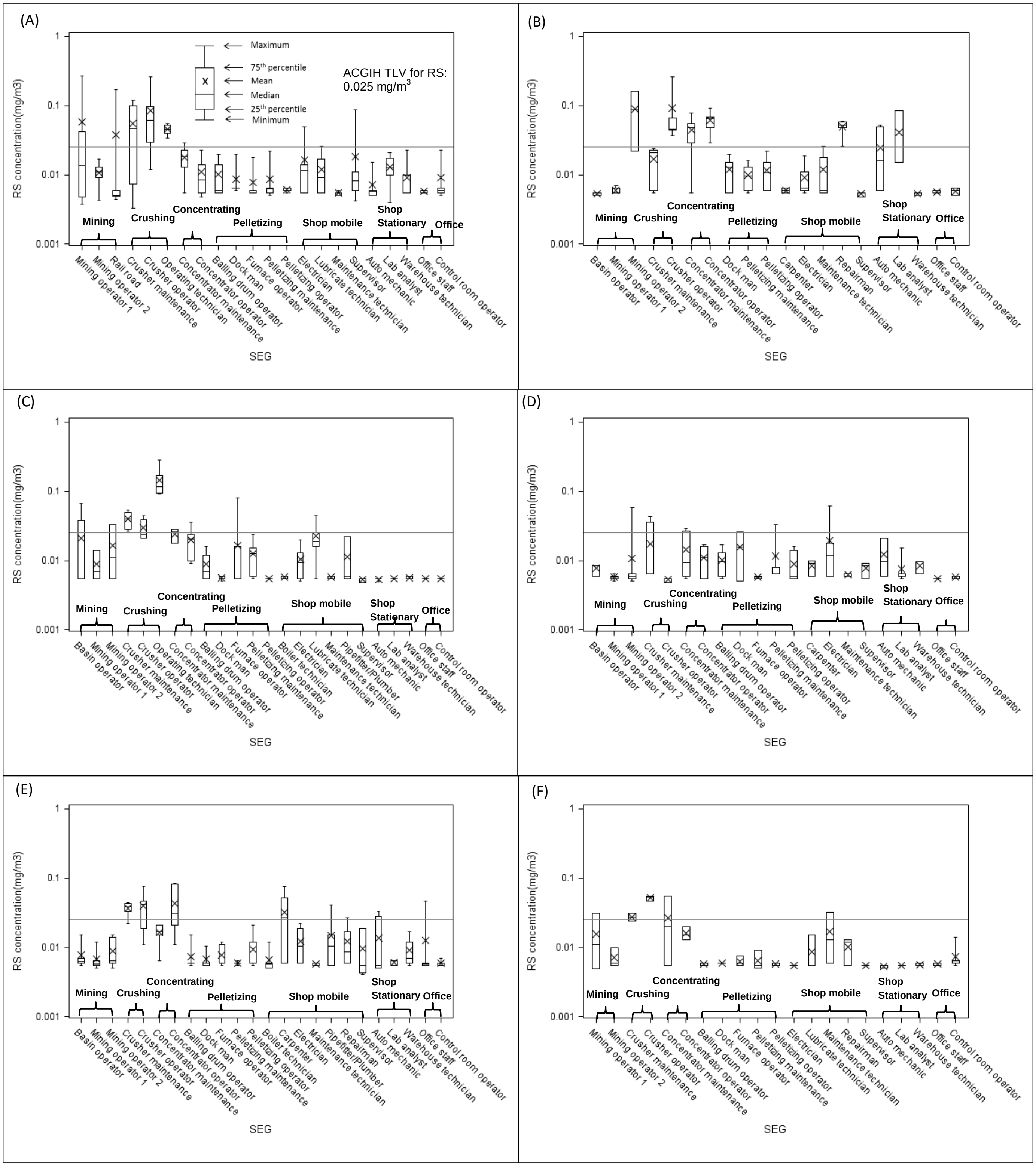

Figure 2 Box plots for respirable silica for each SEG in all mines (the horizontal line indicates the ACGIH TLV for RS = 0.025 mg/m^3)

Office

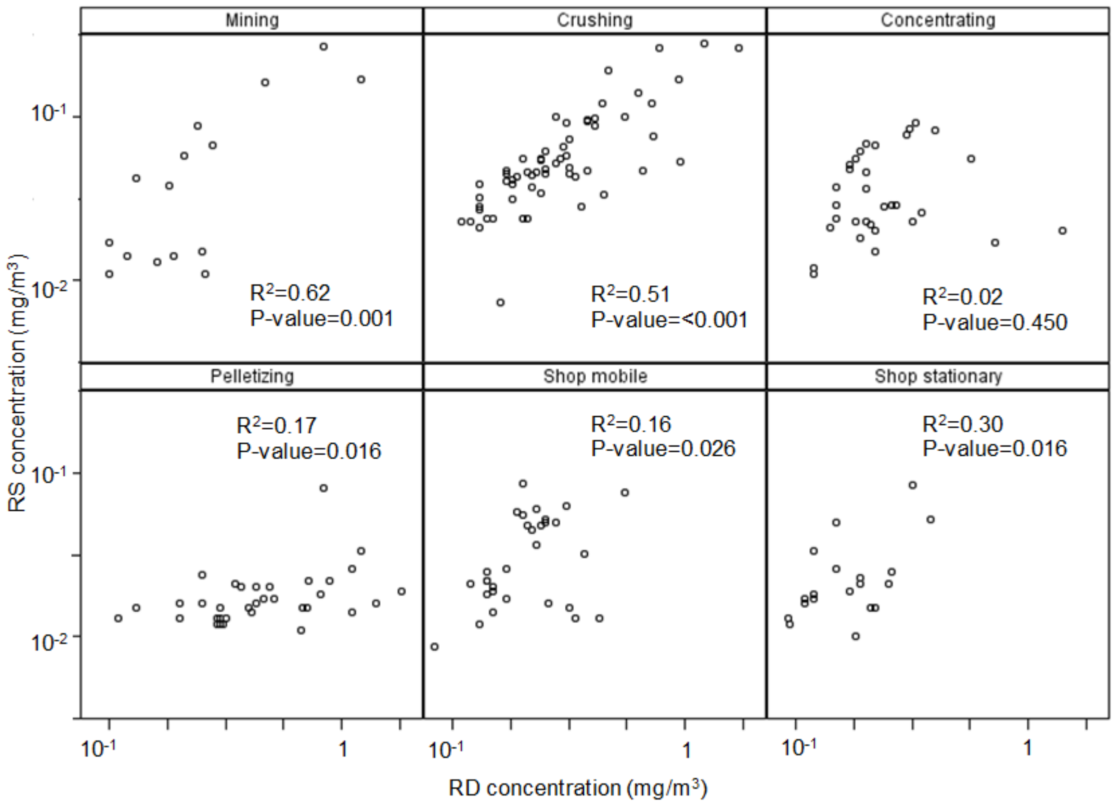

Figure 3 Coefficient of determination (R^2) between respirable dust and respirable silica by department across all mines

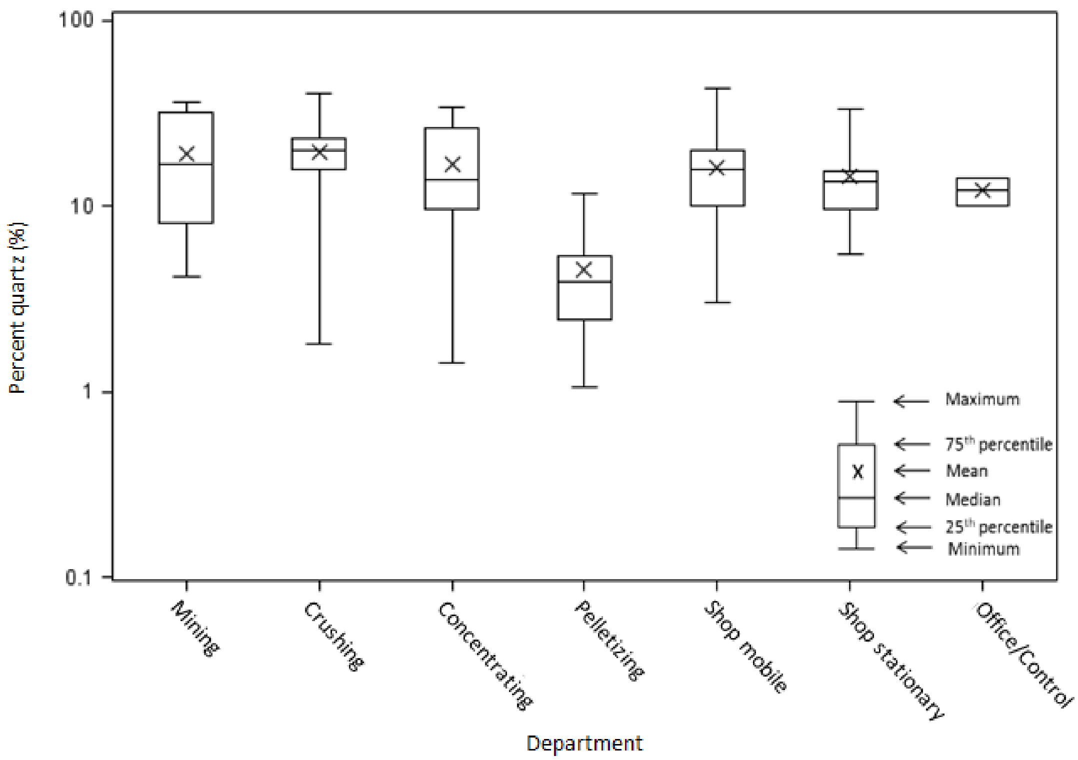

Figure 4 Percent of quartz in respirable dust samples by department

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ORIGINAL ARTICLE

Mortality experience among Minnesota taconite mining industry workers

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ABSTRACT

Objective To evaluate the mortality experience of Minnesota taconite mining industry workers.

Methods Mortality was evaluated between 1960 and 2010 in a cohort of Minnesota taconite mining workers employed by any of the seven companies in operation in 1983. Standardised mortality ratios (SMR) were estimated by comparing observed deaths in the cohort with expected frequencies in the Minnesota population. Standardised rate ratios (SRR) were estimated using an internal analysis to compare mortality by employment duration.

Results The cohort included 31 067 workers with at least 1 year of documented employment. Among those, there were 9094 deaths, of which 949 were from lung cancer, and 30 from mesothelioma. Mortality from all causes was greater than expected in the Minnesota population (SMR=1.04, 95% CI 1.02 to 1.04). Mortality from lung cancer and mesothelioma was higher than expected with SMRs of 1.16 for lung cancer (95% CI 1.09 to 1.23) and 2.77 for mesothelioma (95% CI 1.87 to 3.96). Other elevated SMRs included those for cardiovascular disease (SMR=1.10, 95% CI 1.06 to 1.14), specifically for hypertensive heart disease (SMR=1.81, 95% CI 1.39 to 2.33) and ischemic heart disease (SMR=1.11, 95% CI 1.07 to 1.16). Results of the SRR analysis did not show variation in risk by duration of employment.

Conclusions This study provides evidence that taconite workers may be at increased risk for mortality from lung cancer, mesothelioma, and some cardiovascular disease. Occupational exposures during taconite mining operations may be associated with these increased risks, but non-occupational exposures may also be important contributors.

BACKGROUND AND SIGNIFICANCE

The iron mining industry in Minnesota began in the late 1800s with the discovery of hematite in northeastern Minnesota, within what is now known as the Mesabi Iron Range. Hematite, a high-grade ore, was excavated from the iron formation and shipped directly to steel mills. However, the high-grade ore became less abundant following heavy demand for its use in World War II. In the 1950s, with hematite reserves depleted, the mining and processing of low-grade taconite ore began.[1] Since then, the taconite mining industry in Minnesota has become the largest supplier of iron ore to the steel industry of the USA.[2]

Mining and processing of taconite iron ore results in potential exposure to non-asbestiform amphibole and non-amphibole elongate mineral particles (EMP), respirable silica, quartz and dust, and cleavage fragments.[3] The term 'EMP' refers to any mineral particle with a minimum aspect ratio of 3:1 that is of inhalable size. Cleavage fragments are fractured mineral EMPs created during the crushing and fracturing process.[4]

The Mesabi Iron Range is approximately 2.5 miles wide and 122 miles long and is divided into four mineralogical zones.[5] All zones have deposits of taconite along with quartz and iron silicates, but vary in the type of EMP.[6] The ore body in the eastern range, known as zone 4, contains iron-rich amphibole EMPs (primarily cummingtonite-grunerite), which is believed to be less than 1% fibrous.[7] The western end of the range, zone 1, contains almost exclusively non-asbestiform EMPs, primarily of quartz hematite, siderite, chamosite and greenalite.[6 8] Zone 2 is considered a transitional zone with some amphiboles appearing.[5] One mine operates in zone 4, one mine that is no longer in operation is located in zone 2, the remaining five mines are located in zone 1 which is roughly the western-most two-thirds of the entire Mesabi Iron Range. There is another mineralogical zone, zone 3, however, there are no mines located in this zone. The primary exposure in taconite operations is of non-asbestiform cleavage fragments however, due to the mineralogical differences in the eastern versus western zones, workers in the two zones may be exposed to different types of mineral particles.[3] There is an ongoing debate regarding these exposures and the health of miners which includes (1) whether the amphibole minerals mined in the eastern part of the iron range are a threat to human health and (2) whether exposure to non-asbestiform minerals, including cleavage fragments, poses any risk to human health.[4 9–12]

The history of public concern of the health of taconite miners and residents near the mining and processing facilities began in the early 1970s when EMPs, determined to be primarily grunerite, possibly including some asbestiform grunerite, were found in Duluth's drinking water supply as a result of taconite tailings that were disposed of into Lake Superior.[8 13] This prompted studies of the potential health effects from ingestion of Duluth water which did not show increased risk of malignant tumours in either laboratory animals or human populations.[14 15] The earliest studies of the health of taconite miners were carried out in the early 1980s. The first study[16] focused on a group of miners from Reserve Mining Company. The

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authors reported no increased risk of respiratory cancers among the 5751 miners. Later, studies were conducted in 1988 with an update in 1992[17 18] and, similarly, did not report an excess mortality among the 3431 workers from Erie and Minntac mines. In 1997, the Minnesota Department of Health Cancer Surveillance System reported a 73% excess in cases of mesothelioma among men in the northeastern region of Minnesota between 1988 and 1996 as compared with the rest of the state.[19] This resurrected the concern over whether exposures from taconite mining and processing pose a threat to the health of the workers.

To address these lingering uncertainties regarding the health consequences of taconite mining, we conducted a mortality study of workers from multiple mines to characterise the overall health of the Minnesota taconite worker population.

METHODS

Study population

The occupational cohort for this analysis was enumerated in the early 1980s as part of the Mineral Resources Health Assessment Program (MRHAP). The program was developed by the University of Minnesota, School of Public Health, with the support of the Iron Range Resources and Rehabilitation Board. This was done as part of an effort to further research on health effects of mining and mineral processing. Investigators assembled a database of 68 737 individuals from employment records of the seven mines in operation in 1983, US Steel Corporation, Hanna Mining Company, Pickands-Mather and Company, Reserve Mining Company, Eveleth Taconite Company, Inland Steel Company, and Jones and Laughlin Corporation.

In 2008, the University of Minnesota launched the Taconite Workers Health Study (TWHS). The current mortality analysis was one component of the overall TWHS with an objective to update the health assessment of the cohort of 68 737 miners collected by MRHAP in 1983. The cohort included taconite workers and those who had worked in the earlier hematite mining operations. To focus the study on workers most likely to have been working after taconite mining began in the 1950s, the cohort used in this analysis was limited to those born in 1920 or later, leaving 46 170 individuals. Of these, 1927 were excluded, including 477 whose only record on file was an application with no further evidence of employment, 679 whose records were insufficient for vital status follow-up, and 539 for whom employment information was improbable, for example, began working at age 14 or younger. Those who died before reference mortality rates were available (before 1960, n=232), were also excluded, leaving 44 243 workers. To focus on workers with more stable employment in the taconite industry, this analysis was restricted to workers with at least 1 year of documented employment giving a study population of 31 067 workers. This exclusion removed workers who did not stay in the industry, and also summer workers, often students who only worked a few months.

Vital status ascertainment

The mortality analyses covered the period from 1960 (when complete reference mortality rates were available) through 2010. The vital status of cohort members as of 31 December 2010 was ascertained through several sources including the Social Security Administration (SSA), the National Death Index (NDI), Minnesota Department of Health, and other state health departments. Social security numbers and names of all cohort members were sent to the SSA and were returned with a vital status of *deceased*, *alive*, or *unknown*, with the state of death and date of death identified for decedents. Cohort members who died in Minnesota, or whose state of death was unknown, were sent to the Minnesota Department of Health to ascertain causes of death. NDI, established in 1979, is a national death registry designed to facilitate health investigations. For those who died outside of Minnesota in the year 1979 or later, causes of death were obtained from NDI Plus. For individuals who died before 1979, death certificates were obtained from the state health department from the state in which the individual died. Additional tracing was done on those whose vital status was unknown and, if found to be deceased, their death certificates were obtained. Underlying and contributing causes of death were coded to the International Classification of Disease (ICD) version current at the year of death. The ICD codes were obtained directly from the Minnesota Department of Health and the NDI. All other death certificates were reviewed and coded by a nosologist.

Individuals who were identified as deceased, but whose death certificates were not found, were classified as 'Presumed Dead'. The date of death provided by the SSA was recorded as the vital status date and the cause of death was classified as 'Unknown.' Individuals identified as 'Unknown' by the SSA were traced via a commercial tracing vendor that uses credit bureau address updates. For those who were found to have had recent address activity, their vital status was recorded as 'Presumed Alive' with a vital status date as the most recent date recorded from the web tracing tools. The vital status date for the remaining individuals with an unknown vital status was their last date of employment.

Given the size of the cohort, detailed abstraction of all work histories in the cohort was not feasible, and duration of employment was the primary exposure measure of interest. For this analysis, work records of cohort members were reviewed with the first and last dates of employment abstracted, as well as the last date of activity on the work record. In 4.5% of the data, the work records contained start dates but were missing end dates. In this case, the last date of activity was used as the end date to calculate duration of employment. For roughly 92% of the study population, we also had location (zone 1, 2, or 4) of employment.

Data analysis

The mortality rate of the cohort was compared with that of the Minnesota population to estimate standardised mortality ratios (SMR), and 95% CIs adjusted for sex, and 5-year age and calendar period. Person-time at risk was accrued from the first date of employment until the date of death or the end of the follow-up period (31 December 2010). The expected number of deaths was calculated by applying age, calendar time, and cause-specific mortality rates of the Minnesota population to the person-year observations of the study population. SMRs were obtained by computing the ratio of the observed-to-expected number of deaths for the overall mortality and specific causes of death. In addition to overall SMRs, workers with any evidence of employment in zones 1, 2, and 4 were grouped and SMRs for mesothelioma and lung cancer were estimated for each zone.

To further explore summary results for selected causes of death from the SMR analysis, an internal analysis of mesothelioma, lung cancer, hypertensive heart disease, and ischemic heart disease by duration of employment was undertaken. Mesothelioma was captured under ICD-10 code C45, lung cancer was captured under ICD-7 code 162, ICD-8 code 162, ICD-9 code 162, and ICD-10 codes C33 and C34, hypertensive heart disease was captured under ICD-7 codes 440–443, ICD-8 codes 400.1, 400.9, 402, and 404, ICD-9 codes 402 and 404, and ICD-10 codes I11 and I13, and ischemic heart disease was captured under ICD-7 code 420, ICD-8 codes 410–414, ICD-9 codes 410–414 and 429.2, and ICD-10 codes I20, I21, I22, I24, I25, I51.3, and I51.6. Exposure categories were grouped by duration of employment into four exposure categories (1 year, 2–5 years, 6–14 years, and 15+ years). Those who worked 2–5 years were considered most representative of taconite workers with low but stable employment; those who worked less than 2 years were thought to be either transient workers or individuals whose work records were incomplete. Therefore, the 2–5 year exposure group, representing 35% of the study cohort, was used as the reference. Standardised Rate Ratios (SRRs) were computed by standardising to the age and sex distribution of the total study population. Taylor-series-based 95% CIs were calculated for each specific SRR. All SMRs and SRRs were calculated using the Life Table Analysis System (LTAS) V.3.0 software.[20]

RESULTS

This cohort of 31 067 taconite workers with at least 1 year of documented employment was predominantly male (93%), contributed 1 152 966 person-years of observation, and experienced 9094 deaths. Their mean and median durations of employment were 9.4 and 6 years, respectively. Table 1 shows demographic information of the entire cohort and for those with selected causes of death.

The mortality rates from all causes (SMR=1.04, 95% CI 1.02 to 1.06) and all cancers (SMR=1.04, 95% CI 1.00 to 1.08) were higher than the Minnesota population. Among specific cancers, mortality rates for lung cancer (SMR=1.16, 95% CI 1.09 to 1.24) and mesothelioma (SMR=2.77, 95% CI 1.87 to 3.96) were significantly higher than expected. The mortality rate for cardiovascular disease was also elevated (SMR=1.10, 95% CI 1.06 to 1.14), specifically for hypertensive heart disease (SMR=1.81, 95% CI 1.39 to 2.33) and ischemic heart disease (SMR=1.11, 95% CI 1.07 to 1.16). Table 2 shows selected SMRs for the taconite workers cohort. Only one death each for asbestosis and silicosis was observed.

The mortality rates were elevated for mesothelioma and lung cancer in all three zones of the iron range. Among the 20 282 workers who ever worked in zone 1, the SMRs for mesothelioma and lung cancer were 1.85 (95% CI 0.98 to 3.16) and 1.18 (95% CI 1.09 to 1.27) respectively. Among the 5580 workers who ever worked in zone 2, the SMRs for mesothelioma and lung cancer were 7.38 (95% CI 4.30 to 11.82) and 1.43 (95% CI 1.26 to 1.63) respectively. Among the 6501 workers who ever worked in zone 4, the SMRs for mesothelioma and lung cancer were 3.17 (95% CI 1.37 to 6.25) and 1.23 (95% CI 1.07 to 1.40), respectively.

The internal analysis of mesothelioma, lung cancer, hypertensive heart disease, and ischemic heart disease by duration of employment showed elevated but imprecise SRRs when comparing those with 6–14 years, and 15+ years, to those with 2–5 documented work years for hypertensive heart disease. There was no significant elevation in SRRs for mesothelioma, ischemic heart disease and lung cancer (table 3).

DISCUSSION

In this study of Minnesota taconite iron ore miners, an overall higher than expected mortality rate from all causes was observed among taconite workers. Specifically, elevated causes of death from respiratory cancers (including lung cancer and mesothelioma) and cardiovascular disease (including hypertensive heart disease and ischemic heart disease) were identified. These rates were elevated in all three zones of the iron range for mesothelioma and lung cancer. An internal analysis comparing the association between duration of employment and these causes of death did not show a statistically significant elevation in risk for any duration of employment category for mesothelioma, lung cancer, hypertensive heart disease and ischemic heart disease mortality.

Studies of the morbidity and mortality of miners were first carried out in the early 1980s. Higgins *et al*[16] followed a cohort of 5751 men employed at Reserve Mining Company from 1952 to 1976. The study showed no increases in observed respiratory cancers compared to the USA and Minnesota. Cooper *et al*[17 18] studied mortality through 1988 in a cohort of 3431 male workers from Erie and Minntac mines between 1959 and 1977. Total observed deaths were fewer than expected when compared to US and Minnesota death rates. The investigators reported no significantly elevated SMRs for any cause of death. Though these first studies of the health of taconite miners did not show increased risk of mortality, it is important to note that mesothelioma was not captured systematically in mortality registries until 1999 when the ICD V.10 was introduced giving mesothelioma a unique ICD code. Additionally, the follow-up times were not long enough to capture many of the potential cases given the relatively long latency period which, for mesothelioma, is estimated to have a median duration of 32 years.[21] Aside from these two studies that followed a small number of workers over a relatively short amount of time, there has been no comprehensive look at the health of taconite miners across the entire Mesabi iron range.

