

## ORIGINAL ARTICLE

## Occupational exposures and lung cancer risk among Minnesota taconite mining workers

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**ABSTRACT****Objective** To examine the association between employment duration, elongate mineral particle (EMP) exposure, 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. ORs and 95% CIs were estimated using conditional logistic regression. We evaluated total lung cancer risk and risk of histological subtype by total work duration and by cumulative EMP, and silica exposure by quartile of the exposure distribution.**Results** A total of 1706 cases and 3381 controls were included in the analysis. After adjusting for work in haematite mining, asbestos exposure and sex, the OR for total duration of employment was 0.99 (95% CI 0.96 to 1.01). The ORs for quartile 4 versus 1 of EMP and silica exposure were 0.82 (95% CI 0.57 to 1.19) and 0.97 (95% CI 0.70 to 1.35), respectively. The risk of each histological subtype of lung cancer did not change with increasing exposure.**Conclusions** This study suggests that the estimated taconite mining exposures do not increase the risk of developing lung cancer.**BACKGROUND**The iron mining industry in Minnesota began in 1865 with the discovery of iron ore on the Mesabi Iron Range. Initially, the target ore was haematite, a high-grade iron ore that could be excavated from the iron deposits and shipped directly to steel mills with minimal processing. However, following the high demand for its use during World War II, haematite reserves were depleted, and in the 1950s, the mining and processing of lower grade taconite ore began.<sup>1</sup> 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**What this paper adds**

- ▶ Mining and processing of taconite results predominantly in exposure to non-asbestiform amphibole and non-amphibole minerals.
- ▶ Risk of exposure to non-asbestiform minerals is not understood.
- ▶ No increase in risk of lung cancer was observed.

amphibole and non-amphibole elongate mineral particles (EMP), respirable silica and cleavage fragments.<sup>2</sup>The term 'EMP' refers to any mineral particle with a minimum aspect ratio of 3:1 that is of inhalable size, and EMPs with a length greater than 5 µm are regulated. 'Amphibole EMP' refers to a subset of silicate minerals that can be asbestiform or non-asbestiform.<sup>3</sup> Asbestiform EMPs are likely to be thinner, longer and more flexible than non-asbestiform. They tend to have very large aspect ratios, generally >20:1 for fibres >5 µm in length.<sup>4</sup> By contrast, non-asbestiform EMPs have aspect ratios >3:1 and have widths much larger than asbestiform fibres of the same length. Although the chemical composition of asbestiform and non-asbestiform EMP can be the same, they do not share the same physical structure.<sup>5</sup> Cleavage fragments are mineral EMPs that have broken along a cleavage plane during the crushing and fracturing process.<sup>3,4</sup> The health consequences of exposure to cleavage fragments has not been comprehensively studied.<sup>6</sup> 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.<sup>7</sup> All zones have deposits of taconite along with quartz and iron silicates, but vary in the type of EMP.<sup>8</sup> The eastern part of the range, known as zone 4, contains iron-rich amphibole EMPs, believed to be less than 1% fibrous.<sup>9</sup> 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

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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 and lung cancer is well documented.<sup>3 10–12</sup> 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.<sup>3</sup> These include studies of talc miners in upstate New York,<sup>13–15</sup> and gold miners in South Dakota.<sup>16–18</sup>

In 1996, the International Agency for Research on Cancer concluded that crystalline silica was carcinogenic to humans (group 1).<sup>19</sup> Although the association between crystalline silica and lung cancer has been debated, recent occupational studies have provided evidence supporting the risk of lung cancer after silica exposure.<sup>20 21</sup>

Health risks associated with taconite mining have been of concern to the public for several decades, but few studies have evaluated the health of miners in Minnesota. In 1983, a mortality analysis of 5751 miners showed no increase in risk of respiratory cancer.<sup>22</sup> A similar mortality analysis of 3431 workers published in 1988 and 1992, likewise did not report an excess of mortality for any cause of death.<sup>23 24</sup> 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 SMRs for lung cancer (SMR=1.2, 95% CI 1.2 to 1.2) and mesothelioma (SMR=2.8, 95% CI 1.9 to 4.0) among taconite mining workers.<sup>25</sup> 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<sup>26 27</sup> conducted by the University of Minnesota. The original cohort was established 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 haematite 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. Mortality follow-up occurred between 1960, when comprehensive mortality data were available, and 2010. The vital status and causes of death of cohort members were ascertained by linking social security numbers, names and dates of birth to 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 between 1988 and 2010.

### 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 for each case by age (year of birth  $\pm 5$  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<sup>2</sup> and summarised below.

Mining industry jobs were condensed into 28 similarly exposed groups (SEG) 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.<sup>2</sup>

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 6 h of a work shift on three separate occasions. The filter samples were analysed for EMPs by phase contrast microscopy which identifies all EMPs longer than 5  $\mu\text{m}$ , with a diameter of 0.25  $\mu\text{m}$  and with an aspect ratio  $\geq 3$ . Respirable silica was analysed using the NIOSH method 7500 for crystalline silica by X-