Several occupational studies have been conducted that evaluate the health risk to workers exposed to non-asbestiform EMPs in other occupational settings. These include studies of talc miners in upstate New York and Homestake gold miners in South Dakota. In a 2002 mortality study of talc miners, Honda *et al*[22] reported an excess in mortality from all cancers, lung cancer, ischemic heart disease, and non-malignant respiratory disease. A 2012 follow-up commentary argued that talc ore exposure also increases the risk of mesothelioma,[11] though that conclusion has been debated.[12] Though the authors argue, the lack of an exposure-response relationship indicates the lung cancer excess may not be related to talc ore dust; rather it might be explained by a relatively high smoking rate in the population,[22] it is unlikely that confounding by smoking accounts fully for the lung cancer excess observed in the study.[4] The results of these studies have been argued further, as the composition of industrial-grade talc has been redefined. Industrial-grade talc deposits are a complex mixture of mineral particles that vary substantially and may rarely include asbestos fibers.[23] Price[23] argues that elevated rates of mesothelioma found in New York talc miners are a result of previous occupational exposure to commercial asbestos. Several studies of miners at the Homestake gold mine in South Dakota were done in the 1970s and 1980s.[24–26] An excess of respiratory cancer was reported in the earliest study,[24] and a small excess of lung cancer was reported in the studies by McDonald *et al*[25] and Steenland and Brown.[26] The results of these studies suggest a weak association between dust exposure and lung cancer and like the studies of talc miners, no dose-response relationship was observed.[4] The studies of New York talc miners and Homestake gold miners cannot definitively conclude whether exposure to non-asbestiform minerals poses any risk to human health.

The elevated risk of lung cancer and mesothelioma as a result of exposure to asbestiform EMPs is well documented in the

Table 1 Characteristic of taconite workers with selected causes of death

	Selected cause of death									
	Mesothelioma		Lung cancer		Hypertensive heart disease		Ischemic heart disease		Total cohort	
	N	Per cent	N	Per cent	N	Per cent	N	Per cent	N	Per cent
Duration of employment (years)										
1	4	13.33	123	12.96	6	9.68	241	11.03	4353	14.01
2–5	8	26.67	250	26.34	14	22.58	576	26.36	10 839	34.89
6–14	6	20.00	239	25.18	18	29.03	545	24.94	9072	29.20
15+	12	40.00	337	35.51	24	38.71	823	37.67	6803	21.90
Sex										
Male	30	100.0	915	96.42	58	93.55	2143	98.08	28 860	92.90
Female	0	0	34	3.58	4	6.45	42	1.92	2202	7.09
Unknown	0	0	0	0	0	0	0	0	5	0.02
Age at hire (yrs)										
<20	12	40.00	247	26.03	15	24.19	628	28.74	11 635	37.45
20–29	14	46.67	494	52.05	34	54.84	1163	53.23	15 962	51.38
30–39	4	13.33	165	17.39	10	16.13	312	14.28	2851	9.18
40+	0		43	4.53	3	4.84	82	3.75	619	1.99
Decade of hire										
<1950	6	20.00	289	30.45	20	32.26	799	36.57	4557	14.67
1950–1959	17	56.67	442	46.58	21	33.87	954	43.66	9072	29.20
1960–1969	6	20.00	143	15.07	14	22.58	272	12.45	6897	22.20
1970–1979	1	3.33	72	7.59	6	9.68	157	7.19	10 332	33.26
>1980	0		3	0.32	1	1.61	3	0.14	209	0.67
Vital status										
Alive									20 814	67.00
Dead	30	100.0	949	100.0	62	100.0	2185	100.0	8952	28.82
Presumed alive									1157	3.72
Presumed dead									144	0.46
Total	30	100.0	949	100.0	62	100.0	2185	100.0	31 067	100.0

literature.[4 27–29] However, risk of exposure to non-asbestiform ampbibole and non-amphibole EMPs as found in taconite mining operations, is not understood, and evidence of their toxicity is inconclusive.[4] Our results indicate an increased risk for mesothelioma and lung cancer among taconite workers with at least 1 year of employment, but no exposure-response association for duration of employment was detected. Mortality from cardiovascular disease, specifically hypertensive heart disease and ischemic heart disease, were also increased. Major risk factors for the development of heart disease include hypertension, diabetes and cholesterol. Lifestyle factors, such as smoking, physical activity, and diet also play a role in disease risk. This study result suggests that lifestyle factors likely contribute to disease burden in this working population. However, occupational risk cannot be ruled out entirely. Other workplace factors, such as stress, noise, vibration, extreme temperature and shift work, may also affect cardiovascular disease risk.[30 31] Additionally, environmental factors, such as particulate air pollution, have also been shown to increase the risk of cardiovascular events from short and long-term exposure,[32–36] and elevated cardiovascular mortality has been identified in other working cohorts.[37] Thus, a combination of workplace and lifestyle factors may be contributing to the excess in cardiovascular disease in this taconite workers cohort.

The following limitations should be considered when interpreting the results of this analysis. Instead of specific exposure measurements for this analysis, duration of employment in the taconite mining industry was meant as a proxy for exposure averaged across all jobs and locations on the range. Our estimate of employment duration was measured as the last date of employment minus the start date. This crude measure of employment duration does not take into account any gaps in work history which could result in employment duration misclassification. Individuals who appear to have worked more than 15 years may have a much shorter cumulative work history when considering gaps in employment. We did not have access to information on some confounding variables, most notably smoking status which is a major risk factor for lung cancer and cardiovascular disease. Though we could not adjust for smoking in this analysis, it is possible that smoking explains at least some of this excess risk in lung cancer mortality especially given that working cohorts typically have higher smoking rates than the general population, and because of the high attributable risk for smoking.[38] Smoking however, is not a risk factor for mesothelioma, thus, the high mortality ratio of mesothelioma suggests that there may be occupational exposures to account for some of the increased risk of these diseases.

The risk of mesothelioma may also be underestimated, as the specific ICD code for this disease was not available until 1999, thus, earlier cases were misclassified as another disease. The lower percentage of mesothelioma cases, as compared to other causes of death (table 1) of those who were hired prior to 1950, the earliest exposed, may represent this misclassification. These undercounted mesotheliomas may have had more hematite exposure or exposure to the taconite processes in their earlier work. However, identifying other potential mesothelioma cases

Table 2 Selected SMRs for Minnesota Taconite Workers with ≥1 year employment*

Underlying cause of death	Observed	Expected	SMR	95% CI
All causes	9094	8764.69	1.04	1.02 to 1.06
All cancers	2710	2609.86	1.04	1.00 to 1.08
Respiratory	981	846.74	1.16	1.09 to 1.23
Larynx	26	23.84	1.09	0.71 to 1.60
Trachea, bronchus, lung	949	815.67	1.16	1.09 to 1.24
Pleura	1	1.81	0.55	0.01 to 3.08
Mesothelioma	30	10.82	2.77	1.87 to 3.96
Heart diseases	2676	2435.81	1.10	1.06 to 1.14
Hypertensive heart disease	62	34.17	1.81	1.39 to 2.33
Ischemic heart disease	2185	1964.93	1.11	1.07 to 1.16
Cerebrovascular disease	391	384.30	1.02	0.92 to 1.12
Hypertension w/o heart disease	35	52.80	0.66	0.46 to 0.92
Respiratory Diseases	582	621.19	0.94	0.86 to 1.02
COPD	363	369.89	0.98	0.88 to 1.09
Asbestosis	1	2.90	0.35	0.01 to 1.92
Silicosis	1	1.09	0.91	0.02 to 5.09
Transportation injuries	339	329.15	1.03	0.92 to 1.15
Other injury	239	221.75	1.08	0.95 to 1.22
Violence	289	258.41	1.12	0.99 to 1.26

*Adjusted for age, calendar period, and sex.
SMR, Standardised mortality ratios.

using previously used rubrics[39] would not change the interpretation that taconite workers have elevated rates of mesothelioma. It is also important to note that the cases were identified as primary causes of death, and do not capture incident cases or contributing causes of death and, therefore, do not accurately reflect the total disease burden in the cohort.

Although the SMR for mesothelioma was elevated, the internal analysis did not identify an association by duration of employment. One possible explanation of this is if the elevated risk of mesothelioma is related to work in the taconite industry, that risk may not be a function of time, rather a function of specific exposures while performing certain job tasks. Likewise, the internal analysis did not show an increased risk of lung cancer, hypertensive heart disease, and ischemic heart disease by duration of employment, suggesting that other lifestyle factors are potentially contributing to the elevated SMRs. These results could also have been affected by the crude employment duration measure resulting in misclassification of time worked.

The analysis by zone was a cursory examination of the risk across the iron range, since it evaluated any work in a zone. It does not allow for comparison of risk between zones, but only suggests the risk of mesothelioma and lung cancer is elevated with employment in each zone of the iron range. We limited the analysis to iron mining workers who were born in 1920 or later and who had at least 1 year of documented employment. Restricting the cohort further to those born in 1930 or later (excluding an additional 8504 workers) in order to potentially better focus on taconite mining did not substantially change the results and interpretation of this study (lung cancer SMR=1.15, 95% CI 1.04 to 1.27, mesothelioma SMR=3.59, 95% CI 2.16 to 5.60). Examination of the entire cohort of 44 243 individuals, including those with less than 1 year of documented employment, likewise did not substantially change the results and interpretation of this study (lung cancer SMR=1.20, 95% CI 1.14 to 1.27, mesothelioma SMR=2.89, 95% CI 2.11 to 3.87).

This study has some notable strengths, including the large size and long follow-up of the cohort and the high proportion of workers whose vital status was ascertained. Vital status was found on 98% of the eligible cohort, and few workers (4%) were excluded from the analysis due to data quality problems. Additionally, this study captured mortality from mesothelioma; early mortality studies of taconite workers were unable to evaluate mesothelioma until 1999 when ICD-10 became available.

Table 3 Standardised rate ratios by duration of employment, adjusted for age, calendar period, and sex

	Cause of death							
	Mesothelioma		Lung cancer		Hypertensive heart disease		Ischemic heart disease	
Employment duration (years)	Obs	SRR (95% CI)	Obs	SRR (95% CI)	Obs	SRR (95% CI)	Obs	SRR (95% CI)
1	4	1.14 (0.34 to 3.81)	123	1.01 (0.81 to 1.26)	6	0.90 (0.34 to 2.41)	241	0.88 (0.76 to 1.03)
2–5 (ref)	8	1.0	250	1.0	14	1.0	576	1.0
6–14	6	0.77 (0.26 to 2.25)	239	1.01 (0.85 to 1.21)	18	1.29 (0.63 to 2.63)	545	0.99 (0.88 to 1.11)
15+	12	1.08 (0.44 to 2.67)	337	0.94 (0.79 to 1.13)	24	1.84 (0.82 to 4.11)	823	0.98 (0.88 to 1.10)

SRR, Standardised rate ratios.

This study allowed us to characterise the mortality of the entire Minnesota mining population as compared to the rest of Minnesota, as well as capture information specific to where miners worked by zone which has not been done before. The analysis identifies a need for future studies with more refined exposure estimates to evaluate the extent to which mining-related exposures specifically contribute to disease burden and will be the next step in our evaluation of the health of taconite mining workers.

CONCLUSION

In summary, this analysis suggests taconite workers may be at increased risk for mortality from some cancers and cardiovascular diseases. Duration of employment did not appear to be associated with the mortality risk. However, based on the limited way exposure potential was evaluated, we cannot say for sure what the role of actual workplace exposures play in the disease excess. Additional investigation is warranted.

What this paper adds

- Mining and processing of taconite results predominantly in exposure to non-asbestiform amphibole and non-amphibole minerals.
- The health risks of these exposures are uncertain.
- Increased mortality rates from mesothelioma, lung cancer and some cardiovascular disease among taconite workers were observed.

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REFERENCES

1 Berndt ME, Brice WC. The origins of public concern with taconite and human health: reserve mining and the asbestos case. *Regul Toxicol Pharmacol* 2008;52(S1):S31–9.
2 Minnesota Department of Natural Resources. Digging in MN minerals: Taconite 2011 (Retrieved 22 August 2011). http://www.dnr.state.mn.us/education/geology/digging/mining.html
3 Hwang J, Gurumurthy R, Raynor P, *et al*. Comprehensive assessment of exposures to elongate mineral particles in the taconite mining industry. *Ann Occup Hyg* 2013;57:966–78.
4 Department of Health and Human Services, National Institute for Occupational Safety and Health. Asbestos fibers and other elongate mineral particles: State of the science and roadmap for research, 2011: Publication No. 2011-159.
5 McSwiggin PL, Morey GB. Overview of the mineralogy of the Biwabik Iron Formation, Mesabi Iron Range, northern Minnesota. *Regul Toxicol Pharmacol* 2008;52(S1):S11–25.
6 Jirsa MA, Miller JD, Morey GB. Geology of the Biwabik Iron Formation and Duluth Complex. *Regul Toxicol Pharmacol* 2008;52(S1):S5–10.
7 Wilson R, McConnell EE, Ross M, *et al*. Risk assessment due to environmental exposures to fibrous particulates associated with taconite ore. *Regul Toxicol Pharmacol* 2008;52(S1):S232–45.
8 Langer AM, Maggiore CM, Nicholson WJ, *et al*. The contamination of Lake Superior with amphibole gangue minerals. *Ann NY Acad Sci* 1979;330:549–72.
9 Williams C, Dell L, Adams R, *et al*. State-of-the-science assessment of non-asbestos amphibole exposure: is there a cancer risk? *Environ Geochem Health* 2013;35:357–77.
10 Yang H-Y, Shie R-H, Chen P-C. Carving of non-asbestiform tremolite and the risk of lung cancer: a follow-up mortality study in a historical nephrite processing cohort. *Occup Environ Med* 2013;70:852–7.
11 Finkelstein MM. Malignant Mesothelioma Incidence Among Talc Miners and Millers in New York State. *Am J Ind Med* 2012;868(April):863–8.
12 Nolan RP, Gamble JF, Gibbs GW. Letter to the editor on commentary: malignant mesothelioma incidence among talc miners and millers in New York state by M M Finkelstein. *Am J Ind Med* 2013;56:1116–18.
13 Gamble JF, Gibbs GW. An evaluation of the risks of lung cancer and mesothelioma from exposure to amphibole cleavage fragments. *Regul Toxicol Pharmacol* 2008;52(S1):S154–86.
14 Hilding AC, Hilding DA, Larson DM, *et al*. Biological effects of ingested amosite asbestos, taconite tailings, diatomaceous earth and Lake Superior water in rats. *Arch Environ Health* 1981;36:298–303.
15 Levy BS, Sigurdson E, Mandel J, *et al*. Investigating possible effects of asbestos in city water: surveillance of gastrointestinal cancer incidence in Duluth, Minnesota. *Am J Epidemiol* 1976;103:362–8.
16 Higgins IT, Glassman JH, Oh MS, *et al*. Mortality of Reserve Mining Company employees in relation to taconite dust exposure. *Am J Epidemiol* 1983;118:710–19.
17 Cooper WC, Wong O, Graebner R. Mortality of workers in two Minnesota taconite mining and milling operations. *J Occup Med* 1988;30:506–11.
18 Cooper WC, Wong O, Trent LS, *et al*. An updated study of taconite miners and millers exposed to silica and non-asbestiform amphiboles. *J Occup Med* 1992;34:1173–80.
19 Minnesota Cancer Surveillance System Epidemiology Report. *Cancer incidence rates in Northeastern Minnesota*. Minnesota Department of Health, 1999.
20 Centers for Disease Control and Prevention. Life Table Analysis System. 2013. http://www.cdc.gov/niosh/ltas
21 Lanphear BP, Buncher CR. Laten period for malignant mesothelioma of occupational origin. *J Occup Med* 1992;34:718–21.
22 Honda Y, Beall C, Delzell E, *et al*. Mortality among workers at a Talc mining and milling facility. *Ann Occup Hyg* 2002;46:575–85.
23 Price B. Industrial-grade talc exposure and the risk of mesothelioma. *Crit Rev Toxicol* 2010;40:513–30.
24 Gillam JD, Dement JM, Lemen RA, *et al*. Mortality patterns among hard rock gold miners exposed to an Asbestiform mineral. *Ann N Y Acad Sci* 1976;336–44.
25 McDonald JC, Gibbs GW, Liddel FDK, *et al*. Mortality after long exposure to cummingtonite-grunerite. *Am Rev Respir Dis* 1978;118:271–7.
26 Steenland K, Brown D. Mortality study of gold miners exposed to silica and nonasbestiform amphibole minerals: an update with 14 more years of followup. *Am J Ind Med* 1995;27:217–29.
27 McDonald JC, McDonald AD. The epidemiology of mesothelioma in historical context. *Eur Respir J* 1996;9:1932–42.
28 Robinson BWS, Musk AW, Lake RA. Malignant mesothelioma. *Lancet* 2005;366:397–408.
29 Robinson BM. Malignant pleural mesothelioma: an epidemiological perspective. *Ann Cardiothorac Surg* 2012;1:491–6.
30 Kawachi I, Colditz GA, Stampfer MJ, *et al*. Prospective study of shift work and risk of coronary heart disease in women. *Circulation* 1995;92:3178–82.
31 Price AE. Heart disease and work. *Heart* 2004;90:1077–84.
32 Brook RD, Rajagopalan S, Pope CA, *et al*. Particulate matter air pollution and cardiovascular disease: an update to the scientific statement from the American Heart Association. *Circulation* 2010;121:2331–78.
33 Dockery DW, Pope CA, Xu X, *et al*. An Association between Air Pollution and Mortality in Six U.S. Cities. *N Engl J Med* 1993;329:1753–9.
34 Miller KA, Siscovick DS, Sheppard L, *et al*. Long-term exposure to air pollution and incidence of cardiovascular events in women. *N Engl J Med* 2007;356:447–58.
35 Pope CA III, Burnett RT, Thurston GD, *et al*. Cardiovascular mortality and long-term exposure to particulate air pollution: epidemiological evidence of general pathophysiological pathways of disease. *Circulation* 2004;109:71–7.
36 Bhatnagar A. Environmental cardiology: studying mechanistic links between pollution and heart disease. *Cir Res* 2006;99:692–705.
37 Gallagher LG, Ray RM, Li W, *et al*. Occupational exposures and mortality from cardiovascular disease among women textile workers in Shanghai, China. *Am J Ind Med* 2012;55:991–9.
38 Centers for Disease Control and Prevention. Current cigarette smoking prevalence among working adults-United States 2004–2009. *MMWR Morb Mortal Wkly Rep* 2011;60:1305–9.
39 Sullivan PA. Vermiculite, respiratory disease, and asbestos exposure in Libby, Montana: update of a Cohort Mortality Study. *Environ Health Perspect* 2007;115:579–85.

Mortality experience among Minnesota taconite mining industry workers

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Cancer Incidence among Minnesota Taconite Mining Industry Workers

Objective: To evaluate cancer morbidity among Minnesota Taconite mining industry workers.

Methods: Cancer morbidity between 1988 and 2010 was evaluated in a cohort of 40,720 Minnesota taconite mining workers employed between 1930 and 1983. Standardized incidence ratios (SIRs) with 95% confidence intervals (CI) were determined by comparing observed numbers of incident cancers with frequencies in the Minnesota Cancer Surveillance System. SIRs for lung cancer by histological subtypes were also estimated. SIRs were adjusted to account for out-of-state migration and a bias factor was estimated to adjust smoking related cancers.

Results: A total of 5,700 cancers were identified in the study cohort including 51 mesotheliomas and 973 lung cancers. After adjusting for out-of-state migration, the SIR for lung cancer and mesothelioma were 1.3 (95% CI: 1.2-1.4) and 2.4 (95% CI: 1.8-3.2) respectively. Other elevated cancers included stomach (SIR = 1.4, 95% CI: 1.1-1.6), laryngeal (SIR = 1.4, 95% CI: 1.1-1.7), and bladder (SIR = 1.1, 95% CI: 1.0-1.2). Among the lung cancers, SIRs for adenocarcinoma (SIR = 1.2, 95% CI: 1.1-1.4), squamous cell (SIR = 1.3, 95% CI: 1.2-1.5) non-specified (SIR = 1.6, 95% CI: 1.4-1.8), and other (SIR = 1.4, 95% CI: 1.1-1.8) were elevated. Adjusting with a bias factor for smoking attenuated the lung cancer SIR (SIR = 1.1, 95% CI: 1.0-1.1).

Conclusions*:* Taconite workers have an increased risk for certain cancers. Adjustment for smoking attenuates but does not eliminate the risk of lung cancer in this population. Lifestyle and work-related factors may play an important role in elevated morbidity. The extent to which mining-related exposures contribute to disease burden is being further investigated.

BACKGROUND AND SIGNIFICANCE

Full scale taconite mining began in northeastern Minnesota in the 1950s along the 120 mile long Mesabi Iron Range. This open pit mining is a multi-stage process that involves blasting rock with dynamite, crushing the rock down to a fine powder, magnetically extracting the iron, and reforming the more concentrated product into iron ore pellets. This process generates a significant amount of dust that results in potential exposure to long and short non-asbestiform amphibole and non-amphibole elongate mineral particles (EMPs), respirable silica, quartz, and cleavage fragments.[Hwang, 2013] Several studies have examined the risk of exposure to non-asbestiform EMPs[Steenland and Brown, 1995; Honda *et al*., 2002; Gillam *et al*., 1976 McDonald *et al*., 1978], but the toxicity of these exposures is uncertain.[DHHS, 2011] A limited number of animal studies in this field have provided evidence to suggest that non-asbestiform amphiboles might pose different risks than asbestos,[Davis *et al*, 1991; Mossman 1990; Mossman, 2008] but that risk remains unclear.[DHHS, 2011; Finkelstein, 2012, Nolan, 2013]

Elevated age-adjusted rates of mesothelioma have been reported in northeastern Minnesota counties in proximity to where taconite is mined. [NIOSH, 2008] This apparent increase in cases has been concerning to the mining communities. Despite community-wide health concerns and the lack of knowledge of these potential health effects, there is limited health research related to taconite mining industry workers. Several small-scale mortality studies conducted in the early 1980s and 1990s produced null findings. [Higgins, 1983; Cooper, 1988; Cooper, 1992] A larger mortality study in the population used for this analysis found an excess of death from lung cancer and mesothelioma. In this study, we examine incident cancers in a taconite workers cohort.

METHODS

Study population

The study cohort was enumerated in the early 1980s as part of the Mineral Resources Health Assessment Program (MRHAP). The program was developed by the University of Minnesota, School of Public Health, along with the Iron Range Resources and Rehabilitation Board. Its goals were to develop expertise concerning hazards of the mining and processing of minerals in Minnesota and to research health effects of mining and mineral processing. Investigators assembled a database of 68,737 individuals who had ever worked in one of the mines in operation in 1983. (Allen *et al.*, 2014) Work history information was collected through 1983, though some individuals worked beyond this point.

In 2008, the University of Minnesota launched the Taconite Workers Health Study (TWHS). [UMN TWHS, 2013] One objective of the TWHS was to update the health assessment of the cohort of 68,737 miners collected by MRHAP in 1983. The cohort included both taconite workers and those who had also worked in the earlier hematite mining operations. In order to capture workers who were most likely to have been working after taconite mining began in the 1950s, the cohort was limited to those born in 1920 or later, reducing the cohort size to 46,170 individuals. An additional 1,691 were excluded including 477 whose only record on file was an application with no further evidence of employment, 679 whose vital status remained unknown after follow-up, and 535 for whom employment information was improbable, e.g. began working at age fourteen or younger. For this analysis of cancer incidence, the cohort was further restricted to individuals living to at least 1988 when the Minnesota Cancer

Surveillance System would capture the incident cases, which eliminated 3,759 workers who were deceased before 1988. The final study cohort included 40,720 individuals.

Cancer Incidence

To identify incident cancers, the cohort was linked to the Minnesota Cancer Surveillance System (MCSS). The MCSS is Minnesota's statewide, population-based cancer registry that collects histological information of newly diagnosed cancers on all Minnesota residents. The system was established in 1988 by state statute as a mandatory reporting system to monitor cancers in Minnesota, inform health professionals, answer the public's questions, and promote cancer research. Cancer incidence including date of diagnosis, cancer site, and histology were obtained for cohort members matched to the MCSS.

Data analysis

The cancer morbidity analyses covered the period from 1988 (when the Minnesota Cancer Surveillance System began collecting data) through 2010. The cancer rate of the cohort was compared with that of the Minnesota population to estimate standardized cancer incidence ratios (SIRs) and 95% confidence intervals (CIs) adjusted for sex, and five-year age and calendar period. Person-time at risk was accrued from January 1, 1988 until cancer diagnosis date, date of death, or the end of the follow-up period (December 31, 2010). For individuals with more than one diagnosis of the same cancer, they were followed only to the date of first diagnosis. The expected number of cancers was calculated by applying age, calendar time, and sex specific cancer rates of the Minnesota population to the person-year observations of the study population. SIRs were obtained by computing the ratio of the observed-to-expected number of cancers. Selected cancers of interest were mesothelioma, lung, esophageal, kidney, laryngeal, liver and bile duct, oral, pancreatic, stomach, and bladder cancers. These cancers were of interest to study investigators because of their association with asbestos exposure. DHHS, 2011; National Tox Program 2011; ATSDR] All SIRs were computed using STATA 12.1 software.

We further explored lung cancer incidence by histological type. Lung cancer in the study and reference populations were grouped into one of five subtypes: adenocarcinoma, squamous cell, small cell, other/rare (including large cell), and non-specified carcinomas. The International Classification of Diseases for Oncology (ICD-O) histology code groupings were determined by study investigators. These groupings can be found in Appendix Table A. Standardized incidence ratios and 95% CIs were estimated for each of the five lung cancer histological subtypes.

Accurate estimation of cancer incidence rates in the study population requires individuals to remain in the state of Minnesota, and thus under MCSS surveillance. In order to adjust for potential migration, out-of-state deaths were used as an estimate of out-of-state migration by age group in the study population. As part of the Taconite Workers Health Study, the cohort was followed up for mortality with state of death identified for decedents. Details of the mortality follow-up have been described elsewhere.[Allen *et al*., 2014] The proportion of in-state deaths by age group was used as an estimate of the proportion of workers who stayed in Minnesota. Person-years were adjusted by age-group accordingly.

No information on tobacco smoking was available for cohort members however, because some of the cancers of interest (lung, oral, laryngeal, and bladder) are strongly associated with smoking, [WHO, 2014; Secretan *et al*., 2009] a bias factor for smoking was calculated to adjust the SIRs for smoking related cancers. A subset of 1,313 taconite mining industry workers participated in a cross-sectional survey where data collection included a questionnaire with smoking history. This subset analysis was one part of the overall TWHS and details of this study can be found elsewhere. [Odo *et al.*, 2013] The smoking prevalence in this subset of workers was used as an estimate of the smoking prevalence in the target population. Minnesota smoking data from the Behavioral Risk Factor Surveillance System (BRFSS) [CDC BRFSS, 2013] was weighted by the sex and age distribution of the questionnaire participants and used as an estimate of the smoking prevalence for the reference population. Questionnaire data were summarized into ever and never smokers. Among the 1,313 current and former taconite workers, 38.2% reported never having smoked. After weighting the BRFSS smoking data to the age and sex distribution of the questionnaire respondents, 50.1% of Minnesotans fell into the never smoked category. Cancer rates in smokers versus non-smokers obtained from World Health Organization (WHO) estimates for lung cancer was 10, for oral cancer, 27, for laryngeal cancer, 12, and for bladder cancer, 3.[WHO, 2014] These data were used in the following formulas, adapted from Steenland and Greenland, 2004, to estimate a bias factor: [Steenland and Greenland, 2004]

$$I_{+} = I_0(C_x)(S_1) + I_0(1 - S_1)$$

$$I_{-} = I_0(C_x)(S_0) + I_0(1 - S_0)$$

Where: I_+ = cancer incidence rate in study population

I_- = cancer incidence rate in Minnesota

S_1 = smoking prevalence in study population

S_0 = smoking prevalence in Minnesota

I_0 = cancer rate in non-smokers

C_x = cancer rate in smokers versus non-smokers

A bias factor for smoking was estimated with I_+/I_- and smoking related cancers were divided by this bias factor to adjust for potential differences in smoking between the study and reference populations. Using the smoking prevalence estimates in the study population, the Minnesota general population, and the cancer rates among smokers versus non-smokers, the bias factor for four of the smoking related cancers (lung, laryngeal, oral, and bladder cancers) was estimated.

RESULTS

This cohort of Minnesota taconite mining industry workers was predominantly male (93%) with an average work history of 6.5 years. Among the 40,720 workers, 5,700 cancers were identified by MCSS (5408 for men and 292 for women). Of those, 973 lung cancers and 51 mesotheliomas were identified.

After adjusting for age, sex, calendar period, and out-of-state migration, the cohort members experienced elevated rates of mesothelioma (SIR = 2.4, 95% CI: 1.8-3.2), lung (SIR = 1.3, 95% CI: 1.2-1.4), laryngeal (SIR = 1.4, 95% CI: 1.1-1.7), stomach (SIR = 1.4, 95% CI: 1.1-1.6), and bladder (SIR = 1.1, 95% CI: 1.0-1.2) cancers. SIRs and 95% CIs for selected cancers of interest are summarized in table 1.

Table 1. Selected SIRs for Minnesota Taconite Workers

Cancer	Observed	Expected	SIR*	95% CI
Mesothelioma	51	21.1	2.4	1.8-3.2
Lung	973	750.9	1.3	1.2-1.4
Esophagus	87	76.9	1.1	0.9-1.4
Kidney	170	178.2	1.0	0.8-1.1
Larynx	94	68.6	1.4	1.1-1.7
Liver and bile duct	52	49.4	1.1	0.8-1.4
Oral	172	162.5	1.1	0.9-1.2
Pancreas	120	105.9	1.1	0.9-1.4
Stomach	105	77.7	1.4	1.1-1.6
Bladder	363	338.5	1.1	1.0-1.2

*Adjusted for age, sex, calendar period, and out-of-state migration

A closer look at lung cancer by histological subtypes showed that among the 973 incident lung cancers, 313 were adenocarcinomas, 260 were squamous cell carcinomas, 138 were small cell carcinomas, 201 were non-specified lung cancers, and 61 were other or rare types of lung cancer. SIRs were elevated for adenocarcinoma (SIR = 1.2, 95% CI: 1.1-1.4), squamous cell (SIR = 1.3, 95% CI: 1.2-1.5), non-specified (SIR = 1.6, 95% CI: 1.3-1.8), and rare cancers (SIR = 1.3, 95% CI: 1.0-1.7) after adjusting for age, sex, calendar period, and out-of-state migration. Table 2 shows SIRs for lung cancer by histological subtype.

Table 2. SIRs for lung cancer by histological subtype

Lung cancer histological subtype	**N**	**SIR***
Adenocarcinoma	313	1.2 (1.1, 1.4)
Squamous cell	260	1.3 (1.2, 1.5)
Small Cell	138	1.1 (1.0, 1.3)
Non-specified	201	1.6 (1.3, 1.8)
Rare/other (including large cell)	61	1.3 (1.0, 1.7)
Total	973	1.3 (1.2, 1.4)

*Adjusted for age, sex, calendar period, and out-of-state migration

The estimated bias factors for lung, laryngeal, oral, and bladder cancers were 1.2, 1.2, 1.2, and 1.1 respectively. The bias factor for lung cancer (1.2) was similar to the one estimated in the adapted example (1.18) from Steenland and Greenland, 2004. After adjustment using the smoking bias factor, the SIR for lung cancer was attenuated but remained above what would be expected in the Minnesota population (SIR = 1.1, 95% CI: 1.0-1.2). The rates of laryngeal, oral, and bladder cancers were as expected in the Minnesota population after the bias factor adjustment (laryngeal SIR = 1.1, 95% CI: 0.9-1.4, oral SIR = 0.9, 95% CI: 0.7-1.0, bladder SIR = 1.0, 95% CI: 0.9-1.1). Though the effect of smoking on lung cancer risk by histological subtype varies, squamous and small cell carcinomas are found to be the most strongly associated with smoking (Khuder, 2001). The same sensitivity analysis was applied to squamous and small cell carcinomas. The SIRs were attenuated to what would be expected in the Minnesota population for both squamous (SIR = 1.1, 95% CI: 0.9-1.2) and small cell carcinoma (SIR = 0.9, 95% CI: 0.8-1.1). SIRs with adjustments for smoking are summarized in table 3.

Table 3. SIRs for smoking related cancers before and after bias factor adjustment for smoking.

Cancer	SIR*	95% CI	Smoking adjusted SIR**	95% CI
Lung	1.3	1.2-1.4	1.1	1.0-1.2
Squamous cell	1.3	1.2-1.5	1.1	0.9-1.2
Small cell	1.1	1.0-1.3	0.9	0.8-1.1
Larynx	1.4	1.1-1.7	1.1	0.9-1.4
Oral	1.1	0.9-1.2	0.9	0.7-1.0
Bladder	1.1	1.0-1.2	1.0	0.9-1.1

*Adjusted for age, sex, calendar period, and out-of-state migration

**Bias factor for lung, laryngeal, oral and bladder cancers = 1.2, 1.2, 1.2, and 1.1 respectively

DISCUSSION

In this analysis of cancer incidence among Minnesota taconite mining industry workers, there were higher than expected rates of certain cancers as compared to the general Minnesota population, specifically for mesothelioma, lung, laryngeal, stomach, and bladder cancers. Each lung cancer by histological subtype showed an increased SIR. A sensitivity analysis to account for differences in smoking rates between the study and reference populations attenuated the association between laryngeal, bladder, and oral cancers substantially as well as squamous cell and small cell carcinomas of the lung. However, even after smoking bias adjustment, the overall lung cancer SIR remained elevated. In total, these data support an elevated SIR for those cancers that have historically had the strongest relationship to asbestos and EMP exposure. These observations are in a population of workers exposed to a variety of mineral dusts including asbestiform and non-asbestiform elongate mineral particles.

The strong association between asbestos exposure and mesothelioma and lung cancer is well documented [DHHS, 2011; McDonald and McDonald, 1996; Robinson *et al*., 2005; Robinson, 2012] however, the toxicity of their non-asbestiform analogs is not understood. Results from recent studies have suggested that exposure to non-asbestiform EMPs does not have high potential for disease [Mossman 2008; Berry and Gibbs, 2008; Gamble and Gibbs, 2007] however, NIOSH has specifically identified non-asbestiform EMPs as a needed area of research. [DHHS, 2011] Non-asbestiform EMPs are included in NIOSH recommended exposure limits due to technical limitations of routine EMP assessments and uncertainty about the potential toxicity of non-asbestiform fibers. There is inconclusive evidence in epidemiological studies of New York talc miners [Honda *et al*., 2002] and Homestake gold miners [Gillam *et al*., 1976; McDonald *et al*., 1978; Steenland and Brown, 1995], and evidence from animal studies suggests that fiber dimension, and not composition, is the major determinant of carcinogenicity for mineral fibers. There remains a need to determine conclusively whether non-asbestiform amphibole mineral particles that are chemically similar to asbestos, but with different physical forms that are also capable of causing disease.[DHHS, 2011] These mineral particles, including low-levels of non-asbestiform mineral particles, are present in taconite mining operations. Additionally, the predominant exposure potential during the mining and processing of taconite is of short mineral particles, less than five microns in length.[Hwang *et al*., 2013] These short mineral particles are currently not included in NIOSH regulatory standards[DHHS, 2011; OSHA] and have not been studied to the extent that regulated particles have been.[Aust *et al*., 2011]

We observed elevated SIRs for all types of lung cancer. Small-cell lung cancer is rarely observed in never-smokers[Pallis and Syrigos, 2013] while adenocarcinoma is the predominant histological type in never-smokers.[Pallis and Syrigos, 2013; Toh *et al*., 2006] Moreover, adenocarcinoma has been shown to be the most common histological subtype in asbestos-exposed individuals.[Raffn *et al*., 1993; de Klerk *et al*., 1996] The results of our study show that of the 973 lung cancers identified in the study cohort, 138 were small-cell and 313 were adenocarcinoma. The smoking adjusted results suggest that smoking habit does not account for all of the lung cancer excess in this population. Occupational exposures may also contribute to the elevation in cancer incidence.

The earliest studies of taconite mining exposures focused on ingestion exposure and showed no association between cancers and EMP ingestion.[Hilding *et al*., 1981; Levy *et al*., 1976] These were followed by mortality assessments in specific mining companies.[Higgins *et al*., 1983; Cooper *et al*., 1988; Cooper *et al*., 1992] Though these mortality studies did not show a significant excess in respiratory cancers, they had small study populations, short follow-up periods and thus limited statistical power. In 2007, the Minnesota Department of Health reported a 73% excess in cases of mesothelioma for men in northeastern Minnesota between 1988 and 1996,[MCSS, 1999] consistent with the elevated SIR reported here. The cause of this excess remains unknown.

The few studies of other occupational cohorts who experience exposures to non-asbestiform mineral particles have been inconclusive. Talc miners in upstate New York and gold miners in South Dakota experience potential exposures to non-asbestiform EMPs. The studies of talc miners reported an excess in mortality from all cancers, lung cancer, ischemic heart disease, and non-malignant repiratory disease, however a lack of exposure-response relationship was seen. Studies of the Homestake gold mine in South Dakota published in the 1970s and 1980s reported an excess of respiratory cancer and a small excess of lung cancer[Gillam *et al*., 1976; McDonald *et al*., 1978; Steenland and Brown, 1995] with no observed dose-response relationship, suggesting a weak association between dust exposure and lung cancer. Due to the limitations of these epidemiology studies, NIOSH has concluded that the findings provide inconclusive evidence regarding the health effects associated with exposures to non-asbestiform EMPs.[DHHS, 2011] This analysis provided evidence of a possible association between non-asbestiform exposures and cancer.

Some limitations should be considered when interpreting the results of this analysis. Utilizing the Minnesota state cancer registry data requires cohort members to remain in Minnesota in order to capture newly diagnosed cancers. Because it was not feasible to identify if an individual was diagnosed with cancer outside of Minnesota before the end of follow up, adjustments in person-years were required to correct for potential underestimation of SIRs. This study used out-of-state deaths by age group as an estimate of the proportion of individuals in each age group who left Minnesota. We also did not have information on lifestyle factors, most importantly smoking history, a known risk factor for several of the cancers of interest. Differences in smoking in our study cohort and reference population were likely given the documented higher rates of smoking in working cohorts.[CDC MMWR, 2011] We were able to address this issue with a sensitivity analysis which estimated smoking rates of the study population using data from a smaller study of Minnesota taconite workers. However, there are potential limitations with using this subset of miners as an estimate of smoking habits in our study population. There is potential selection bias of those who participated in the subset analysis by smoking status. We do not know if our study population is representative of the smoking habits of the entire taconite cohort. Additionally, those who participated in the subset analysis were alive in 2010 and thus may have very different smoking habits than their historic counterparts due to generational differences in smoking patterns. However, because smoking habits for the reference population were taken from BRFSS 2010 data, the relative differences in smoking between the two groups were taken at the same time. We assumed that population smoking rates changed at the same rate as cohort smoking rates and thus the bias factor analysis accounted for this relative difference in smoking between the two groups and adjusted the SIRs accordingly. The sensitivity analysis also required knowing the cancer rate is smokers versus non-smokers. This estimation can vary among different sources[WHO, 2014; Steenland and Greenland, 2004] however changing this variable in the bias factor calculation did not substantially change the results of the sensitivity analysis.

One of the main strengths of this study is the large size of the cohort. The study population included all taconite mining industry workers with any work experience across the entire Minnesota Iron Range with very few workers (4%) excluded from the analysis due to data quality problems. Having mortality data including state of death for the study population allowed for an estimation of out-of-state migration which can be challenging for other cancer incidence studies of this nature.

CONCLUSION

In summary, this analysis suggests that Minnesota taconite mining industry workers are at risk for development of mesothelioma, lung cancer, and other cancers. The elevated risk of lung and other cancers may be due to elevated smoking and other unmeasured confounders among the workers. However, because confounding variables were not measured and workplace exposure measurements were not evaluated in this analysis, we cannot say for sure if actual work place exposures contribute to that excess in cancer incidence. A detailed examination of taconite workplace exposures is warranted.

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References

1. Agency for Toxic Substances and Disease Registry. *Toxicological Profile for Asbestos*. September 2001. Retrieved January 28, 2014, from: http://www.atsdr.cdc.gov/toxprofiles/tp61.pdf.
2. Allen E, Alexander B, MacLehose R, *et al*. Mortality Experience Among Minnesota Taconite Mining Industry Workers, *Occupational and Environmental Medicine*. *Accepted for publication; date pending.*
3. Aust AE, Cook PM, Dodson RF. Morphological and chemical mechanisms of elongate mineral particle toxicities. *J Toxicol Environ Health B Crit Rev* 2011;14:40-75.
4. Berry G, Gibbs GW. An overview of the risk of lung cancer in relation to exposure to asbestos and of taconite miners. *Regul Toxicol Pharmacol* 2008;52(S1):S218-22.
5. Centers for Disease Control and Prevention. Current cigarette smoking prevalence among working adults-United States 2004-2009. *MMWR Morb Mortal Wkly Rep* 2011;60(38):1305-1309.
6. Centers for Disease Control and Prevention. Behavioral Risk Factor Surveillance System 2013. Available from: http://www.cdc.gov/brfss/data_tools.htm.
7. Cooper WC, Wong O, Graebner R. Mortality of workers in two Minnesota taconite mining and milling operations. *J Occup Med* 1988;30(6):506-511.
8. Cooper WC, Wong O, Trent LS, *et al*. An updated study of taconite miners and millers exposed to silica and non-asbestiform amphiboles. *J Occup Med* 1992;34(12):1173-1180.
9. Davis JM, Addison J, McIntosh C, *et al*. Variations in the carcinogenicity of tremolite dust samples of differing morphology. *Ann NY Acad Sci* 1991;643:473-490.
10. Department of Health and Human Services, National Institute for Occupational Safety and Health. Asbestos fibers and other elongate mineral particles: State of the science and roadmap for research, 2011: Publication No. 2011-159.

11. Finkelstein MM. Malignant Mesothelioma Incidence Among Talc Miners and Millers in New York State. *Am J Ind Med* 2012;868(April):863–868.
12. Gamble JF, Gibbs GW. Evaluation of the risks of lung cancer and mesothelioma from exposure to amphibole cleavage fragments. *Regul Toxicol Pharmacol* 2007;52(S1):S154-S186.
13. Gillam JD, Dement JM, Lemen RA, *et al*. Mortality Patterns Among Hard Rock Gold Miners Exposed to an Asbestiform Mineral. *Ann N Y Acad Sci* 1976;336–344.
14. Higgins IT, Glassman JH, Oh MS, *et al*. Mortality of Reserve Mining Company employees in relation to taconite dust exposure. *Am J Epidemiol* 1983;118(5):710-9.
15. Hilding AC, Hilding DA, Larson DM, *et al*. Biological effects of ingested amosite asbestos, taconite tailings, diatomaceous earth and Lake Superior water in rats. *Arch Environ Health* 1981;36:298-303.
16. Honda Y, Beall C, Delzell E, *et al*. Mortality among Workers at a Talc Mining and Milling Facility. *Ann Occup Hyg* 2002;46(7):575–585.
17. Hwang J, Gurumurthy R, Raynor P, *et al*. Comprehensive Assessment of Exposures to Elongate Mineral Particles in the Taconite Mining Industry. *Ann Occup Hyg* 2013;doi:10.1093.
18. Khuder SA. Effect of cigarette smoking on major histological types of lung cancer: a meta-analysis. *Lung Cancer* 2001 Feb-Mar;31(2-3):139-48.
19. de Klerk, NH, Musk AW, Eccles J *et al*. Exposure to crocidolite and the incidence of different histological types of lung cancer. *Occup Environ Med* 1996;53:157-159.
20. Levy BS, Sigurdson E, Mandel J, *et al*. Investigating possible effects of asbestos in city water: surveillance of gastrointestinal cancer incidence in Duluth, Minnesota. *Am J Epidemiol* 1976;103:362-368.
21. Minnesota Cancer Surveillance System Epidemiology Report. Cancer incidence Rates in Northeastern Minnesota. Minnesota Department of Health, 1999.

22. McDonald JC, Gibbs GW, Liddel FDK, *et al*. Mortality after long exposure to cummingtonite-grunerite. *Am Rev Respir Dis* 1978;118:271-277.

23. McDonald JC, McDonald AD. The epidemiology of mesothelioma in historical context. *Eur Respir J* 1996;9(9):1932–1942.

24. Mossman B, Sesko A. In vitro assays to predict the pathogenicity of mineral fibers. *Toxicology* 1990;60:53-61.

25. Mossman BT. Assessment of the pathogenic potential of asbestos vs. nonasbestiform particulates (cleavage fragments) in in vitro (cell or organ culture) models and bioassays. *Regul Toxicol Pharmacol* 2008;52(S1):S200-3.

26. National Institute for Occupational Safety and Health. Malignant mesothelioma: Counties with highest age-adjusted death rates (per million population), U.S. residents age 15 and over, 2000-2004. Work-Related Lung Disease (WoRLD) Surveilllance Report Update, 2008: http://www2.cdc.gov/drds/WorldReportData/FigureTableDetails.asp?FigureTableID=901andGroupRefNumber=T07-10, accessed January 17, 2014.

27. National Toxicology Program. Asbestos. In: *Report on Carcinogens. Twelfth Edition*. U.S. Department of Health and Human Services, Public Health Service, National Toxicology Program, 2011.

28. Nolan RP, Gammble JF, Gibbs GW. Letter to the editor on commentary: malignant mesothelioma incidence among talc miners and millers in New York state by M M Finkelstein. *Am J Ind Med* 2013;56(9):1116-8.

29. Odo NU, Majdel JH, Perlman DM, *et al*. Estimates of restrictive ventilator defect in the mining industry. Considerations for epidemiological investigations: a cross-sectional study. BMJ Open 2013; *3:e002561 doi:10.1136/bmjopen-2013-00256.*

30. Occupational Safety and Health Association. OSHA Standards 1910.1001 Asbestos. Available at https://www.osha.gov/pls/oshaweb/owadisp.show_document?p_table=standardsandp_id=9995. Accessed J.
31. Pallis AG, Syrigos KN. Lung cancer in never smokers: disease charateristics and risk factors. *Crit Rev Oncol Hematol* 2013 Dec;88(3):494-503 .
32. Raffn E, Lynge E, Korsgaard B. Incidence of lung cancer by histological type among asbestos cement workers in Denmark. *Br J Ind Med* 1993 January;50(1):85-89.
33. Robinson BWS, Musk AW, Lake RA. Malignant mesothelioma. *Lancet* 2005;366(9483):397–408.
34. Robinson BM. Malignant pleural mesothelioma: an epidemiological perspective. *Ann Cardiothorac Surg* 2012;1(4):491–6.
35. Secretan B, Straif K, Baan R, *et al*. A review of human carcinogens-Part E: tobacco, areca nut, alcohol, coal smoke, and salted fish. *The Lancet Oncol* 2009;10:1022-4.
36. Steenland K, Greenland S. Monte Carlo Sensitivity Analysis and Bayesian Analysis of Smoking as an Unmeasured Confounder in a Study of Silica and Lung Cancer. *Am J Epidemiol* 2004;160:384-392.
37. Steenland K, Brown D. Mortality study of gold miners exposed to silica and nonasbestiform amphibole minerals: an update with 14 more years of followup. *Am J Ind Med* 1995;27:217-229.
38. Toh CK, Gao F, Lim WT, *et al*. Never-smokers with lung cancer: epidemiologic evidence of a distinct disease entity. *Journal of Clinical Oncology* 2006;24:2245-51.
39. University of Minnesota. *Taconite workers health study* 2013. Available from: http://taconiteworkers.umn.edu/

40. World Health Organization. Tobacco Free Initiative 2014. Available from: http://www.who.int/tobacco/research/cancer/en/.

APPENDIX

Table A. Lung cancer major histology groupings

Histology	ICD-O code	count
ADENOCARCINOMA		313
Acinic Cell Adenocarcinoma	85503	1
Adenocarcinoma NOS	81403	263
Bronchiolo-Alveolar Adenocarcinoma	82503	23
Bronchiolo-Alveolar Mucinous	82533	1
Bronchiolo-Alveolar non-mucinous	82523	4
Mixed Cell Adenocarcinoma	83233	1
Mucin Producing Adenocarcinoma	84813	11
Clear Cell Adenocarcinoma	83103	1
Mucinous Adenocarcinoma	84803	5
Papillary Adenocarcinoma NOS	82603	3
SMALL CELL CARCINOMA		139
Combined Small Cell Carcinoma	80453	2
Intermediate Cell Small Cell Carcinoma	80443	5
Neuroendocrine Carcinoma	82463	9
Oat Cell Carcinoma	80423	4
Small Cell Tumor	80023	1
Small Cell Carcinoma NOS	80413	118
SQUAMOUS CELL CARCINOMA		258
Basaloid Squamous Cell Carcinoma	80833	1
Squamous Cell Carcinoma Spindle Cell	80743	1
Squamous Cell Carcinoma Keratinizing	80713	9
Squamous Cell Carcinoma Non- Keratinizing	80723	10
Squamous Cell Carcinoma	80703	237
NON-SPECIFIED		202
Neoplasm Malignant	80003	19
Non-Small Cell Carcinoma	80463	97
Carcinoma NOS	80103	68
Undifferentiated Carcinoma	80203	11
Carcinoid Tumor	82403	4
Atypical Carcinoid Tumor	82493	1
Tumor cells Malignant	80013	2
RARE/OTHER		61
Anaplastic Carcinoma	80213	2
Spindle Cell Carcinoma	80323	1
Large Cell Carcinoma NOS	80123	38
Large Cell Carcinoma rhabdoidphenotype	80143	1
Adenosquamous Carcinoma	85603	12
Fibrous histiocytoma	88303	1
Large Cell Neuroendocrine Carcinoma	80133	5
Sarcome NOS	88003	1

Appendix 6

A Case-Control Study of Mesothelioma in Taconite Miners Exposed to Elongate Mineral Particles (EMPs)

Background

During the past several decades, Minnesota's taconite industry has been plagued by controversy over potential health problems. Concerns were initially expressed in the 1970s regarding the disposal of taconite waste rock, which contained fibrous minerals, into Lake Superior and ultimately into the city of Duluth's drinking water (Wilson *et al.*, 2008). In follow-up of this issue, occupational studies were conducted that did not demonstrate evidence of disease excess (Cooper *et al.*, 1988, 1992; Higgins *et al.*, 1983). In 2007, the Minnesota Department of Health identified an apparent excess of mesothelioma in a cohort of taconite miners (MDH Report, 2007), using the state's cancer registry to identify cases. This finding was confirmed in a general cohort mortality analysis, which indicated a 2.77 fold increase in the rate of mesothelioma in taconite industry workers when compared to the rest of Minnesota (Allen *et al.*, 2014). While this finding suggested that people working in the industry were at higher risk for mortality from mesothelioma, it did not reveal specifically how work in the industry may be related to this risk. The present report attempts to determine further details about the role of the workplace in this finding.

Assessments of workplace mineral exposure and lung disease have been hampered by a confusing terminology that may deal with different measurement techniques and/or different definitions of exposure. As an example, although mesothelioma has been strongly linked to asbestos exposure, the term "asbestos" may have different meanings. It may have a commercial connotation, as the six regulated types of asbestos [chrysotile (serpentine) and five types of amphiboles: anthophyllite, tremolite, cummingonite-grunerite (amosite), riebeckite (crocidolite) and actinolite] may be used in various industrial applications. From a mineralogical view, all types may exhibit the "asbestiform" habit (morphology), meaning they can be separated in their natural environmental state into hair-like fibers along the longitudinal axis (Gunter *et al.*, 2007). The asbestiform type has the highest potential for lung exposure. All regulated types may also exist naturally in a non-asbestiform habit, with lower lung exposure potential. The term "fiber" is another ambiguous term, as mineralogical and regulatory definitions of fiber are inconsistent. The mineralogical definition refers to the smallest elongate crystalline unit that can be separated from a bundle or appears to have grown individually in that shape. Polycrystalline aggregates of mineral fibers give rise to a fibrous habit, one specific type of which is referred to as "asbestiform".

Use of the term "elongate mineral particle" (EMP) has been employed to clarify some of the confusion around the use of these terms (NIOSH, 2011). An EMP refers to any mineral that has an aspect ratio (length to width ratio) of 3:1 or greater. EMPs may be classified as amphibole or non-amphibole and amphibole EMPs may be further described as asbestiform or non-asbestiform (NIOSH, 2011). Mineral composition, dimension and habit are important parameters in the definition of EMPs. The regulatory definition of "fiber" is based solely on dimensional criteria and refers to particles with aspect ratios of at least 3:1 and a length greater than 5 µm (NIOSH Method 7400, 2003). EMPs defined in this way are counted with the use of phase contrast microscopy (PCM). The NIOSH recommended exposure limit (REL) is 0.1 fibers (EMP) per cubic centimeter of air, measured as a time-weighted average (TWA), although this method is not able to distinguish amphibole from non-amphibole EMP or asbestiform from non-asbestiform EMP. These subtleties in how EMPs are defined may be important considerations in epidemiological investigations.

In the taconite industry, relevant exposures to EMPs may be generated from a natural component of the ore or from commercial grade asbestos, which was used historically in various parts of the mining facilities as an insulator. While the mineral dust in taconite mining is a complex mixture, predominant exposures of relevance are to non-amphibole EMPs and to non-asbestiform amphibole EMPs. EMPs may also include cleavage fragments (CFs), which are produced as a result of mechanical fracturing of the mineral by crushing or grinding. In many cases CFs are produced by the breaking of crystals in preferred directions, related to their molecular structures, but this is not always the case as some minerals do not break along cleavage planes (e.g. quartz). It may be difficult to distinguish between amphibole asbestos and amphibole CF because their dimensional attributes may overlap (Harper *et al.*, 2012). NIOSH, OSHA and the U.S. EPA include CFs in their fiber counting methods. Chatfield has suggested that amphibole CFs can be distinguished from asbestiform amphibole fibers when investigated by transmission electron microscope by aspect ratio (>20:1) and width criteria (width ranges from 0.04-1.5 µm) in the latter (Chatfield, 2008).

There is a well-established, causal relationship between mesothelioma and asbestiform EMPs (IOM, 2006; ATSDR, 2001; IARC, 1987), likely related to fiber dimension, chemical composition, surface reactivity and persistence (IOM, 2006; Lippmann, 1990). Although controversies exist around the health effects of non-asbestiform exposure, existing reports suggest that these minerals are less pathogenic (Mossman, 2008; Gibbs and Berry, 2008; Gamble and Gibbs, 2008; Wilson *et al.*, 2008).

The objective of this investigation was to perform a nested case-control study to determine if risk of developing mesothelioma was related to exposure to elongate mineral particles (EMPs), a specific component of dust generated by the mining and processing of taconite ore. Descriptions of EMPs within the Mesabi Range suggest that only a small (1% or less) of the naturally-occurring amphibole is thought to be of the asbestiform type (Jirsa, 2008; Ross, 2008). Non-asbestiform amphibole exposure is the prevalent exposure as naturally-occurring cummingonite and grunerite are part of the taconite ore body on the eastern end of the Mesabi Range (Jirsa, 2008). Cleavage fragment EMP exposure is also likely to involve amphibole and non-amphibole types that are also non-asbestiform. These are released during the crushing and processing of the ore.

Since the amount of exposure may vary by the definition of EMP, several definitions have been considered in this report. The EMP definition most utilized by United States government agencies is any mineral over 5 µm in length and 0.5 µm in diameter with a 3 to 1 aspect ratio or greater. Because the predominant EMP exposure in this industry is less than 5 µm (Hwang *et al.*, 2013), we have attempted to assess exposure using other definitions including the Suzuki and Chatfield cleavage fragment types, defined in the exposure assessment below (Suzuki *et al.*, 2005; Chatfield, 2009).

Methods

The protocol for this study was reviewed and approved annually by the Human Subjects Committee of the University of Minnesota Institutional Review Board. All data in this study were held under strict control for the protection of confidentiality and privacy.

Study Design

We conducted a nested case-control study of mesothelioma in a cohort of taconite iron mining workers. The cohort was enumerated by the University of Minnesota in 1983 and included 68,737 individuals who ever worked in the iron ore mining industry sometime before 1983. This study was called the Mineral Resources Health Assessment Program (MRHAP). In the present effort, the previously-identified cohort was followed for vital status and causes of death were obtained through 2007. Vital status was ascertained using the Social Security Administration, the National Death Index, the Minnesota Department of Health, and death certificates obtained from the state where death occurred. All deaths were coded to the International Classification of Disease (ICD) codes in effect at the time of death. The cohort contained individuals from the following mining companies: Eveleth Taconite Company, Hanna Mining Company, Inland Steel Company, Jones and Laughlin, Pickands-Mather, which became Erie Mining Company (which later became LTV Mining), Hibbing Taconite Company, Reserve Mining Company (which later became Northshore Mining Company), and U.S. Steel Company.

Mesothelioma Case and Control Identification

All cases and controls were nested within the MRHAP cohort, and had to have evidence of employment in the taconite mining industry. Mesothelioma cases were identified using two sources, the Minnesota Cancer Surveillance System (MCSS) and death certificate records. MCSS has pathologically confirmed cancer information dating back to 1988 for cancer cases diagnosed within the state of Minnesota. Four controls were selected for each case using an incidence density sampling approach. For each case, controls were selected from those cohort members of similar age (years of birth +/- two years) who were alive and without a diagnosis of mesothelioma on the date of diagnosis or death of the case. Five controls were eliminated from the study due to lack of employment in mining, giving 315 controls, 80 cases and a total study population of 395 miners.

Exposure Assessment

Years worked along with on-site and historical EMP measurements and work histories were used to estimate cumulative EMP exposures. The initial step in the assessment of current exposures was to identify the major job titles in connection with taconite ore mining and processing (Hwang *et al.*, 2013). From these job titles, a list was developed of 28 unique, similarly exposed groups (SEGs), which occurred in all of the mines.

Personal and area exposures to EMPs were sampled on site in 2010 and 2011 by study investigators and counted using the NIOSH 7400 (PCM) method. Two workers were sampled per SEG in the eastern zone, while eight workers per SEG were sampled in the western zone to account for the multiple mines in this zone. Three exposure measurements for each sampled worker were obtained. On-site exposure monitoring was conducted within all six active mines within zones 1 and 4 (Figure 1). Zones 2 and 3 had no active mines at the time of the exposure monitoring for this investigation.

For personal monitoring, volunteers wore an air-sampling pump for six-hours during their work shift. PCM was used for counting EMPs on all samples with 20% of the samples also analyzed using NIOSH 7402 (TEM). This latter method can detect EMPs that are 0.25-0.5 µm in diameter and may provide more accurate counting with small diameters that could be missed by PCM. The NIOSH 7402 method included an expanded characterization of elemental composition with energy dispersive x-ray analysis (EDXA) and crystalline structure by selected area electron diffraction (SAED). In this way, EMPs that were amphiboles or chrysotile could be identified. The estimates of percent amphibole EMPs obtained for a given SEG analyzed using NIOSH 7402 were then applied to the remaining samples in that SEG which were analyzed using only the NIOSH 7400 method. The difference between these two measurements (*i.e.* between total EMPs and amphibole EMPs) provided an estimate of non-amphibole EMPs that included cleavage fragments.

Area air monitoring was conducted for each SEG using a cascade impactor (nano-MOUDI Model 125R, MSP Corp., Shoreview, MN) that was capable of collecting size-fractionated samples between 32 nm to greater than 5600 nm in aerodynamic diameter. EMPs had dimensions measured with an indirect-transfer (ISO 13794) TEM method. Identification of amphibole EMPs was accomplished using EDXA (Energy Dispersive X-ray Analysis) (Hwang *et al*., 2014). Each MOUDI sample was obtained as a 4-hour time-weighted average. With the use of these area samples and measurement techniques, EMPs could be counted by several definitions, including the NIOSH definition (length > width by at least 3:1 and length > 5 µm; the Suzuki definition (width $\leq$ 0.25 µm, length $\leq$ 5 µm; the Chatfield definition (width < 0.04 µm, aspect ratio > 20; the cleavage fragment definition (everything not categorized as Chatfield EMPs with aspect ratio < 20). Regression estimates were made between the personal and area counts based on the NIOSH definition and the alternate definitions. These regression relationships derived from area measurements were then applied to the current and historical personal measurements (NIOSH 7400) to obtain sets of personal exposures based on the different definitions of interest. The personal exposures were then used to compute cumulative exposures based on the definition of interest (Hwang *et al.*, 2014).

Work History

The work records from MRHAP for all cases and controls were abstracted to record, in increasing order of detail, the company, mine, department, and specific job titles with respective start and stop dates through 1982, the last date that work history information from MRHAP was available. Mining job titles varied across companies and time, and were standardized to the greatest extent possible. Job title abbreviations were expanded and duplicate job titles removed. Once job titles were standardized, mapping phrases for each job title were created and used to assign jobs to similarly-exposed groups (SEGs). If information from the job title was not sufficient to classify to a specific SEG, the job was assigned to an SEG using department information. For some work records, the job titles were missing or were too vague to be assigned to a specific SEG. Three additional SEGs (general mine, general plant or general shop) were created for jobs that could be broadly classified at the departmental level. Job titles that couldn't be assigned to a general or specific SEG or were missing were assigned a mine-specific "unknown" SEG.

A job-exposure matrix was created using the SEGs to estimate an EMP exposure value for each individual and each EMP definition in the following way. Historical EMP measurements (n=682) were extracted from databases maintained by the three active mining companies (six sites), the Mine Safety and Health Administration and a previous exposure assessment done by the University of Minnesota in the 1980s (Sheehy, 1986). These were combined with present-day EMP concentrations (n=1298). Using the measured data and a time-varying regression model, we reconstructed the exposure history for each SEG by mine for each year between 1955 and 2010. The reconstruction allowed for the assignment of exposures based on historical estimates for which we had no direct measurement data. Each SEG had a daily exposure estimate, based on a time weighted average (TWA) for an 8-hour day. The exposure values for department level SEGs were based on the average of other SEGs in that department. Exposures for unknown SEGs were an average of all SEGs in that mine for that year.

Each case and control's work history was combined with the job-exposure matrix to generate each individual's cumulative EMP occupational exposure. Using the work history for each case and control, a cumulative exposure value was calculated by the summation of the exposure value for each SEG multiplied by the time spent working in that SEG to give the cumulative exposure for a worker in EMP/cc/days. This value was divided by 365 to convert it to EMP/cc/years.

Exposure to commercial asbestos and dust from hematite operations may have also occurred among workers as this material was used throughout the industry historically for construction purposes. There were also some process specific jobs that may have used commercial asbestos directly. Commercial asbestos could have included serpentine chrysotile, as well as amphiboles. The potential for exposure to commercial asbestos was categorized as low, medium or high for each specific SEG. Expert industrial hygienists reviewed all jobs in each SEG and scored each SEG as having a high, medium or low probability of working with commercial asbestos and the subsequent frequency of exposure. The classifications were also reviewed by industrial hygienists in the taconite industry to validate jobs with potential commercial asbestos exposure. A consensus was developed for each classification. The estimates of commercial asbestos exposure for each individual were summarized as ever working in one of these jobs with high, medium, or low exposure, and the cumulative time working at each level. Ever/never classifications were also made for analytic purposes.

A portion of the taconite cohort worked in the earlier hematite industry. As hematite is a high-grade iron ore, it does not require the extensive processing and concentrating techniques used in taconite, and does not have the same exposures as the taconite industry. Hematite mining work histories were distinguished from taconite. Historical data on mining operations and yearly taconite production totals were used to determine a taconite start date for each company (1950s and 1960s, depending on the company). Jobs held before the taconite start dates were assigned to a specific hematite SEG.

Data Analysis

The cases and controls were compared by year of first employment, gender, type of ore mining, zones of employment, and departments of employment. They were compared by employment duration (years) across the Iron Range and by cumulative exposure, as EMP/cc/years, across the range and by specific zone worked. Categories were formed based on whether miners had ever worked in a geological zone, controlling for time worked in other zones. Since no on-site EMP measurements were available for the mine in the intermediate mineralogical zone, and since this zone is also known to contain amphibole EMPs, the eastern zone measures within SEGs were used to estimate historical exposures in this zone.

Rate ratios and 95% confidence intervals were estimated using separate logistic regression models to estimate the association between risk of mesothelioma and both duration of employment in taconite operations and cumulative exposure to EMPs. The association between mesothelioma and cumulative EMP/cc/years for each specific EMP definition categorized as high, medium and low (using tertiles), and high and low (median split) was evaluated. Rate ratios were also estimated for employment and EMP exposure by specific Iron Range mineralogical zone to see if associations varied by zone. The estimates of exposure to commercial asbestos were included in the models of cumulative EMP exposure and mesothelioma to control for potential confounding. Length of time employed in hematite mining was also included in all statistical models to account for any effects from this type of mining. Models were estimated with no latency, where all obtained exposures were included, and with 20-year latency. In the latter instance, only exposures that occurred at least twenty years prior to the date of case diagnosis or death were accounted for in the model (20-year lag). Although smoking information was not available in this assessment, smoking has not been associated with risk for mesothelioma.

Results

Exposure assessment

Results from the occupational exposure assessment for current levels have been published in detail elsewhere (Hwang *et al.*, 2013). Briefly, using the NIOSH 7400 counting method, the exposure level for total EMPs was higher than the NIOSH Recommended Exposure Limit (REL) in several SEGs for several mines. However, these measures do not reflect only regulated EMPs as this method is unable to distinguish asbestiform and non-asbestiform EMPs. The concentrations of amphibole EMPs were much lower than the concentrations of total EMPs, indicating that amphibole EMPs is not a major component of total EMPs generated in taconite operations. Amphibole EMP concentrations that were detected were almost exclusively limited to the eastern Mesabi Range and, with a few exceptions, were lower than the NIOSH REL of 0.1 fibers/cm^{-3} by an order of magnitude.

Study population

Standardized mortality ratios (SMRs) are presented elsewhere (Allen *et al.*, 2014). Records from MCSS identified 63 mesothelioma cases and an additional 17 cases outside of Minnesota and not captured by MCSS. A total of 80 cases and 315 controls were included in the analysis (Table 1). All of the cases were male with females making up 5% of controls. The median year of birth for both cases and controls was 1927. Cases and controls who ever worked in Zone 2 or Zone 4 were slightly younger than those who ever worked in Zone 1. Approximately one-third of cases and one-fourth of controls worked in both taconite and hematite mining. A larger proportion of cases worked exclusively in taconite, while a larger proportion of controls worked exclusively in hematite. The largest percentage of cases occurred in workers who ever worked in Zone 2. The departments in which the greatest number of both cases and controls worked at some point were the mining and shop departments. Among those who worked in the taconite industry 22 percent of cases and 11 percent of controls ever held a job with probable high commercial asbestos exposure. The median years of employment in these high exposure jobs were 6.5 years for cases and 1.4 years for controls.

The median length of employment in all iron ore mining and in taconite mining specifically was longer for cases, while the median length of employment in hematite was longer for controls (Table 2). Median length of taconite employment was greatest in Zone 1 for both cases and controls. Within departments, median length of employment was greatest for cases in the mining and shop departments versus the shop and office departments for controls.

Table 3 lists characteristics of cases and controls by exposure definition and by zone of the Iron Range. More cases worked in zone 2 whereas the highest exposure estimates occurred in zone 4. The rate of mesothelioma increased slightly for each additional year worked in taconite mining (Table 4). The rate ratio of 1.03 represents, on average, a three percent increase in the risk of mesothelioma for each additional year worked in the taconite industry. The risk of mesothelioma was increased with duration of employment in both Zone 1 and Zone 2, but was not associated with employment duration in Zone 4. The rate ratio estimates for taconite years were adjusted for years in hematite mining. Models that incorporated a 20 year lagged exposure had similar results as models without lagged exposure.

EMP exposures among cases and controls

Table 5 lists cumulative exposure estimates for cases and controls overall and by mineralogical zone, using the NIOSH 7400 method. Cases had higher exposure estimates than controls in western zones but not in the eastern zone. This pattern persisted for each EMP definition.

Higher exposure to EMPs, as defined by the NIOSH 7400 measurement method, was associated with increased risk of mesothelioma. Each additional EMP/cc/year of exposure was associated with an elevated but not statistically significant risk of mesothelioma (RR=1.10, 95% CI=0.97-1.24) (Table 6). When the cumulative exposure was divided into high and low based on the median cumulative exposures of the cases, the rate of mesothelioma was 1.93 times greater for workers in the highest exposure category relative to those in the lowest (95% CI=1.00-3.72). When the cumulative exposure was categorized as high, medium and low based on tertiles, the rate ratio increased incrementally, although none were statistically significant. As with duration of employment, the associations varied across zones in a parallel fashion. The effect estimates for EMP/cc/year were adjusted for years in hematite mining and years of employment with high probability of exposure to commercial asbestos. Using other classifications of commercial asbestos exposure (ever/never) did not change the interpretation of the models, nor did use of the 20 year lagged exposure data.

Excluding the 17 female controls did not change the associations appreciably. For example, removing the 17 female controls resulted in a rate ratio of 1.02 (95% CI=1.0-1.05) for each year worked in the industry (vs. 1.03 with female controls in the analysis). Without female controls, the rate ratio for cumulative exposure using EMP/cc/years was 1.07 (95% CI=0.97-1.17) compared to 1.10 (95% CI=0.97-1.24) with them included.

Although the NIOSH 7400 measurement of EMPs (> 5 µm) is the measure used by United States government agencies, in this setting it was not the most frequent EMP exposure type. The most frequent EMP dimensions were between 1-3 µm in length and 0.2-0.5 µm in width (Figure 2). We attempted to assess the risk with these smaller EMP exposures. The correlation coefficients between the EMP definitions were distinctly high and ranged from 0.6-0.96. Using the Suzuki EMP definition (≤5 µm length; ≤ 0.25 µm width), risk for mesothelioma was not elevated in the analysis that included all zones (RR=0.99, 95% CI=0.98-1.0). Rate ratios by zone appeared to be elevated in the west and intermediate geological areas (zones 1 and 2). The rate ratios for cleavage fragment EMP exposure estimates paralleled the Suzuki findings without evidence of increased risk in the overall analysis (RR=0.99, 95% CI=0.99-1.0) and with increased risk estimates for zones 1 and 2 (RR=1.05, 95% CI=1.01-1.10 for zone 1; RR=1.10, 95% CI=1.04-1.16 for zone 2) but not for zone 4 (RR=0.99, 95% CI=0.98-1.0). The rate ratios for the Chatfield EMPs (long EMPs) paralleled the NIOSH definition with elevated rate ratios in the overall analysis (RR=1.05, 95% CI=0.89-1.25) and in zones 1 and 2 (RR=1.73, 95% CI=1.06-2.83 for zone 1; RR= 1.56, 95%CI=1.16-2.09 for zone 2) but not for zone 4 (RR=1.0, 95% CI=0.95-1.05). Due to the high degree of correlation between these definitions, we were not able to estimate the independent effects of each EMP type.

Discussion

In this analysis of workers employed in the taconite mining industry of Minnesota, an overall association was observed between duration of employment in taconite mining operations and rate of mesothelioma. There was also some evidence of an increased rate of mesothelioma with increasing exposure to EMPs as identified by several measurement definitions. However, these definitions were highly correlated and did not distinguish amphibole from non-amphibole or asbestiform from non-asbestiform EMPs. The high correlation by EMP type limited the ability to distinguish the individual effects of the different EMP definitions.

The results for employment duration showed an association corresponding to an average of a 3 percent increase in the risk of mesothelioma with each additional year of employment in taconite operations. These excess cases are not exposure-specific. The overall rate of mesothelioma was also associated with cumulative EMP (NIOSH 7400 definition) exposure. For each EMP/cc/year of exposure the rate of mesothelioma increased approximately 10 percent. This measure of cumulative exposure is based on time and intensity of exposure. One EMP/cc/year is equivalent, for example, to one year working at an average of 1.0 EMP/cc or 10 years working at an average 0.1 EMP/cc. Workers above the median level of exposure had approximately twice the rate of mesothelioma as those below the median level. This analysis lends support to the hypothesis that workers who had higher cumulative exposure to EMPs had a higher rate of mesothelioma. However, the absolute risk for mesothelioma in the cohort was small compared to other disease frequencies. Because mesothelioma is a rare disease it is helpful to consider these results in the context of lifetime risk of mesothelioma. An average person who lives to be 80 years old has on average a 0.144 percent chance of developing mesothelioma in their lifetime, or about 1.4 cases per 1,000 individuals. A taconite miner who worked for 30 years in the taconite industry has on average a 0.333 percent chance of getting mesothelioma in their lifetime or about 3.33 cases per 1,000 taconite miners working for 30 years and living to be 80 years old.

When the NIOSH EMP definition was used in the zone-specific analyses, there was evidence of increased risks within Zones 1 and 2, but not Zone 4. This pattern was not consistent with the estimated levels of EMP exposures which were lowest in zone 1 than the other zones for both cases and controls (Tables 5, 6). The incongruity of this finding could suggest the impact of uncontrolled confounding factors and points to the need for further study of zone-specific results. The overall rate with the other definitions was not elevated (RR_{Suzuki}=0.99, 95%CI=0.98-1.00) and ($RR_{cleavage\ fragment}$=0.99, 95%CI=0.99-1.00).

Amphibole asbestiform EMP exposures are known causes of mesothelioma. Although amphibole EMP exposures exist in the eastern Iron Range zone, these are believed to be predominantly of the non-asbestiform variety (Gamble and Gibbs, 2008; Ross *et al.*, 2008; Wilson *et al.*, 2008), a type that has not had clearly-established mesothelioma or lung cancer risk associated with exposure in studies of Homestake gold miners and New York talc workers (Steenland and Brown, 1995; Gamble, 1993 and 2008; Honda *et al.*, 2002; Finkelstein, 2012; Nolan *et al.*, 2013).

Limitations

Similar to the circumstances involving other industries, the early study period (1950s and 1960s) was a time when exposures were likely to have been the highest, as the facilities were new and not as well equipped with dust control technologies, and where exposure measurements were less frequently taken. This time was also in advance of the regulatory era in the United States and, as a result, we have limited data to use in dose reconstructions for this period.

The cases in this study were identified from death certificates and via a state cancer registry. Additional cases may have occurred outside of Minnesota prior to 1999, the year ICD-10 went into effect, and which was the first edition to include a code for mesothelioma mortality. Cases may also have occurred within Minnesota prior to 1988, the initial year for the state's cancer surveillance system. Since mesothelioma mortality codes first existed in ICD-10, death cases identified prior to this time may have existed but lacked accompanying population estimates and couldn't be used to estimate observed and expected values. Use of additional algorithms to enumerate possible cases was done and revealed one additional cancer of the pleura and 14 connective tissue cancers (Sullivan, 2007). There was potential for mesothelioma to exist within these categories, but no further information was available on them and they were not used in any of the analyses.

There have been two occupational cohorts in northeastern Minnesota with documented increases in mesothelioma rates, the cohort of miners addressed in this study and the Conwed cohort with asbestiform EMP exposures (MDH Report, 2007). Through the assistance of the Minnesota Department of Health, we were able to identify whether workers in the mining cohort also worked in that industry. No such cases were found.

While several factors could lead to the exposures being categorized higher or lower, the exposure reconstruction was based on all available work history without regard to case or control status. Due to important gaps in exposure measures, particularly during the early years of the industry, there was a potential for exposure misclassification. In this study, since work histories were abstracted without knowledge of case status, misclassification should be non-differential.

However, it is also possible that job information was collected in error systematically, creating the potential for differential bias. In fact, we were not able to state which way this misclassification occurred, if it was a factor.

The risk associated with non-asbestiform dust exposure is obviously dependent on adequate control of asbestiform minerals. The facilities were constructed in the 1950s and 60s, a time when commercial asbestos materials were not regulated and were regularly used in many industrial applications. The analysis of EMP exposures controlled for potential commercial asbestos exposure in the jobs held in the taconite industry, but the ability to do this was limited by the absence of data on the amount of exposure and type of commercial asbestos used. We had no evidence that our classification approach was flawed. Nevertheless, it is possible that exposure to commercial asbestos remained as a residual confounding variable in this assessment.

Strengths

There are a number of strengths in this study. The exposure assessment, especially the current, on-site component, was comprehensive. It was, in fact, the first to be incorporated into an epidemiologic investigation within Minnesota's taconite industry. On-site exposures were obtained for all active mines utilizing both traditional phase contrast and electron microscopy. The potential impact from non-taconite mining exposures (hematite) was controlled in the analysis. Even though smoking information was not available for cases or controls, smoking has not been demonstrated as a risk for mesothelioma. The study population was large which enabled the examination of a rare disease like mesothelioma. Finally, the follow-up of the cohort and ascertainment of vital status was thorough.

CONCLUSION

The results from this case-control study suggested an association between duration of employment in the taconite industry and risk of mesothelioma. There was also an association with mesothelioma and exposure to cumulative EMPs, as measured by the NIOSH 7400 method. Due to high correlations between the different EMP definitions, the specific details of size and type of EMP exposure (asbestiform, non-asbestiform) could not be further ascertained. The effect of exposure to commercial asbestos could not be completely ruled out as a factor in this finding.

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References

Agency for Toxic Substances and Disease Registry (ATSDR), 2001. Toxicological Profile for Asbestos. ATSDR; Centers for Disease Control.

Allen EM, Alexander BH, MacLehose RF, Ramachandran G, Mandel JH. Mortality experience among Minnesota taconite mining industry workers. Occup Environ Med, Occup Environ Med. 2014 May 9. doi: 10.1136/oemed-2013-102000. [Epub ahead of print] PMID:24816518

Chatfield EJ. A procedure for quantitative description of fibrosity in amphibole minerals. Presentation delivered at the ASTM Johnson Conference, Burlington, VT, 2008.

Cooper WC, Wong O, Graebner R. Mortality of workers in two Minnesota taconite mining and milling operations. J Occup Med 1988, 30(6):506-511.

Cooper WC, Wong O, Trent LS, Harris F. An updated study of taconite miners and millers exposed to silica and non-asbestiform amphiboles. J Occup Med, 1992, 34(12):1173-1180.

Finkelstein MM. Malignant mesothelioma incidence among talc miners and millers in New York State. AJIM 2012, 55(10):863-8. (doi: 10.1002/ajim.22063. Epub 2012 Apr 27.)

Gamble JF. A nested case control study of lung cancer among New York talc workers. International Arch. Occup. Env Hlth 1993, 64:449-456.

Gamble JF, Gibbs GW. An evaluation of the risks of lung cancer and mesothelioma from exposure to amphibole cleavage fragments. Regulatory Toxicology and Pharmacology2008, 52 (1 supp):154-186.

Gibbs GW, Berry G. Mesothelioma and asbestos. Regulatory Toxicology and Pharmacology 2008, 52 (1 supp):223-231.

Gunter ME, Belluso E, Mottana A. Amphiboles: environmental and health concerns. Reviews in Mineralogy and Geochemistry 2007, 67:453-516.

Harper M, Lee EG, Slaven JE, Bartley DL. An inter-laboratory study to determine the effectiveness of procedures for discriminating amphibole asbestos fibers from amphibole cleavage fragments in fiber counting by phase-contrast microscopy. Ann Occup. Hygiene 2012, 56(6):645-659.

Higgins IT, Glassman JH, Oh MS, Cornell RG. Mortality of Reserve Mining Company employees in relation to taconite dust exposure. Am J Epidemiol 1983, 118: 710-719.

Hinds WC. Aerosol Technology-Properties, Behavior and Measurement of Airborne Particles, 2nd Edition (1999) John Wiley and Sons, Inc., New York, NY, p. 9.

Honda Y, Beall C, Delzell E, Oestenstad K, Brill I, Matthews R. Mortality among workers at a talc mining and milling facility. Ann Occup Hyg 2002, 46:575-585.

Hwang J, Ramachandran G, Raynor PC, Alexander BH, Mandel JH. A comprehensive assessment of exposures to elongate mineral particles (EMPs) in the taconite mining industry. Ann Occup Hyg Published Online First: 22 June 2013. Doi:10.1093/annhyg/met026.

Hwang J, Ramachandran G, Raynor PC, Alexander BH, Mandel JH. The Relationship between Various Exposure Metrics for Elongate Mineral Particles (EMPs) in the Taconite Mining and Processing Industry._J Occup Environ Hyg. 2014 Feb 10. [Epub ahead of print].

International Agency for Research on Cancer (IARC), 1987. Overall Evaluation of Carcinogenity: An Updating of IARC Monographs, Supplement 7. Lyon, France: World Health Organization.

Institute of Medicine of the National Academies, 2006. Background information on asbestos. In: Asbestos: Selected cancers committee on asbestos: Selected health effects 49-61.

Jirsa MA, Miller JD, Morey GB. Geology of the Biwabik Iron Formation and Duluth Complex. Regul Toxicol Pharmacol 2008, 52:S5-S10.

Lippmann M. Effects of fiber characteristics on lung deposition, retention, and disease. Environ Health Perspectives 1990; 88:311-317.

Minnesota Department of Health. *Mesothelioma in Northeastern Minnesota and Two Occupational Cohorts: 2007 Update*. Available at: http://www.health.state.mn.us/divs/hpcd/cdee/mcss/ documents/nemeso1207.pdf. Accessed July 10, 2013.

Mossman BT. Assessment of the pathogenic potential of asbestiform vs. nonasbestiform particulates (cleavage fragments) in *in vitro* (cell or organ culture) models and bioassays. Regulatory Toxicology and Pharmacology 2008, 52 (1 supp): 200-203.

NIOSH Current Bulletin No. 62. Asbestos Fibers and Other Elongate Mineral Particles: State of the Science and Roadmap for Research (Revised Edition). Department of Health and Human Services, Centers for Disease Control and Prevention, National Institute for Occupational Safety and Health. April, 2011.

NIOSH. NIOSH Manual of Analytical Methods: Asbestos and Other Fibers by PCM 7400. Avaliable at:http://www.cdc.gov/niosh/docs/2003-154/pdfs/7400.pdf.

NOISH. NIOSH Manual of Analytical Methods: Asbestos by TEM 7402. Available at http://www.cdc.gov/niosh/docs/2003-154/pdfs/7402.pdf.

Nolan RP, Gamble JF, Gibbs GW. Letter to the Editor on Commentary: Malignant

Mesothelioma Incidence Among Talc Miners and Millers in New York State by MM Finkelstein. AJIM 2013 56:1116–1118.

Ross M, Nolan RP, Nord GL. The search for asbestos within the Peter Mitchell taconite iron ore mine, near Babbitt, Minnesota. Regul Toxicol Pharmacol 2008, 52 (1 suppl):43-40.

Sheehy JW, McJilton CE. Development of a model to aid in reconstruction of historical silica dust exposures in the taconite industry. Am Ind Hyg Assoc J, 1987 48: 914–918.

Steenland K, Brown D. Mortality study of gold miners exposed to silica and non-asbestiform amphibole minerals: an update with 14 more years of follow-up. Am J Ind Med 1995, 27:217-229.

Sullivan PA. Vermiculite, Respiratory Disease, and Asbestos Exposure in Libby, Montana: Update of a Cohort Mortality Study. Environ Health perspect 2007, 115(4):579-585.

Suzuki Y, Yuen SR, Ashley R. Short, thin asbestos fibers contribute to the development of human malignant mesothelioma: pathological evidence. Int J Hyg Environ Health, 2005 208:201-210.

University of Minnesota Report to the Legislature, 2013. Available at: http://www.taconiteworkers.umn.edu.

Wilson R, McConnell EE, Ross M, Axten CW, Nolan RP. Risk assessment due to environmental exposures to fibrous particulates associated with taconite ore. Regulatory Toxicology and Pharmacology 2008, 52 (1 supp): 232-245.

Table 1. Demographic and work history characteristics of mesothelioma cases and controls

	Cases		Controls	
	N	Median	N	Median
Birth Year	80	1927	315	1927
First Year of employment				
Overall	80	1953	315	1952
Ever worked Zone 1	45	1948	220	1950
Ever worked Zone 2	33	1957	64	1957
Ever worked Zone 4	12	1957	66	1956
	N	%	N	%
Gender				
Female	0	0	17	5.4
Male	80	100	298	94.6
Type of Ore Mining				
Hematite and Taconite	25	31.3	81	25.7
Hematite only	23	28.7	131	41.6
Taconite only	32	40.0	103	32.7
Taconite Mineralogical Zone				
Ever worked Zone 1	18	22.5	74	23.5
Ever worked Zone 2	31	38.8	58	18.4
Ever worked Zone 4	12	15.0	66	21.0
Department –Ever worked				
Mining	20	25.0	73	23.2
Crushing	6	7.5	37	11.7
Concentrating	12	15.0	35	11.1
Pelletizing	14	17.5	43	13.7
General Plant	0	0.0	7	2.2
Shop Mobile	33	41.3	82	26.0
Shop Stationary	9	11.3	35	11.1
General Shop	0	0	3	1.0
Office	4	5.0	20	6.3
Unknown/Missing	16	20.0	63	20.0
Hematite	48	60.0	212	67.3
Commercial Asbestos Exposure*				
High exposure	13	22.8	35	11.1
Low/Moderate	44	77.2	149	80.9

*Commercial asbestos exposure estimated for SEGs in taconite processing only.

Table 2. Years of employment in all taconite mining operations, by zone, and in specific departments in taconite production for mesothelioma cases and controls

	Cases				Controls			
	N	Median	Min	Max	N	Median	Min	Max
Ore Type								
All Mining	80	4.05	0.01	35.23	315	2.42	0.003	37.31
Hematite	48	0.69	0.01	27.69	212	1.29	0.003	29.74
Taconite	57	8.1	0.01	31.06	184	6.79	0.003	30.62
Geologic Zone								
Zone 1	18	11.68	0.05	31.06	74	8.75	0.01	22.21
Zone 2	31	6.02	0.06	26.00	58	1.95	0.01	28.61
Zone 4	12	2.4	0.01	27.09	66	6.11	0.003	30.62
Department								
Mining	20	4.53	0.07	22.36	73	1.12	0.01	24.58
Crushing	6	1.36	0.19	3.51	37	0.65	0.01	13.68
Concentrating	12	0.53	0.03	7.67	35	0.49	0.02	17.30
Pelletizing	14	0.49	0.01	12.24	43	0.44	0.003	14.50
General Plant	0	0	0	0	7	0.08	0.01	5.33
Shop Mobile	33	5.75	0.01	24.87	82	4.79	0.003	30.62
Shop Stationary	9	6.18	1.29	30.66	35	1.15	0.02	22.02
General Shop	0	0	0	0	3	0.41	0.08	2.93
Office	4	1.74	0.32	9.21	20	4.2	0.03	25.36
Unknown	16	1	0.01	11.31	63	1.74	0.01	19.77
Hematite	48	0.69	0.01	27.69	212	1.29	0.003	29.74

Table 3. Descriptive findings and cumulative EMP exposure estimates by definition for cases and controls who worked in taconite

	Cases (n=80)	**Controls (n=315)**
Type of Ore Mining (%)		
Hematite Only	23 (28.7)	131 (41.6)
Taconite & Hematite	25 (31.3)	81 (25.7)
Taconite Only	32 (40)	103 (32.7)
TACONITE WORKERS	**Cases (n=57)**	**Controls (n=184)**
Gender (%)		
Female	0 (0.0)	9 (4.9)
Male	57(100.0)	175 (95.1)
Geologic Zone Ever Worked (%)		
Zone 1	18 (31.6)	74 (40.2)
Zone 2	31 (54.4)	58 (31.5)
Zone 4	12 (21.1)	66 (35.9)
Mean years in SEGs with high commercial asbestos score[1]	7.1	4.0
Mean Chatfield EMP/cc/years[2]		
Overall	1.5	1.3
Zone 1	1.2	0.3
Zone 2	1.4	0.9
Zone 4	1.6	2.4
Mean Suzuki EMP/cc/years[3]		
Overall	16.8	23.2
Zone 1	20.0	1.9
Zone 2	7.5	5.0
Zone 4	34.8	58.3
Mean Cleavage EMP/cc/years[3]		
Overall	10.8	16.6
Zone 1	10.2	1.2
Zone 2	4.9	3.2
Zone 4	23.5	42.0

[1] SEGs with a high commercial asbestos score are crusher maintenance, furnace operator, electrician, carpenter, auto mechanic, pipefitter/plumber, and lubricate technician
[2] Measured by NIOSH 7400 method
[3] Converted to personal results from NIOSH 7400 using ISO 13794 method

Table 4. Overall and zone specific rate ratio estimates for mesothelioma by years of employment in taconite

	Cases	Controls	RR[1]	95% CI[2]
Taconite Years	57	184	1.03	1.00-1.06
Any hematite	48	212	0.99	0.94-1.04
High vs low[3]				
Low employment	28	97	1.00	--
High employment	29	87	1.15	0.62-2.11
Years employment (tertiles)				
≤ 2 years (REF)	16	66	1.00	--
2 to < 12 years	17	55	1.45	0.64-3.27
12+ years	25	63	1.78	0.84-3.75
Zone 1 Taconite years	18[4]	74[4]	1.05	1.00-1.11
Zone 2 Taconite years	31[4]	58[4]	1.06	1.02-1.09
Zone 4 Taconite years	12[4]	66[4]	0.97	0.92-1.02

[1] Rate ratio; adjusted for age, and years of employment in hematite
[2] 95% CI= 95% confidence interval
[3] The high group represents workers with employment duration greater than that of the case median duration
[4] Cases and controls may have worked in more than one zone

Table 5. Overall and zone specific cumulative exposure estimates (EMP/cc)-years for mesothelioma cases and controls who ever worked in taconite operations[1,2]

	Cases			Controls		
	N	Median[3]	75th Percentile[3]	N	Median[3]	75th Percentile[3]
Overall	57	1.15	2.95	184	0.24	2.63
Zone 1	18	0.22	0.73	74	0.12	0.18
Zone 2	31	1.88	2.95	58	0.58	2.61
Zone 4	12	1.10	3.23	66	2.09	5.97

[1] Measured by NIOSH 7400 method
[2] Cases and controls may have worked in more than one zone
[3] Cumulative exposures for median and 75th percentile expressed as EMP/cc-year

Table 6. Rate Ratios for cumulative EMP exposure in taconite and mesothelioma

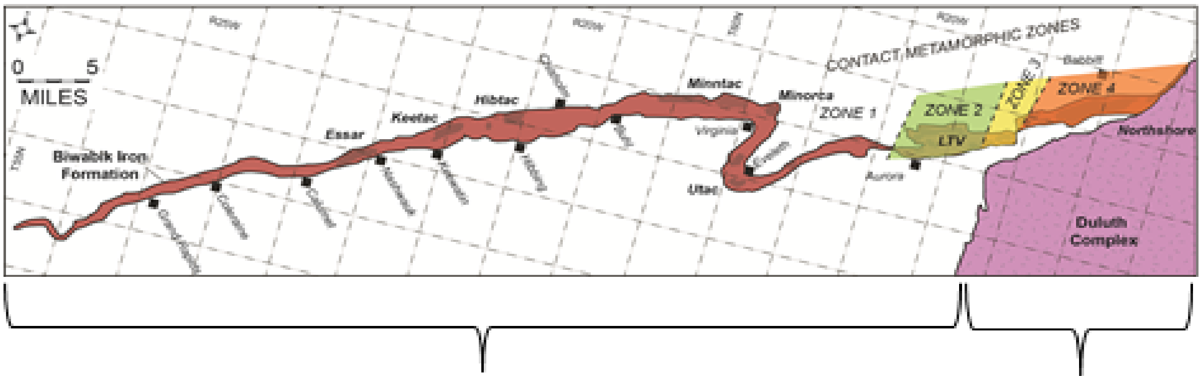
Exposure	Cases	Controls	RR[1]	95% CI
EMP/cc/yr[2]	57	184	1.10	0.97-1.24
Low: <1.15[3] EMP/cc/yr	29	124	1.00	--
High: ≥ 1.15[3] EMP/cc/yr	28	60	1.93	1.00-3.72
Tertiles[2,4]				
0 to<0.25 (REF)	16	77	1.00	--
0.25 to <2.0	19	57	1.66	0.75-3.68
2.0+	22	50	1.84	0.80-4.23
EMP/cc/yr[5] Zone 1	18	74	1.96	1.15-3.34
EMP/cc/yr[5] Zone 2	31	58	1.31	1.12-1.54
EMP/cc/yr[5] Zone 4	12	66	0.88	0.71-1.09
Hematite	48	212	0.99	0.94-1.04

[1] Measured by NIOSH 7400 method (NIOSH EMP definition: > 5 µm length, aspect ratio ≥ 3)
[2] Results adjusted for age, employment in hematite, and potential for commercial asbestos exposure
[3] Based on the upper and lower half of the case exposure distribution
[4] Based on the lower, middle and upper one-third of the case exposure distribution
[5] Results adjusted for age, employment in hematite, potential for commercial asbestos, and exposures in other zones. Cases and controls may have worked in more than one zone.

Figure 1.

Biwabik Iron Formation Mineralogy

West to East

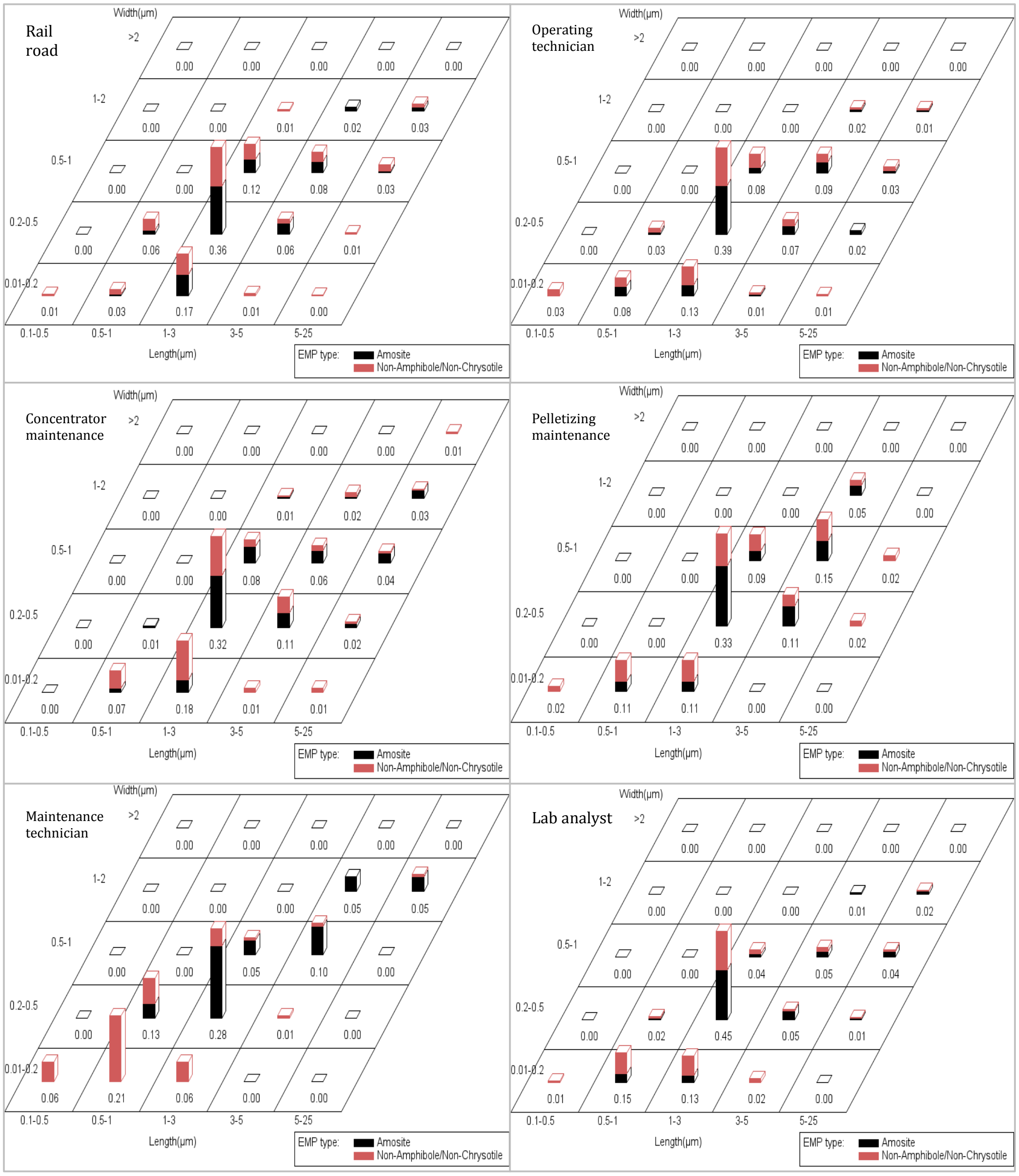


Zones 1 and 2: quartz, magnetite, hematite, carbonates, talc, chamosite, greenalite, minnesotaite and stilpnomelane

Modified from: OVERVIEW OF THE MINERALOGY OF THE BIWABIK IRON FORMATION, MESABI IRON RANGE, NORTHERN MINNESOTA Peter L. McSwiggen and G.B. Morey (2008).

Zones 3 and 4: quartz, magnetite, grunerite, hornblende, hedenbergite, ferrohypersthene (ferrosilite), and fayalite

Figure 2. Occurrence of EMP dimensions for six SEGs within the taconite mining industry



Appendix 7

Lung Cancer Risk among Minnesota Taconite Mining Workers

ABSTRACT

Objective: To examine the association between employment duration, elongate mineral particle (EMP) exposure, and silica exposure and the risk of lung cancer in the taconite mining industry.

Methods: We conducted a nested case control study of lung cancer within a cohort of Minnesota taconite iron mining workers employed by any of the mining companies in operation in 1983. Lung cancer cases were identified by vital records and cancer registry data through 2010. Two age-matched controls were selected from risk sets of cohort members alive and lung cancer free at the time of case diagnosis. Calendar time-specific exposure estimates were made for every job and were used to estimate workers' cumulative exposures. Odds ratios (OR) and 95% confidence intervals (CI) were estimated using conditional logistic regression. We evaluated lung cancer risk by total work duration and by cumulative EMP and silica exposure modeled continuously and by quartile of the exposure distribution.

Results: A total of 1,706 cases and 3,381 controls were included in the analysis. After adjusting for work in hematite mining, asbestos exposure, and sex, the OR for total duration of employment was 1.00 (95% CI: 0.96-1.01). The ORs for total exposure were 0.94 (95% CI: 0.89-1.01) for EMPs and 1.22 (95% CI: 0.81-1.83) for silica. The risk of lung cancer did not appear to change with increasing exposure when examined by quartiles.

Conclusions: This study suggests that the estimated taconite mining exposures do not increase the risk for the development of lung cancer.

BACKGROUND

Taconite mining is an open pit, multi-stage process that involves blasting rock with explosives, crushing it into small pieces, magnetically extracting iron, and reforming a more concentrated product into high-grade iron ore pellets, the process of which can result in a dusty environment. The mining and processing of taconite iron ore results in potential exposure to non-asbestiform amphibole and non-amphibole elongate mineral particles (EMPs), respirable silica, and cleavage fragments.[Hwang et al., 2013] The term 'EMP' refers to any mineral particle with a minimum aspect ratio of 3:1 that is of inhalable size. Cleavage fragments are mineral EMPs created during the crushing and fracturing process.[DHHS, 2011]

The Mesabi Iron Range, located in northeastern Minnesota, is a narrow belt approximately three miles wide and 120 miles long, consisting of iron-rich sedimentary rocks. The mineralogy of the Mesabi Iron Range changes from east to west and is broken into four distinct mineralogical zones.[McSwiggin et al., 2008] All zones have deposits of taconite along with quartz and iron silicates, but vary in the type of EMP.[Jirsa et al., 2008] The eastern part of the range, known as zone 4, contains iron-rich amphibole EMPs, believed to be less than 1% fibrous [Wilson et al., 2008]. The western part of the range, known as zone 1, includes approximately two-thirds of the entire Mesabi Iron Range and contains almost exclusively non-asbestiform EMPs. Zone 2 is considered a transitional zone and contains some amphiboles. There are no mines located in zone 3. The primary exposure in taconite operations is non-asbestiform cleavage fragments however, due to the mineralogical differences in the zones, workers in each zone may be exposed to different types of mineral particles.

The causal relationship between exposure to asbestiform EMPs minerals and lung cancer is well documented.[DHHS, 2011; McDonald & McDonald, 1996; Robinson et al., 2005; Robinson, 2012] However, evidence from epidemiological studies of workers exposed to non-asbestiform EMPs is inconclusive. Since 1990, non-asbestiform EMPs have been included within the NIOSH recommended exposure limits of asbestiform EMPs due to the inconclusive findings of epidemiological studies.[DHHS, 2011] These include studies of talc miners in upstate New York[Honda et al. 2002; Finkelstein, 2012; Nolan et al., 2013), and gold miners in South Dakota.[Gillam et al, 1976; McDonald et al., 1978; Steenland & Brown, 1995]

Historically, the association between silica and lung cancer has been debated but recent occupational studies have provided evidence supporting the risk of lung cancer after silica exposure (DHHS, 2011-120). In 1996, the International Agency for Research on Cancer concluded that respirable silica was carcinogenic in occupational settings despite the lack of good-quality datasets available to quantitatively evaluate the relationship.[IARC, 2012]

Health risks associated with taconite mining have been a concern to the public for several decades, but few studies have evaluated the health of miners in Minnesota. In 1983, a mortality analysis of 5,751 miners showed no increase in risk of respiratory cancer.[Higgins et al., 1983] A similar mortality analysis of 3,431 workers published in 1988 and 1992, likewise did not report an excess of mortality for any cause of death.[Cooper et al., 1988; Cooper et al., 1992] These early studies had small study populations, focused on single mining companies, and had relatively short follow-up periods with limited power. However, a recent comprehensive mortality analysis found elevated lung cancer mortality among taconite mining workers.[Allen et al. 2014] No mortality study to date has evaluated the association between quantitative exposure level and cancer risk.

The purpose of this study is to address uncertainties regarding the health consequences of taconite mining by examining the association between employment duration, EMP exposure, and silica exposure in the taconite mining industry with the risk of lung cancer. This study also provides a unique opportunity to examine some of the key questions surrounding risk associated with exposure to non-asbestiform EMP exposure.

METHODS

Study population and follow-up

We conducted a nested case-control study of lung cancer within a cohort of Minnesota taconite iron mining workers as part of the Taconite Workers Health Study conducted by the University of Minnesota.[www.taconiteworkers.umn.edu] The original cohort was enumerated in 1983 by the University of Minnesota and included 68,737 individuals with any employment in the mining industry. The earliest records were found to have sparse work history information, unreliable data for vital records linkages and early workers would have spent a majority of their working life in hematite mining. In order to restrict the cohort to those thought to have the most complete records and focus on employment in taconite, the study cohort was limited to those born in 1920 or later leaving 46,170 individuals.

Lung cancer cases were identified by mortality records and cancer registry data through 2010. The vital status and causes of death of cohort members were ascertained through several sources including the Social Security Administration, the National Death Index (NDI), Minnesota Department of Health, and other state health departments. The Minnesota Department of Health provided causes of death for those who died within the state. For those who died outside of Minnesota in 1979 or later, causes of death were obtained from NDI Plus. For those who died prior to the establishment of NDI Plus in 1979, death certificates were obtained from state health departments. Underlying causes of death were coded to the International Classification of Disease (ICD) version in place at the year of death. The ICD codes were obtained directly from the Minnesota Department of Health and the NDI. All other death certificates were reviewed and coded by a nosologist.

To identify incident cancers, the cohort was linked to the Minnesota Cancer Surveillance System (MCSS). The MCSS, established in 1988 by state statute, is Minnesota's statewide, population-based cancer registry that collects histological information of newly diagnosed cancers on all Minnesota residents. Incident cancers including date of diagnosis, cancer site and histology were obtained for cohort members matched to the MCSS.

Selection of cases and controls

In this nested case-control study, all lung cancer cases identified via death record or MCSS were included. Two controls for each case were selected using an incidence density sampling protocol. Eligible controls were selected from risk-sets for each case by age (year of birth +/- five years) and were alive without a lung cancer diagnosis on the date of death or date of diagnosis of their index case.

Exposure assessment

A job-exposure matrix was developed using work history records and quantitative, time-specific exposure estimates for each job and department (specific job groupings) to generate a cumulative exposure for each worker. Exposures for controls were truncated at the date of diagnosis or death of the matched case. Details of the exposure assessment and historical reconstruction are provided elsewhere[Hwang at al., 2013] and summarized below.

Mining industry jobs were condensed into 28 similarly exposed groups (SEGs) based on job title, task, location, and procedure. The SEGs were used to systematically capture work history records and link estimates of exposure to EMPs and respirable silica for the exposure data matrix. Quantitative exposure estimates were derived from an exposure reconstruction that incorporated data from a comprehensive exposure assessment conducted as part of the Taconite Workers Health Study and from historical industrial hygiene monitoring data collected by Mine Safety and Health Administration (MSHA) and the mining companies.[Hwang at al., 2013]

For the Taconite Workers Health Study exposure assessment, personal exposure measures were collected for all SEGs in all operating mines in the Mesabi Iron Range between January 2010 and May 2011. Several workers per SEG were selected for sampling and each participant wore a personal air-sampling pump for approximately six hours of a work shift on three separate occasions. The filter samples were analyzed for EMPs by phase contrast microscopy which identifies all EMPs longer than 5 µm, with a diameter of 0.25 µm and with an aspect ratio ≥ 3. Respirable silica was analyzed using NIOSH 7500 Crystalline silica X-ray diffraction. The results from the samples were used to calculate a single average concentration for the shift for each participant.

Historical exposures data were obtained from the Mine Data Retrieval System maintained by MSHA and the internal databases of two currently operating taconite mining companies. Available personal exposure data were used to create the historical reconstruction. Historical and current EMP and respirable silica data were combined into a master database to estimate an SEG specific exposure. Annual average exposures were estimated for each combinations of SEG, year, and mine using a time-varying linear regression model. The final exposure matrix included seven mines, 28 SEGs, and 56 years between 1955 and 2010. Five of the mines are located in zone 1, one mine is located in zone 4, and one mine that is no longer in operation is located in zone 2.

Company work records were abstracted to collect job title, mine, and dates of employment. Job titles were standardized and mapped into one of the original 28 SEGs. Additional SEGs were created at the department level for jobs that had insufficient description to classify into a specific SEG. Jobs with no specific information about where or what the individual did was classified into a missing/unknown SEG. Exposure levels for department level SEGs were based on the average of other SEGs in that department. Exposures for the missing/unknown SEG were an average of all SEGs within that mine. Employment history was combined with the exposure matrix to estimate a cumulative exposure for each worker. Each SEG had an EMP and silica concentration that differed by company and year. This concentration was multiplied by the length of time spent working in the SEG and then summed to give a cumulative EMP exposure for each workers measured in EMP/cc/years and a cumulative silica exposure measured in mg/m^3/years.

Many of the workers had employment history in the mining industry before taconite mining began in the 1950s and 60s. The transition from hematite to taconite mining occurred at different times for different companies. Historical data on mining operations and yearly taconite production totals was used to determine the year in which taconite mining began for each company. Any jobs held prior to that year were assigned to a hematite SEG for which EMP and silica exposure estimates were not available.

It is possible that commercial asbestos was used throughout the mines for maintenance and building and was a potential additional exposure to some of the workers. Each SEG was evaluated to determine whether it involved potential exposure to commercial asbestos. A high or low commercial asbestos score was assigned based on the likelihood and frequency of exposure for that SEG. These scores were reviewed by industrial hygiene experts within the taconite industry. Time spent in an SEG with a high probability of exposure to commercial asbestos was used as a covariate in the statistical models (below).

Data analysis

Conditional logistic regression was used to estimate the odds ratios (OR) and 95% confidence intervals (CI) for the association between taconite mining exposures and the development of lung cancer. Because of the risk set sampling design, ORs from the logistic models are estimates of hazard ratios. In the final models, ORs were adjusted for sex, hematite mining exposure (measured in years), and number of years spent in SEGs believed to have the potential for high commercial asbestos. Taconite mining exposure was characterized in three ways using separate regression models for each: employment duration, cumulative EMP and cumulative silica exposure. Employment duration and EMP exposure were examined in an overall and zone specific analysis divided into years worked or EMP exposure in each zone of the iron range (zone 1, 2, or 4). Both EMPs and silica distributions were incorporated into models by quartile and by continuous exposure. Analyses were repeated restricting the cases to those only identified by death certificate, eliminating those only identified through MCSS and thus living in Minnesota at the time of diagnosis.

The histological subtype of lung cancer was available for the cases identified by MCSS. Separate analyses were done for each of five major histological subtypes: squamous cell, adenocarcinoma, small cell, non-specified, and other/rare carcinomas.

All statistical analyses were conducted using SAS 9.2.

RESULTS

Follow-up of the 46,170 workers identified 1,725 cases corresponding to 3,450 controls. After work history abstraction, 3 cases along with their 6 corresponding controls, and 4 additional controls were excluded due to poor data quality, e.g. conflicting dates of birth in different records. Another 16 cases and their 32 corresponding controls along with an additional 27 controls were excluded because the only record on file was an application of employment with no evidence of actual employment in the taconite mining industry. The final analysis included 1,706 lung cancer cases and 3,381 controls. Of the 1,706 cases, 309 were identified only through MCSS, 723 were identified only through death certificates, and 674 cases were identified by both MCSS and death certificates.

The general characteristics of the study population are presented in Table 1. The study population was mostly male (96% of cases and 94% of controls). The mean duration of employment in taconite mining of the cases and controls was 7.7 and 8.5 years respectively. The total cumulative exposure of EMPs and silica was higher in the controls than in the cases (1.7 EMP/cc/years and 0.31 mg/m^3/years for controls and 1.5 EMP/cc/years and 0.28 mg/m^3/years for cases). Total employment duration and cumulative EMP exposure was greatest in zone 4 for both cases and controls. The mobile shop department had the greatest employment duration for both cases and controls followed by the mining department.

Table 1. Characteristics of cases and controls

	CASES (N=1706)	CONTROLS (N=3381)
	N (%)	N (%)
Sex		
Male	1637 (95.96)	3183 (94.14)
Female	69 (4.04)	198 (5.86)
Ore type		
Taconite only	668 (39.16)	1239 (36.67)
Hematite only	738 (43.26)	1530 (45.28)
Taconite & hematite	300 (17.58)	610 (18.05)
Ever worked by zone		
Zone 1	347 (20.34)	642 (18.99)
Zone 2	366 (21.45)	618 (18.28)
Zone 4	327 (19.17)	699 (20.67)
	Mean	**Mean**
Birthyear (min, max)	1930 (1920, 1959)	1930 (1920, 1961)
Years of employment		
Taconite	7.67	8.52
Hematite	3.57	3.67
Years of taconite employment by zone		
Zone 1	7.38	7.60
Zone 2	5.41	7.11
Zone 4	8.81	9.27
EMP/cc/years		
Total	1.478	1.679
Zone 1	0.520	0.521
Zone 2	1.173	1.537
Zone 4	2.509	2.605
Silica mg/m^3/years		
Total	0.2809	0.3070
Years of employment by department		
Mining	1.28	1.36
Crushing	0.16	0.20
Concentrating	0.20	0.22
Pelletizing	0.25	0.24
Shop mobile	2.59	2.98
Shop stationary	0.68	0.71
Office	0.30	0.65
Missing/unknown	0.48	0.46
General mine	0.69	0.47
General plant	0.38	0.44
General shop	0.68	0.79

Total duration of employment in taconite mining did not appear to increase the risk of lung cancer (OR = 0.99, 95% CI: 0.96-1.01). The ORs for total exposure were 0.95 (95% CI: 0.89-1.01) for EMPs and 1.22 (95% CI: 0.81-1.83) for silica. A decrease in ORs with increasing exposure was observed across quartiles for EMP and silica exposure however, none of the quartiles exhibited a significant increase in risk. As compared to quartile 1 exposure levels, those with no taconite exposure showed a decrease in risk of lung cancer (EMP OR = 0.81, 95% CI: 0.67-0.98; silica OR = 0.81, 95% CI: 0.68-0.98). Odds ratios and 95% CIs for the analysis by employment duration, total exposure, and exposure quartiles can be found in table 2. The risk of lung cancer did not appear to change in any particular zone of the iron range by employment duration or cumulative EMP exposure. Results of the analysis by zone can be found in table 3. When we restricted the study population to the 1,397 cases identified through death certificates and their corresponding controls, the results did not change substantially.

Table 2. Risk of lung cancer by employment duration, cumulative EMP, and cumulative silica exposure

	OR	95% CI
Years of employment		
Total		
Taconite years[a]	0.99	0.96-1.01
Hematite years[b]	0.99	0.98-1.01
By Department[c]		
Mining	0.99	0.97-1.01
Crushing	0.96	0.88-1.05
Concentrating	0.99	0.93-1.06
Pelletizing	1.02	0.97-1.07
Shop Mobile	0.99	0.98-1.01
Shop Stationary	1.01	0.98-1.05
Office	0.95	0.92-0.99
EMP exposure		
Total		
EMP/cc/years[a]	0.95	0.89-1.01
By quartiles[e]		
Q1	1	
Q2	1.00	0.79-1.25
Q3	0.98	0.77-1.24
Q4	0.82	0.57-1.19
Unexposed[f]	0.81	0.67-0.98
Silica exposure		
Total		
Silica mg/m^3/years[d]	1.22	0.81-1.83
By quartiles[g]		
Q1	1	
Q2	1.04	0.84-1.29
Q3	0.95	0.74-1.22
Q4	0.97	0.70-1.35
Unexposed[f]	0.81	0.68-0.98

a Adjusted for hematite exposure, silica exposure, asbestos exposure, and sex
b Adjusted for taconite exposure, silica exposure, asbestos exposure, and sex
c Adjusted for years in unknown SEGs, hematite, general mine, general plant, general shop, sex, and asbestos
d Adjusted for taconite exposure, hematite exposure, asbestos exposure, and sex
e Lower cut point for Q1-4 = 0, 0.1298, 0.4527, and 2.353 EMP/cc/years
f Worked only in hematite production and did not have taconite exposure
g Lower cut point for Q1-4 = 0, 0.0373, 0.2064, 0.5189 mg/m^3/years

Table 3. Risk of lung cancer by employment duration and cumulative EMP exposure in each zone of the iron range

	OR	95% CI
Taconite years by zone[a]		
Zone 1	1.01	0.97-1.04
Zone 2	0.99	0.96-1.02
Zone 4	0.99	0.96-1.01
EMP/cc/years by zone[a]		
Zone 1	1.00	0.87-1.16
Zone 2	0.94	0.85-1.02
Zone 4	0.95	0.89-1.01

a adjusted for hematite exposure, silica exposure, asbestos exposure, exposure in other zones, and sex

A total of 973 lung cancer cases were identified by MCSS and were included in the sub analysis by histological subtype. No significant association was found with EMP or silica quartiles for squamous cell, adenocarcinoma, small cell, non-specified, or other carcinomas of the lung. ORs were greatest for squamous cell and non-specified carcinoma; however, none of these effects were statistically significant and most were imprecise. Results of the analysis by histological subtype can be found in table 4.

Table 4. Risk of major histological subtypes of lung cancer by cumulative EMP and silica exposure

	Odds Ratios (95% CIs)				
	Squamous N=258	**Adeno N=313**	**Small cell N=139**	**Non-specified N=202**	**Other N=61**
EMP/cc/years (quartiles)[a]					
Unexposed[c]	0.65 (0.40-1.06)	0.78 (0.50-1.22)	0.77 (0.37-1.60)	0.93 (0.53-1.64)	0.89 (0.33-2.43)
Q1	1	1	1	1	1
Q2	1.03 (0.58-1.82)	0.92 (0.55-1.53)	0.99 (0.46-2.14)	0.96 (0.49-1.90)	0.47 (0.13-1.67)
Q3	1.20 (0.66-2.20)	0.79 (0.46-1.36)	0.93 (0.41-2.06)	0.91 (0.47-1.74)	1.01 (0.33-3.07)
Q4	1.04 (0.42-2.58)	0.54 (0.23-1.30)	1.07 (0.31-3.70)	1.44 (0.56-3.72)	0.11 (0.01-1.04)
Silica mg/m^3/years (quartiles)[b]					
Unexposed[c]	0.67 (0.41-1.08)	0.78 (0.51-1.19)	0.64 (0.30-1.34)	1.06 (0.59-1.91)	1.24 (0.44-3.49)
Q1	1	1	1	1	1
Q2	1.11 (0.64-1.95)	0.92 (0.57-1.48)	0.76 (0.36-1.60)	1.15 (0.62-2.16)	2.10 (0.73-6.05)
Q3	1.25 (0.71-2.18)	0.96 (0.59-1.56)	0.71 (0.32-1.57)	1.57 (0.79-3.10)	0.99 (0.22-4.47)
Q4	1.28 (0.73-2.24)	0.96 (0.58-1.59)	0.98 (0.43-2.25)	1.72 (0.88-3.36)	1.90 (0.62-5.83)

a Adjusted for hematite exposure, silica exposure, asbestos exposure, and sex
b Adjusted for hematite exposure, EMP exposure, asbestos exposure, and sex
c Worked only in hematite production and did not have taconite exposure

DISCUSSION

We found little evidence of increased risk of lung cancer associated with duration of employment, cumulative exposure to EMPs or cumulative exposure to silica. Due to geological differences in the rock between zones of the iron range, a zone specific analysis was conducted to evaluate whether or not risk of lung cancer differed by the unique exposure potential in each zone. The zone specific analysis did not show substantial differences in risk for each zone, nor did the risk of lung cancer increase with exposure in any particular zone of the iron range when examined by employment duration, cumulative EMP or cumulative silica exposures. Adenocarcinoma has been shown to be the most common histological subtype of lung cancer in asbestos-exposed individuals, although all types have occurred.[Raffn et al., 1993; de Klerk et al., 1996] This would suggest that if non-asbestiform EMPs did have a carcinogenic affect, it might also vary by histological subtype. In this analysis, histological subtype did not show any increase in risk for any of the five major subtypes. This was true for both EMP and silica exposure quartiles.

Previous analyses from the Taconite Workers Health Study showed an excess in mortality[Allen et al., 2014] and cancer incidence in this taconite workers cohort. Specifically, standardized mortality ratios and standardized incidence ratios were estimated comparing the all cause and cause specific mortality and cancer rates in the overall cohort to the Minnesota population. Mortality was elevated for mesothelioma (SMR = 2.8, 95% CI: 1.9-4.0) and lung cancer (SMR = 1.2, 95% CI: 1.1-1.2). Cancer incidence was elevated for mesothelioma (SIR = 2.4, 95% CI: 1.8-3.2) and lung cancer (SIR = 1.3, 95% CI: 1.2-1.4). Results from the current analysis suggest that the increase in risk for mortality and incidence of lung cancer in this study population is not associated with the exposures that were estimated in this study, rather could be due to non-occupational exposures.

Lung cancer can have a relatively long latency period before diagnosis. Given that the work history records were collected in 1983 and follow-up continued through 2010, much of the study population (those diagnosed after 1993) had at least a 10 year lag built into the data analysis. However, 28% of the cases were diagnosed before 1993. The analyses were repeated using both a 10 and 20 year lag but the study results and interpretations did not change substantially. Analyses were also repeated restricting the cases to those only identified by death certificate. Cases identified through MCSS had to be living in Minnesota at the time of diagnosis but it was not feasible to determine if controls were living in Minnesota. This restricted analysis provided a potentially better comparison between cases and controls due to similar follow-up potential. However, the study results did not change substantially with this restricted analysis which included 1,397 cases identified through death certificates and their corresponding controls.

Various types of asbestiform EMPs can differ chemically, but structurally they are all similar in that they are highly fibrous silicate minerals that are crystallized in an asbestiform habit, causing them to separate into long, thin, strong, flexible fibers.[Mossman, 2008; Gamble & Gibbs, 2008] Asbestiform EMPs tend to have very large aspect ratios, generally >20:1 for fibers > 5µm in length.[Mossman, 2008] In contrast, non-asbestiform EMPs have aspect ratios >3:1 and have widths much larger than asbestiform fibers of the same length. Common non-asbestiform analogs of asbestiform EMPs may share the same chemical composition but they do not share the same crystal structure. Cleavage fragments, or fragments of EMPs that have broken along a cleavage plane, lack the tensile strength and flexibility of asbestos. [Mossman, 2008] The health consequences of exposure to cleavage fragments has not been comprehensively studied.[Gamble & Gibbs, 2008]

The strong association between asbestiform EMP exposure and lung cancer is well documented[DHHS, 2011; McDonald & McDonald, 1996; Robinson et al., 2005; Robinson, 2012] however, the toxicity of non-asbestiform EMPs is less studied. *In vitro* assessments have suggested that non-asbestiform EMPs and cleavage fragments are less potent than asbestiform EMPs,[Mossman, 2008] but epidemiology studies have been inconclusive. NIOSH has specifically identified non-asbestiform EMPs as a needed area of research.[DHHS, 2011] Non-asbestiform EMPs are included in NIOSH recommended exposure limits due to technical limitations of routine exposure assessments and uncertainty about the potential toxicity of non-asbestiform EMPs. Research focused on exposure to non-asbestiform EMPs has consisted largely of mortality studies within a few mining industries. Previous studies of New York talc miners[Honda et al., 2002] and South Dakota gold miners[Gillam et al., 1976; McDonald et al., 1978; Steenland & Brown, 1995] have shown inconclusive evidence of an association between non-asbestiform EMPs and malignant lung disease. Results from some animal studies have suggested that fiber dimension, and not composition, is the major determinant of carcinogenicity for mineral fibers.[DHHS, 2011] There remains a need to determine whether non-asbestiform EMPs in different physical forms are also capable of causing disease.[DHHS, 2011] These mineral particles are present in taconite mining and processing operations, the predominant exposure being non-asbestiform cleavage fragments, making Minnesota taconite miners an important population for research. This study provides evidence to suggest that exposure to non-asbestiform EMPs is not a major risk factor for the development of lung cancer.

Some limitations should be considered when interpreting the results of this analysis. Exposure misclassification is a likely occurrence in this study. Despite an extensive effort to identify all available exposure data, measurements were sparse for some time periods and some SEGs. The exposure reconstruction relied on imputation and regression modeling to estimate historical exposure levels. The results of the current analysis are dependent on the assumptions of our exposure reconstruction, such as a linear trend in historical exposure levels. However, employment duration data, which are less likely to be biased, may serve as a suitable proxy for EMP and silica exposures, provided that there were no major changes in exposure potential over time. Results of employment duration analyses were similar to those for EMP and silica.

Incorrect assignment of SEGs based on work records is another potential area for exposure misclassification. Details in individual work records varied greatly including level of detail in job titles and dates of employment. Though standardization of job titles was done to the greatest extent possible, in many cases there was not enough information in the work record to assign specific SEGs. In these cases general SEGs that averaged exposures across mines were used. Quality of work records varied by mine, therefore SEG misclassification may have occurred in specific mines. This could have masked any significant finding by zone.

Smoking is the major risk factor for lung cancer. However, to be a confounder for an internal exposure response analysis, smoking must be differentially distributed by level of exposure. Though we did not have smoking information for the study population there were data available on the smoking habits from a survey of 1,186 current and former taconite workers conducted in 2010 as part of the Taconite Workers Health Study. Roughly 75% of these individuals were in the cohort from which the cases and controls were identified. We used these data to estimate the association between smoking and EMP exposure as a means to assess the potential for confounding due to smoking. The SEG based exposure algorithms were applied to the reported work histories from the 2010 survey study and cumulative exposure was compared by smoking status (ever/never). Among the workers who participated in the 2010 survey, the 'ever' smokers had higher mean cumulative exposure than the 'never' smokers (3.3 vs 2.5 EMP/cc/years and 0.5 vs 0.4 silica mg/m^3/years). Working under the assumption that the survey participants represent the study population, this would suggest it is unlikely that differential smoking habits in the study population explains a lack of association between the exposures and lung cancer. In fact, the direction of potential confounding would be to overestimate the effect of taconite work exposures and lung cancer.[VanderWeele et al., 2008]

There are notable limitations to using the survey population to examine EMP exposure by smoking. The survey participants had greater cumulative exposure levels than the study population, they had to be alive in 2010, and they were subject to selection bias as we relied on volunteers for participation. Despite these limitations, the survey participants are the only comparison group available for identifying smoking variation among exposure levels.

Exposure to commercial asbestos is another known cause of lung cancer and was used regularly in the early and mid-part of the century. It is likely that commercial asbestos was used in the building and maintenance of taconite plants however there is limited information on its use and no quantitative data on asbestos type or exposure level. This analysis accounted for commercial asbestos by relying on industrial hygiene experts to identify the probability of exposure in each SEG and final models included years of work in an SEG with a high probability of asbestos exposure. Without a quantitative measure of commercial asbestos exposure, our estimate has potential for misclassification. For asbestos exposure to have confounded an association between taconite mining exposures and lung cancer, the lower exposure workers would have to have had high levels of asbestos exposure. However, asbestos probability was assigned based on job descriptions, not exposure assessment. It is unlikely that systematic misclassification occurred for only lower or higher exposed workers.

This study has notable strengths. The large study population provided enough statistical power to examine the exposure disease relationship in various ways. The 2010 exposure assessment was the most comprehensive assessment in the taconite mining industry. All mines in operation, departments, and SEGs were represented in the assessment and direct measurements of EMPs were used for a portion of the exposure assessment. The cohort from which the cases were identified was thorough and included all taconite miners ever employed by seven mining companies up to 1983. Use of both mortality records and Minnesota cancer surveillance allowed us to capture a near complete set of lung cancer cases in the cohort. Work history information came directly from mining company records and did not rely upon individual workers, eliminating the possibility of recall bias. The case-control design allowed for comprehensive examination of lung cancer risk that has not been possible in previous mortality studies of workers exposure to non-asbestiform EMPs.

CONCLUSIONS

This study provides evidence to suggest that exposure to non-asbestiform EMPs and to silica are not major risk factors for development of lung cancer in this population of miners.

References

1. Allen EM, Alexander BH, MacLehose RF, Ramachandran G, Mandel JH. Mortality Experience among Minnesota Taconite Mining Industry Workers. *Occup Environ Med,* accepted for publication April 2014, awaiting citation.
2. Cooper WC, Wong O, Graebner R. Mortality of workers in two Minnesota taconite mining and milling operations. *J Occup Med* 1988;30(6):506-511.
3. Cooper WC, Wong O, Trent LS, et al. An updated study of taconite miners and millers exposed to silica and non-asbestiform amphiboles. *J Occup Med* 1992;34(12):1173-1180.
4. de Klerk, NH, Musk AW, Eccles J et al. Exposure to crocidolite and the incidence of different histological types of lung cancer. *Occup Environ Med* 1996;53:157-159.
5. Department of Health and Human Services, National Institute for Occupational Safety and Health. Asbestos fibers and other elongate mineral particles: State of the science and roadmap for research, 2011: Publication No. 2011-159.
6. Department of Health and Human Services, National Institute for Occupational Safety and Health. Silica, lung cancer, and respiratory disease quantitative risk. A project from the first 10 years of NORA: High Impact, Publication No. 2011-120.
7. Finkelstein MM. Malignant Mesothelioma Incidence Among Talc Miners and Millers in New York State. *Am J Ind Med* 2012;868(April):863–868.
8. Gamble JF, Gibbs GW. Evaluation of the risks of lung cancer and mesothelioma from exposure to amphibole cleavage fragments. *Regul Toxicol Pharmacol* 2007;52(S1):S154-S186.
9. Gillam JD, Dement JM, Lemen RA, et al. Mortality Patterns Among Hard Rock Gold Miners Exposed to an Asbestiform Mineral. *Ann N Y Acad Sci* 1976;336–344.

10. Higgins IT, Glassman JH, Oh MS, et al. Mortality of Reserve Mining Company employees in relation to taconite dust exposure. *Am J Epidemiol* 1983;118(5):710-9.
11. Honda Y, Beall C, Delzell E, et al. Mortality among Workers at a Talc Mining and Milling Facility. *Ann Occup Hyg* 2002;46(7):575–585.
12. Hwang J, Gurumurthy R, Raynor P, et al. Comprehensive Assessment of Exposures to Elongate Mineral Particles in the Taconite Mining Industry. *Ann Occup Hyg* 2013;doi:10.1093.
13. International Agency for Research on Cancer. IARC Monographs on the evaluation of carcinogenic risks to humans, Vol 100C, Arsenic, Metals, Fibres, and Dust. International Agency for Research on Cancer: Lyon, 2012.
14. Jirsa MA, Miller JD, Morey GB. Geology of the Biwabik Iron Formation and Duluth Complex. *Regul Toxicol and Pharmacol* 2008;52(S1):S5-S10.
15. McDonald JC, Gibbs GW, Liddel FDK, et al. Mortality after long exposure to cummingtonite-grunerite. *Am Rev Respir Dis* 1978;118:271-277.
16. McDonald JC, McDonald AD. The epidemiology of mesothelioma in historical context. *Eur Respir J* 1996;9(9):1932–1942.
17. McSwiggin PL, Morey GB. Overview of the mineralogy of the Biwabik Iron Formation, Mesabi Iron Range, northern Minnesota. *Regul Toxicol and Pharmacol* 2008;52(S1):S11-S25.
18. Mossman BT. Assessment of the pathogenic potential of asbestos vs. nonasbestiform particulates (cleavage fragments) in in vitro (cell or organ culture) models and bioassays. *Regul Toxicol Pharmacol* 2008;52(S1):S200-3.
19. National Institute of Occupational Safety and Health (NIOSH). Silica, lung cancer, and respiratory disease quantitative risk. A project from the first 10 years of NORA: High Impact. DHHS (NIOSH) Publication No. 2011-120.

20. Nolan RP, Gamble JF, Gibbs GW. Letter to the editor on commentary: malignant mesothelioma incidence among talc miners and millers in New York state by M M Finkelstein. *Am J Ind Med* 2013;56(9):1116-8.

21. Raffn E, Lynge E, Korsgaard B. Incidence of lung cancer by histological type among asbestos cement workers in Denmark. *Br J Ind Med* 1993 January;50(1):85-89.

22. Robinson BWS, Musk AW, Lake RA. Malignant mesothelioma. *Lancet* 2005;366(9483):397–408.

23. Robinson BM. Malignant pleural mesothelioma: an epidemiological perspective. *Ann Cardiothorac Surg* 2012;1(4):491–6.

24. Steenland K, Brown D. Mortality study of gold miners exposed to silica and nonasbestiform amphibole minerals: an update with 14 more years of followup. *Am J Ind Med* 1995;27:217-229.

25. Sogl M, Taeger D, Pallapies D, Bruning T, Dufey F, Schnelzer M, Straif K, Walsh L, Kreuzer M. Quantitatie relationship between silica exposure and lung cancer mortality in German uranium miners, 1946 – 2003. British Journal of Cancer, 2012; 107: 1188 – 1194.

26. VanderWeele TJ, Hernan MA, Robins JM. Causal directed acyclic graphs and the direction of unmeasured confounding bias. *Epidemiology* 2008; 19(5):720-728.

27. Wilson R, McConnell EE, Ross M, et al. Risk assessment due to environmental exposures to fibrous particulates associated with taconite ore. *Regul Toxicol and Pharmacol 2008;52(S1): S232-S245.*

Medical Screening and Exposure Assessment of Current and Former Workers in the Taconite Industry of Minnesota

Background

An investigation into the presence of non-malignant respiratory disease (NMRD) was conducted within the taconite industry of Minnesota. Early investigation into the prevalence of NMRD in taconite miners and controls was undertaken over 30 years ago (Clark *et al.*, 1980; Higgins *et al.*, 1983). Although little NMRD was found in these early studies, the latency between dust and NMRD was such that little was expected to occur at that time.

Because there are no public databases that address this disease category in Minnesota, it was necessary to collect the information prospectively. NMRD, also referred to as pneumoconiosis, is well-described in many jobs where dust control is difficult and refers to those disease processes that typically result in a recognizable pattern of scarring/opacification of the lung substance (parenchyma) or lung lining (pleura) on chest x-ray (Santos Antao, *et al.*, 2007). As the scarring of the lung ensues, physiologic changes may occur in the ability to move air in and out of the lungs. The typical spirometry finding associated with parenchymal scarring is a restrictive pattern, with a decrease in forced vital capacity (FVC) and in forced expiratory volume in one second (FEV1). The former is the total amount of air expelled after a maximum inhalation. The latter is the maximum amount of air expelled in one second. In general, the longer the exposure, and the higher the exposure concentration, the more likely a worker is to develop NMRD.

Measurement of the main components of dust generated in taconite mining in this study included asbestiform and non-asbestiform elongate mineral particles (EMPs), respirable silica and respirable dust. An EMP refers to any mineral that has an aspect ratio (length to width ratio) of 3:1 or greater. EMPs may be classified as amphibole or non-amphibole and amphibole EMPs may be further described as asbestiform or non-asbestiform (NIOSH, 2011). Crystalline silica is a component of the total respirable dust and also has a typical x-ray and spirometric pattern.

The goal of the Respiratory Health Survey (RHS) was to assess the association between exposure to several dusts from taconite operations and NMRD, which was assessed using the degree of lung physiology impairment (spirometry) and anatomical abnormality (chest x-ray). We conducted a cross-sectional study of current and former workers and their spouses to do this.

Methods

The protocol for this study was reviewed and approved annually by the Human Subjects Committee of the University of Minnesota Institutional Review Board. All data in this study were held under strict control for the protection of confidentiality and privacy.

Study design

A cross-sectional survey of current and former taconite workers and spouses was conducted during 2010 and 2011. The survey consisted of a detailed questionnaire, which included health, occupational, military and smoking histories, physiologic lung function (spirometry) and chest x-ray evaluation for all participants.

Study population

The sampling frame for this study was assembled from lists of current and former workers obtained from each of the six active mines and one inactive site. The sampling frame was comprised of workers employed during the late 1980s until 2010 and totaled 16,990 individuals. This group represented the larger industry since mines that closed were typically purchased by one of three currently-active companies. From this population, a random sample was selected based on age, with over sampling of older individuals to increase the chances of identifying dust-related lung disease. The sample included workers who were currently or formerly employed at all seven mines across the entirety of the Mesabi Range. Mines on the eastern end of the Range are known to process an ore containing non-asbestiform amphiboles (Gamble and Gibbs, 2008). The western mines process non-amphibole-containing ore. A sample size of 1200 workers was determined, on the basis of respiratory symptoms in non-smoking, blue-collar workers, adjusting for gender, race, height, weight and education (Petersen and Castellan, 1984), to adequately power this study. Spouses were invited to participate given their potential secondary exposure and subsequent risk (Ferrante, 2007; Magnani, 2001).

Study recruitment

In order to enroll 1200 workers, we attempted to contact 3310 individuals. All randomly selected individuals were invited to participate in the study by mail. For those individuals who didn't respond to three mailings, attempts were made to contact them by phone. After five attempts to reach people by phone, no further recruitment efforts were undertaken. Workers were categorized as "enrolled" (agreed to participate), "refused" (did not agree to participate), "withdrew" (originally consented but later stopped their participation), or "non-responder" (no response from recruitment letter or phone call). This last category did not distinguish whether workers received letters and phone calls and ignored them, or whether their address and phone information was incorrect.

Those who agreed to participate were scheduled for a two-hour clinical evaluation. They filled out a self-administered questionnaire in advance that contained a medical, occupational, military and smoking history. This also contained a list of common respiratory symptoms (ATS, 1994). All individuals underwent informed consent. No remuneration, other than mileage reimbursement was provided for participants. Driving distances and travel times to the survey clinic were calculated using Google Maps Javascript API V3 (Google 2011).

Exposure assessment

One distinguishing characteristic of this study was in the use of work history information. The case-control studies described previously in this report used information from an existing MRHAP work history evaluation. Work history information in this study was obtained from questionnaires administered by the investigative team, in advance of medical testing. Work histories obtained directly from each participant, describing job titles, job locations, and dates of each job were used to create a comprehensive list of job titles.

The exposure assessment process has been described elsewhere and is described briefly here (Hwang *et al.*, 2013 Hwang *et al.*, 2014; Appendix 1, 2, 3). The goals for the exposure assessment component of this research were to (a) identify the major tasks pertinent to the processing of taconite ore, referred to as similarly exposed groups (SEGs); (b) assess current exposures of workers to the relevant components of dust from taconite operations which included asbestiform and non-asbestiform elongate mineral particles (EMPs), respirable silica, and respirable dust in each SEG; (c) estimate historical exposures within each SEG from relevant components of dust generated in taconite operations from 1953 to the present. Historical estimates were based on measurements provided by the companies for all sites and measurements taken by the Mining Safety and Health Administration (MSHA). The one inactive site did not have measurement data available for it, except those taken by MSHA.

Several workers per SEG were selected for sampling. Each participant wore a personal air-sampler for approximately six hours of a work shift on three separate occasions. The filter samples were analyzed for EMPs by phase contrast microscopy which identifies all EMPs longer than 5 µm, with a diameter of 0.25 µm and with an aspect ratio ≥ 3. Respirable silica was analyzed using the NIOSH 7500 analytic method. The samples were used to calculate a single average concentration for the shift per participant. For respirable dust, samples were analyzed with the NIOSH 0600 method.

Standardized exposure assessment approaches were used to assign each of 181 jobs across the active mines to 28 similarly exposed groups (SEGs), in common to all plants. The SEG information was combined with some 2000 on- site measurements that were made (Hwang *et al.*, 2013; Hwang *et al.*, 2014; Appendix 1, 2, 3) for both area and personal samples using traditional as well as more detailed methods for the assessment of EMPs, silica and total respirable dust. These measures were combined with historical measures obtained from each of the mining companies along with MSHA data to form a job (SEG)-exposure matrix for each year dating back to the beginning of the industry and extending through 2010.

Each person's company work record was then linked to the list of SEGs, using a standardized mapping approach. The exposure matrices could then be used to estimate each worker's exposure to EMPs, silica and total respirable dust. Each person's SEG exposure (by type, concentration and duration) was summed across all years worked in that SEG to obtain a cumulative exposure estimate. This information was obtained within the eastern and western most zones of the Mesabi Range. There were no active plants in the other zones (zones 2 and 3). Jobs with insufficient information were assigned to a department SEG, which was the average exposure for all SEGs in it. Jobs with no information were assigned to a missing SEG, which was the average for all SEGs in the mine.

Cross-sectional screening

During the clinical evaluation, participants underwent informed consent followed by a brief history and physical exam determining that they were fit for clinical testing. During this assessment, participants had the following tests performed: standard spirometry, diffusion capacity for carbon monoxide (D_LCO), which includes the determination of alveolar volume, a venous blood draw of 20 ccs and a posterior-anterior (PA) chest x-ray.

Spirometry was measured using a dry rolling seal, volume displacement spirometer by technicians trained in a two-day NIOSH-certified spirometry course. Regular quality checks of equipment and monitoring of procedural performance of technicians was undertaken. Testing followed American Thoracic Society (ATS)/European Respiratory Society (ERS) recommendations (Miller *et al.*, 2005), except that in this study, a minimum of five spirometry efforts was performed. Different categories were assessed, based on whether ATS/ERS guidelines for "acceptability" and "repeatability" of spirometric maneuvers were achieved. Standard reference equations were used for the estimation of expected spirometric results (Hankinson, 1999). A participant was identified as having "airflow/lung/spirometric obstruction" if the FEV1/FVC ratio was less than the lower limit of normal (LLN) (Hankinson, 1999). Spirometric restriction was identified in those whose FEV1/FVC ratio was greater than or equal to the LLN, but their FVC value was under the LLN. A '"mixed pattern" was identified when both FEV1/FVC ratio and FVC values were under the LLN. All spirometric restriction in this paper includes the mixed category. Borderline obstruction, which may represent either a mild obstruction or a normal physiological variant, sometimes called "dysanapsis" was identified by a low FEV1/FVC ratio plus an FEV1 over the LLN (Mead, 1980).

Certified radiologic technicians took all chest x-rays. All films were read blindly by two NIOSH-certified B-Readers using ILO guidelines and standard images (ILO, 2000). For the purposes of this study, parenchymal abnormalities were defined as the presence of small opacities of profusion ILO category 1/0 or above, and pleural abnormalities defined as any finding consistent with pneumoconiosis. When results from the two initial readers differed, a third certified B-reader performed an arbitration reading. For parenchymal abnormalities a third read took place when the two initial readers disagreed by more than two subcategories or one profusion category, or by more than one level in the opacity and distribution questions. Results of chest x-rays are listed herein as a consensus of two reads.

Statistical Analyses

Descriptive analyses examined the characteristics of workers who completed the questionnaire and clinic visit. Separate analyses examined the characteristics of study responders versus non-responders to explore possible selection bias. The association between employment duration in taconite or cumulative exposure and NMRD on chest x-ray was estimated using Poisson regression. Models were also used to estimate rate ratios and 95% confidence intervals for restriction. Employment duration models examined the effect of years worked in operations across the entire Iron Range, with separate models examining the effect of years worked within each of four Iron Range zones (Figure 1). Cumulative exposure models examined exposure in all geologic zones combined, with another model examining cumulative exposure within each zone. Since no EMP exposure measurements were available for zone 2 and mineralogy was most similar to zone 4, those measurements were felt to best represent zone 2 EMP exposures. SAS Version 9.2 was used to run all statistical models. Analyses were done controlling for age, gender, BMI, smoking status, hematite years, commercial asbestos, outside occupation with high probability of asbestos exposure and exposure in other zones.

Models incorporated continuous and categorical covariates for age and BMI. As hematite mining does not require the same processing steps needed for taconite, and since no exposure data were available for the hematite SEGs, models included the number of years spent in the hematite SEG as a separate variable. Commercial asbestos was used in the maintenance and building of the mines, but no quantitative data existed for commercial asbestos levels within the mines. To account for potential commercial asbestos exposure in the mines, each SEG was assigned a commercial asbestos score of low, medium, or high in a blinded fashion, by experienced industrial hygienists, based on the likelihood and frequency of asbestos exposure. Potential non-taconite, occupational asbestos exposure was assessed in the questionnaire, and a variable included in the models that indicated whether an individual had ever been employed in an occupation with a high potential for asbestos exposure.

Separate models were estimated for each of the NMRD outcomes, including spirometry, chest x-rays (pleural and parenchymal abnormalities) and exertional dyspnea. Detailed analyses were conducted for those endpoints that have been most consistently associated with dust exposure in the literature, including restrictive lung disease (via spirometry) and parenchymal abnormalities (via chest x-ray).

Results

We enrolled 1322 workers and 496 spouses (total of 1818 individuals). A total of 1,188 workers and 496 spouses completed the questionnaire and clinical examination over a 14 month period. Testing was performed at a central location on the Mesabi Iron Range, but even so, some individuals had to travel over three hours to get to the test site. Individuals living within one hours of the testing site made up 70% of the participants. Participants made up a lower percent of the random sample between the ages of 35 and 45 years (7.7% vs. 21%) and a higher percent of the random sample between the ages of 66 and 75 years (25.3% vs. 15.4%). Twenty percent of non-participants lived more than two hours from the testing site compared to 12.0% in the participant group. A group of 134 individuals responded to the questionnaire only without taking part in medical testing. From the random sample, 725 individuals could not be located, either related to incorrect address information or because of failure to respond to several mailings and five phone calls. Table 1 lists demographic characteristics of participants and spouses.

A total of 233 workers underwent personal exposure monitoring. Since five of the six currently operating mines were in the western zone, 177 of the workers were from this zone with the remainder from the eastern zone. In general, results for EMP measurements (NIOSH 7400 method) were below the recommended exposure limit (REL), with evidence of amphibole EMP present in the eastern zone plant but not in the western zone plants (Hwang *et al.*, 2013). Amphibole exposures were well below the REL. No asbestiform amphiboles were found in these measurements.

This study also assessed the present-day levels of exposure to respirable dust (RD) and respirable silica (RS) in taconite mines. Personal samples (n=679) were collected to assess the present-day exposure levels of workers to RD and RS at six mines on the Mesabi Iron Range. The silica and respirable dust measurements indicated slightly higher concentrations in the eastern zone (Appendix 3). The concentrations of RD in all mines fell below the ACGIH TLV for RD. With a few exceptions, the concentrations of RS in the crushing and concentrating processes were higher than those measured in the other mining processes with more excursions over the ACGIH TLV for RS than other measured exposures (Appendix 3).

Table 2 contains a comparison of chest x-ray and spirometry findings between workers and spouses. Workers had increased chest x-ray abnormalities in the lung substance (parenchyma) and the tissue surrounding the lungs (pleura) compared to spouses. In workers, most parenchymal abnormalities were in the 1/0 category (52%), with 28% in the 1/1 category, 7% read as 1/2, 3% read as 2/1, 7% as 2/2 and 3% as greater than 2/2. Pleural findings were mostly described as localized (53%), with 4% demonstrating obliteration of the costo-phrenic angle, 3% showing localized calcification and less than 1% with diffuse pleural thickening. When comparing workers and spouses with spirometry, abnormalities were comparable between these groups.

Table 3 lists demographic and exposure variables in workers by whether pleural or parenchymal findings were present. Those workers with abnormalities involving either the pleural or parenchyma were older, had higher rates of current and former smoking, had lower rates of having never smoked, spent more time working in the taconite industry and had slightly higher amounts of exposure to elongate mineral particle concentrations. Those with pleural abnormalities tended to have higher BMI. Neither prior employment in a job with potential asbestiform EMP exposure nor the geological taconite zone worked seemed to vary within those workers with or without lung pleural or parenchymal abnormalities.

Table 4 demonstrates the association between duration of employment in the taconite industry and parenchymal abnormality. The rate ratio was interpreted as the relative increase in the frequency of abnormality associated with a one unit increase in the exposure for continuous measures of exposure, e.g. years of employment, or compared to the reference category (designated as 1.0). Duration of employment was not significantly related to parenchymal abnormalities in these analyses.

Table 5 shows the relationship between exposures to EMP concentration-years to parenchymal abnormalities. As with duration of employment, the findings don't indicate a statistically significant association between these. When the exposures were categorized into two groups, high and low, using the median exposure as the cutoff, the rate ratio of high exposure to low exposure was 1.26. This finding was not statistically significant.

Tables 6 and 7 reveal the relationship between having pleural abnormalities with duration of employment and cumulative exposure, respectively. Analyses for Tables 6 and 7 were done controlling for age, gender, smoking, BMI, hematite years, commercial asbestos, outside occupation with high probability of asbestos exposure and exposure in other zones. In this analysis, the overall effect of employment duration showed an increased risk ratio (RR=1.02, 95% CI=1.0-1.04). This may be interpreted as a 2% increase in the risk of pleural abnormalities for each year worked. For a worker employed 30 years or longer, the risk of pleural abnormality was about 65% increased (RR=1.65, 95% CI=1.02-2.65). The overall relationship suggests a 6% increased risk of abnormalities, per each EMP/cc/year of exposure (RR=1.06, 95% CI=1.0-1.12). As an example, this could represent an exposure of 0.1 EMP/cc for 10 years or an exposure of 1.0 EMP/cc for one year. Looking at exposure concentrations at or greater than 1.16 EMP/cc/year nearly doubled the RR for pleural abnormalities (RR=1.93, 95% CI=1.32-2.83). The effect appeared strongest in zone 2.

Table 8 demonstrates the association between having a restrictive pattern on spirometry, pleural and parenchymal abnormalities and exposure to silica and respirable dust. In this analysis, adjusting for age, gender, BMI, smoking, commercial asbestos exposure score, there were non-significant increases in the RR for silica and, to a lesser extent, respirable dust. Neither silica nor respirable dust had strong associations with chest x-ray or spirometric abnormalities. Exertional dyspnea was also assessed as an endpoint. It also was not related to these exposures.

In an assessment of similarly exposed groups (SEGs), used to determine cumulative exposure for each exposure type, an association with pleural, parenchymal or spirometric abnormalities was not found, nor was one found with groupings of SEGs into broader categories, i.e. departments. Examples of departments included mining, crushing, concentrating and pelletizing.

Discussion

This survey of current and former taconite workers allowed for collection of exposure, lung function and imaging (chest x-ray) measurements, along with medical, occupational, military and smoking history information in workers and their spouses. Chest x-ray and lung function testing (spirometry) are the standard tests used to assess workers with dust exposure. This information provided additional context concerning the potential effects of exposures in this industry.

The response rate of the survey was consistent with recent investigations of this type (Galea and Tracy, 2007). The fact that individuals needed to drive several hours in some cases, without remuneration other than mileage reimbursement, may have played an inhibitive role in participation. Initial comparisons of responders and non-responders have shown that the former group is more likely to have been over age 55 and to have lived closer to the testing facility (within one hour). This may be because younger invitees were working and were unwilling to take time off to participate. Given that 75% of the participants were over age 55, no longer working and able to travel to the screening, they may represent a healthier group than the overall cohort. Over 90% of the participants were male, which parallels the gender makeup of the complete cohort (Allen *et al.*, 2014). A formal comparison of these issues is currently under study.

Despite questions on generalizability to other work settings, inference may be made on the basis of internal comparisons of workers to spouses. Based on chest x-ray evaluation alone, there is evidence of non-specific parenchymal abnormalities in workers. Although not as dramatically elevated as described in other industrial settings, it is higher than abnormalities found in spouses. Work-related silica and respirable dust exposure did not appear to be strongly associated with these abnormalities in our statistical models. Silica has a predilection for the lung parenchyma and was measured as the exposure with the most excursions over the ACGIH TLV in the onsite industrial hygiene assessment. However, the radiologic presentation is not classical of workers highly exposed to silica and is more consistent with mixed dust exposure. In this assessment, spouses do not appear to be at increased risk for chest x-ray abnormalities. The amount of their chest x-ray abnormalities is consistent with reports of findings in the non-occupational setting (Hillerdal, 1997). This is reassuring and suggests that current community exposures to dust from taconite operations are not likely to result in increased risk beyond what would be expected in the general population.

For workers, there was suggestion of an elevated risk for pleural abnormalities associated with duration of employment and exposure to EMPs. Over 16% of worker participants had evidence of pleural abnormalities by a consensus of B-readers, distinctly higher than spouses. It has also been described in relation to lung function impairment (Schwartz *et al.*, 1990; Broderick *et al.*, 1992). Pleural abnormalities can be complicated by other factors, including obesity (Sargent *et al.*, 1984). In statistical models that controlled for these factors, pleural abnormalities remained associated with duration of employment as well as with exposure to EMPs. The most likely exposure that would account for pleural abnormalities is asbestiform EMPs. In this study, we were not able to distinguish which specific type of EMP was associated. Parenchymal abnormalities were not consistently associated with either duration of employment or EMP exposure. The finding of a restrictive pattern on spirometry was not strongly related to either duration of employment or EMP exposure nor was dyspnea on exertion.

Strengths and limitations

Although we used the standard disease screening techniques, each of these medical tests has shortcomings in terms of sensitivity, specificity and predictive value. The cross-sectional design measured diseases at one point in time, which can limit the accuracy of diagnoses and subsequent inference. The healthy worker survivor effect is a concern with this type of study since the sickest workers may have died or been too sick to participate in this study.

Prior investigations in this industry have been limited by statistical power and the lack of exposure assessment data. The current approach had adequate size to detect important differences in exposed vs. unexposed groups. It also utilized spouses as an internal comparison to workers. It used onsite monitoring data, company measures and MSHA compliance monitoring data to project historical exposure estimates. The on-site measures were more complete and could be tied directly to SEGs of interest. Since phase contrast microscopy, which was used to analyze the onsite industrial hygiene samples for EMP, has a resolution of 0.25 µm, it is possible that EMPs under this diameter would be missed, even if greater than 5 µm in length. However, there is no indication that this potential misclassification would differ in those with or without test abnormalities.

The exposure assessment was unique in the incorporation of several dust-related exposures (EMP, silica, respirable dust). Despite the advantages of this exposure assessment approach, it lacked differentiation of asbestiform and non-asbestiform EMP. Due to important gaps in exposure measures, particularly during the early years of the industry, there was a potential for exposure misclassification. While several factors could lead to the exposures being categorized higher or lower, the exposure reconstruction was based on all available work history, without regard to test findings. Since work histories were abstracted without knowledge of test status, misclassification should be non-differential. However, it is also possible that job information was created in some systematic way that enhanced the potential for differential bias. In fact, we were not able to state which way this misclassification occurred, if it was a factor.

The findings of pleural abnormalities were more common in the western-most geological zones. This is contrary to the exposure measures for EMPs, which were higher on the eastern zone (Hwang *et al.*, 2013). The incongruity of this finding could suggest the impact of uncontrolled confounding factors and points to the need for further study of zone-specific results. In addition, although amphibole EMP exposures exist in the eastern Iron Range zone, these are believed to be predominantly of the non-asbestiform variety (Gamble and Gibbs, 2008; Ross *et al.*, 2008; Wilson *et al.*, 2008), a type that did not have clearly-established disease associated with exposure in studies of Homestake gold miners and New York talc workers (Steenland and Brown, 1995; Gamble, 1993 and 2008; Honda *et al.*, 2002; Finkelstein, 2012; Nolan *et al*., 2013).

Pleural abnormalities associated with non-asbestiform dust exposure are dependent on adequate control of asbestiform minerals. The facilities were constructed in the 1950s and 60s, a time when commercial asbestos materials were not strictly regulated and were used commonly in many industrial applications. The analysis of EMP exposures controlled for potential commercial asbestos exposure in the jobs held in the taconite industry, but the ability to do this was limited by the absence of data on the amount of exposure and type of commercial asbestos. It is possible that exposure to commercial asbestos remained as a residual confounding variable in this assessment.

Conclusions

This survey of taconite workers and spouses demonstrated increased findings for both pleural and parenchymal abnormalities in workers compared to spouses. Spouses did not appear to be at risk for dust-related lung disease beyond what would be expected in the general population. The parenchymal findings are consistent with dust exposure to a mixed dust including silica. Worker abnormalities for pleural disease were related to length of employment in the taconite industry and, to a lesser extent, to exposure to EMP. The specific type of EMP exposure could not be determined in this evaluation.

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References

Allen EM, Alexander BH, MacLehose RF, Ramachandran G, Mandel JH. Mortality experience among Minnesota taconite mining industry workers. Occup Environ Med, Occup Environ Med. 2014 May 9. doi: 10.1136/oemed-2013-102000. [Epub ahead of print] PMID:24816518

American Thoracic Society (ATS) Standardization of spirometry: 1994 update. Am J Respir Crit Care Med, 1995: 152:1107-1136.

Broderick A, Fuortes LJ, Merchant JA, *et al*. Pleural determinants of restrictive lung function and respiratory symptoms in an asbestos-exposed population. Chest, 1992 101:684-691.

Clark TC, Harrington VA, Asta J, Morgan WK, Sargent EN. Respiratory effects of exposure to dust in taconite mining and processing. Am Rev Respir Dis, 1980 121(6):959-966.

Ferrante D, Bertolotti M, Todesco A, Mirabelli D, Terracini B, Magnani C. Cancer mortality and the incidence of mesothelioma in a cohort of wives of asbestos workers in Casale Monferrato, Italy. Environ Health Perspect, 2007 115(10):1401-1405.

Finkelstein MM. Malignant mesothelioma incidence among talc miners and millers in New York State. AJIM 2012, 55(10):863-8. (doi: 10.1002/ajim.22063. Epub 2012 Apr 27.)

Galea S, Tracy M. Participation rates in epidemiologic studies. Ann Epidemiology. 2007 17(9):643-653.

Gamble JF. A nested case control study of lung cancer among New York talc workers. International Arch. Occup. Env Hlth 1993, 64:449-456.

Gamble JF, Gibbs GW. An evaluation of the risks of lung cancer and mesothelioma from exposure to amphibole cleavage fragments. Regul Toxicol Pharmacol, 2008 52(1 Suppl):S154-186.

Hankinson JL, Odencrantz JR, Fedan KB. Spirometric reference values from a sample of the general U.S. population. Am J Respir Crit Care Med, 1999 159:179-187.

Higgins IT, Glassman JH, Oh MS. The effect of taconite dust exposure on the health of employees of Reserve Mining Company: Mortality, respiratory symptoms and chest radiography. University of Michigan, Ann Arbor, MI. 1981.

Hillerdal G. Pleural plaques: incidence and epidemiology, exposed workers and the general population: a review. Indoor and Built Environment 1997, 6:86-95.

Honda Y, Beall C, Delzell E, Oestenstad K, Brill I, Matthews R. Mortality among workers at a talc mining and milling facility. Ann Occup Hyg 2002, 46:575-585.

Hwang J, Ramachandran G, Raynor PC, Alexander BH, Mandel JH. A comprehensive assessment of exposures to elongate mineral particles (EMPs) in the taconite mining industry. Ann Occup Hyg Published Online First: 22 June 2013. Doi:10.1093/annhyg/met026.

Hwang J, Ramachandran G, Raynor PC, Alexander BH, Mandel JH. The relationship between various exposure metrics for elongate mineral particles (EMP) in the taconite mining and processing industry. J Occup Environ Hyg. 2014;11(9):613-24. doi: 10.1080/15459624.2014.890287. PMID: 24512074

ILO Guidelines for the use of the International Labor Organization International Classification of Radiographs of Pneumoconioses. Occupational Safety and Health Series No. 22. Geneva International Labor Office, Geneva, Switzerland, revised 2000.

Magnani C, Dalmasso P, Biggeri A, Ivaldi C, Mirabelli D, Terracini B. Increased risk of malignant mesothelioma of the pleura after residential or domestic exposure to asbestos: a case-control study in Casale Monferrato, Italy. Environ Health Pers, 2001 109(9):915-919.

Mead J. Dysanapsis in normal lungs assessed by the relationship between maximal flow, static recoil, and vital capacity. Am Rev Respir Disease 1980 121:339-342.

Miller MR, Hankinson J, Brusasco V, et al. Standardization of spirometry. ATS/ERS task force: standardization of lung function testing. Eur REspir J 2005 26:319-338.

National Institute for Occupational Safety and Health (NIOSH). NIOSH manual of analytical methods (NMAM) 7400. 4th Edition: Asbestos and other fibers by PCM, Issue 2, 1994.

NIOSH Current Bulletin No. 62. Asbestos Fibers and Other Elongate Mineral Particles: State of the Science and Roadmap for Research (Revised Edition). Department of Health and Human Services, Centers for Disease Control and Prevention, National Institute for Occupational Safety and Health. April, 2011.

Nolan RP, Gamble JF, Gibbs GW. Letter to the Editor on Commentary: Malignant Mesothelioma Incidence Among Talc Miners and Millers in New York State by MM Finkelstein. AJIM 2013 56:1116–1118.

Petersen M, Castellan RM. Prevalence of chest symptoms in non-exposed blue collar workers. J Occup Med, 1984 26:367-374.

Ross M, Nolan RP, Nord GL. The search for asbestos within the Peter Mitchell taconite iron ore mine, near Babbitt, Minnesota. Regul Toxicol Pharmacol 2008, 52 (1 suppl):43-40.

Santos Antao VC, Pinheiro GA, Parker JE. Lung diseases associated with silicates and other dusts. Environmental and Occupational Medicine 4th Edition (2007). Rom WE, Editor. Wolters Kluwer/Lippincott Williams & Wilkins, Philadelphia, PA. Chapter 32, p. 525-542.

Sargent EN, Boswell W, Ralls P, *et al.* Subpleural fat pads in patients exposed to asbestos: distinction from non-calcified pleural plaques. Radiology, 1984 152:273-277.

Schwartz DA, Fuortes LJ, Galvin JR, *et al.* Asbestos-induced pleural fibrosis and impaired lung function. Am Rev Respir Dis, 1990 141:321-326.

Steenland K, Brown D. Mortality study of gold miners exposed to silica and nonasbestiform amphibole minerals; an update with 14 more years of follow-up. Am J Ind Med, 1995 276:217-229.

Wilson R, McConnell EE, Ross M, Axten CW, Nolan RP. Risk assessment due to environmental exposures to fibrous particulates associated with taconite ore. Regulatory Toxicology and Pharmacology 2008, 52 (1 supp): 232-245.

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Table 1. Demographic profile of study participants and spouses

	Participants (n=1188)	Spouses (n=455)
Mean age (yrs.)	60.0	59.7
Age groups (%)		
35-45	7.7	6.8
46-55	18.3	28.2
56-65	35.3	29.4
66-75	25.3	28.8
75+	13.5	5.8
Mean BMI	31.4	30.9
Smoking (%)		
Never	38	47
Current	12	10
Former	50	43
Gender (%)		
Male	90.8	3.1
Female	9.2	96.9

Table 2. Summary of chest x-ray and spirometry findings in taconite workers and spouses

Chest x-ray	Workers (n=1188)	Spouses (n=455)
B-reader consensus parenchymal abnormality	63 (5.3%)	3 (0.6%)
B-reader consensus pleural abnormality	198 (16.7)	22 (4.5)
B-reader consensus x-ray diffuse pleural thickening	12 (1.0)	0
B-reader consensus pleural and parenchymal abnormality	29 (2.5)	0

Spirometry	(n=1084)	(n=455)
Obstruction[a]	182 (16.8)	53 (11.6)
Restriction[b]	49 (4.5)	20 (4.4)
Mixed disease[c]	31 (2.9)	13 (2.8)

[a] FEV1/FVC ratio was less than the lower limit of normal
[b] FEV1/FVC ratio was greater than or equal to the LLN and FVC value was under the LLN
[c] Both FEV1/FVC ratio and FVC values under the LLN

Table 3. Demographics and exposure levels of taconite workers by radiographic status

Characteristic	Parenchymal Abnormality		Pleural Abnormality	
	Yes=63	No=1115	Yes=198	No=980
Working Status %				
Former	93.6	69.9	84.9	68.4
Current	6.4	30.1	15.1	31.6
Gender %				
Female	1.6	9.6	2.0	10.6
Male	98.4	90.4	98.0	89.4
Mean Age	67.9	60.1	65.6	59.5
Mean BMI	30.5	31.4	34.3	30.8
Smoking Status %				
Current	15.9	11.7	8.1	12.7
Former	61.9	48.3	66.7	45.5
Never	22.2	40.0	25.2	41.8
Outside Asbestos Occupation %				
No	76.2	77.9	74.2	78.5
Yes	23.8	22.1	25.8	21.5
Zone ever worked %				
Zone 1	57.1	61.5	58.6	61.8
Zone 2	38.1	34.8	36.9	34.6
Zone 4	22.2	25.0	22.7	25.3
Mean years of taconite employment				
Overall	29.0	25.3	28.5	24.9
Zone 1	25.9	20.8	22.7	20.7
Zone 2	22.7	19.2	24.9	18.2
Zone 4	24.1	21.2	24.5	20.8
Mean EMP/cc/year				
Overall	3.8	2.9	3.9	2.8
Zone 1	2.3	1.5	2.0	1.5
Zone 2	3.1	2.4	3.7	2.2
Zone 4	5.7	4.6	5.9	4.5

Table 4. Parenchymal abnormality[a] associated with duration of taconite employment (years) and duration of taconite employment in each Iron Range Zone

Exposure	Abnormalities Yes/No	Rate Ratio (RR)[e]	95%CI
Overall Employment[b]			
Taconite employment duration	63/1115	1.02	0.99-1.04
Hematite employment duration	7/51	1.01	0.94-1.09
Duration Category[b,c]			
0 < years < 22	15/425	1.00	---
22+ years	48/690	1.38	0.75-2.56
Zone Analysis[d]			
Employment duration-Zone 1	36/686	1.03	0.99-1.06
Employment duration-Zone 2	24/388	1.03	0.99-1.06
Employment duration-Zone 4	14/279	1.01	0.98-1.04

[a] Defined as profusion 1/0 or greater by B-reader consensus
[b] Results adjusted for age, gender, BMI, smoking status, hematite years, and outside occupation with high probability of asbestos exposure
[c] Duration category comparison of duration quartile 1 vs duration quartiles 2-4
[d] Results adjusted for age, BMI, hematite years, outside occupation with high probability of asbestos exposure, and duration in other zones
[e] Rate ratio is interpreted as the relative increase in the frequency of abnormality associated with a one unit increase in the exposure for continuous measures of exposure, e.g. years of employment, or compared to the reference category (designated as 1.0).

Table 5. Parenchymal abnormality[a] associated with cumulative EMP/CC/years in each Iron Range Zone

Exposure	Abnormalities Yes/No	RR[d]	95%CI
Overall Employment[b]			
EMP/cc/year	63/1115	1.00	0.92-1.09
Hematite	7/51	1.01	0.93-1.08
Zone Analysis[c]			
EMP/cc/year -Zone 1	36/686	1.06	0.92-1.23
EMP/cc/year -Zone 2	24/388	1.03	0.90-1.18
EMP/cc/year -Zone 4	14/279	0.99	0.90-1.09

[a] Defined as profusion 1/0 or greater by B-reader consensus
[b] Results adjusted for age, gender, BMI, smoking status, hematite years, commercial asbestos exposure score, and outside occupation with high probability of asbestos exposure
[c] Results adjusted for age, BMI, hematite years, commercial asbestos, outside occupation with high probability of asbestos exposure, and exposure in other zones
[d] Rate ratio is interpreted as the relative increase in the frequency of abnormality associated with a one unit increase in the exposure for continuous measures of exposure or compared to the reference category (designated as 1.0).

Table 6. Pleural abnormality[a] associated with duration of taconite employment (years) and duration of taconite employment in each Iron Range Zone

Exposure	Abnormalities Yes/No	RR[d]	95%CI
Overall Employment[b]			
Taconite employment duration	198/980	1.02	1.00-1.04
Hematite employment duration	15/43	1.01	0.95-1.07
Duration Quartile[b]			
0 < years < 21	40/342	1.00	---
21 < years < 30	50/248	1.39	0.86-2.26
30 < years < 35	57/218	1.65	1.02-2.65
35+ years	51/172	1.84	1.11-3.07
Zone Analysis[c]			
Employment duration-Zone 1	116/606	1.02	1.00-1.04
Employment duration-Zone 2	73/339	1.03	1.01-1.05
Employment duration-Zone 4	45/248	1.01	0.99-1.03

[a] Defined as abnormality consistent with pneumoconiosis by B-reader consensus
[b] Results adjusted for age, gender, BMI, hematite years, and outside occupation with high probability of asbestos exposure
[c] Results adjusted for age, gender, BMI, hematite years, outside occupation with high probability of asbestos exposure, and duration in other zones
[d] The rate ratio is interpreted as the relative increase in the frequency of abnormality associated with a one unit increase in the exposure for continuous measures of exposure, e.g. years of employment, or compared to the reference category (designated as 1.0).

Table 7. Pleural abnormality[a] associated with cumulative EMP/cc/years and Iron Range zone

Exposure	Abnormalities[a] Yes/No	RR[f]	95%CI
Overall Employment[b]			
EMP/cc/years	198/980	1.06	1.00-1.12
Hematite	15/43	1.01	0.96-1.07
Exposure Category [b, c]			
0 < EMP/cc/years < 1.16	48/415	1.00	---
1.16 + EMP/cc/years	150/565	1.93	1.32-2.83
Exposure Quartile[b]			
0 < EMP/cc/years < 1.16	48/415	1.00	---
1.16 < EMP/cc/years < 3.29	51/238	1.84	1.18-2.94
3.29 < EMP/cc/years < 5.89	49/176	2.22	1.42-3.63
5.89 + EMP/cc/years	50/151	1.78	1.11-2.98
Zone Analysis[d]			
EMP/cc/year -Zone 1	116/606	1.09	0.99-1.21
EMP/cc/year -Zone 2	73/339	1.16	1.06-1.27
EMP/cc/year -Zone 4	45/248	1.04	0.97-1.10
Zone Analysis[d,e]			
Quartiles 2-4 vs 1-Zone 1	62/205 vs 54/401	1.97	1.27-3.06
Quartiles 2-4 vs 1-Zone 2	56/168 vs 17/171	2.67	1.3-5.48
Quartiles 2-4 vs 1-Zone 4	38/195 vs 7/53	1.05	0.39-2.81

[a] Defined as abnormality consistent with pneumoconiosis as interpreted by B-reader consensus
[b] Results adjusted for age, gender, BMI, hematite years, commercial asbestos exposure score, and outside occupation with high probability of asbestos exposure
[c] Exposure category comparison of exposure quartile 1 vs exposure quartiles 2-4
[d] Results adjusted for age, gender, BMI, hematite years, commercial asbestos, outside occupation with high probability of asbestos exposure, and exposure in other zones
[e] For each zone, cumulative EMP/CC/years for quartiles 2-4 are compared to quartile 1
[f] The rate ratio is interpreted as the relative increase in the frequency of abnormality associated with a one unit increase in the exposure for continuous measures of exposure, e.g. years of employment, or compared to the reference category (designated as 1.0).

Table 8. Pleural[a] and parenchymal chest x-ray abnormality[b] and restrictive pattern on spirometry[c] associated with cumulative exposure to silica and respirable dust

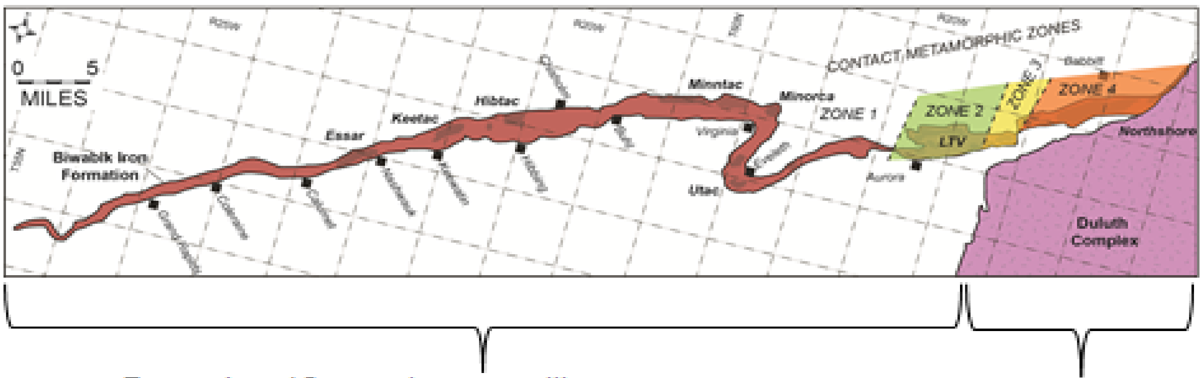
	Pleural		Parenchymal		Spirometric Restriction[c]	
	RR[e]	**95% CI**	**RR[e]**	**95% CI**	**RR[e]**	**95% CI**
Cumulative silica exposure in mg/cc/years	1.06	0.85-1.31	0.97	0.60-1.57	1.19	0.81-1.75
Cumulative respiratory dust exposure in mg/cc/years[d]	1.01	0.99-1.03	1.00	0.96-1.04	1.00	0.96-1.05

[a] Defined as abnormality consistent with pneumoconiosis by B-reader consensus
[b] Defined as consensus read of 1/0 or greater by ILO categorization
[c] Defined as FVC < LLN (includes mixed disease)
[d] Respirable dust is defined as total respiratory dust minus total silica dust
[e] The rate ratio is interpreted as the relative increase in the frequency of abnormality associated with a one unit increase in the exposure for continuous measures of exposure, e.g. years of employment, or compared to the reference category (designated as 1.0). The analysis was adjusted for age, gender, BMI, smoking and commercial asbestos exposure score.

Figure 1.

Biwabik Iron Formation Mineralogy

West to East



Zones 1 and 2: quartz, magnetite, hematite, carbonates, talc, chamosite, greenalite, minnesotaite and stilpnomelane

Modified from: OVERVIEW OF THE MINERALOGY OF THE BIWABIK IRON FORMATION, MESABI IRON RANGE, NORTHERN MINNESOTA Peter L. McSwiggen and G.B. Morey (2008).

Zones 3 and 4: quartz, magnetite, grunerite, hornblende, hedenbergite, ferrohypersthene (ferrosilite), and fayalite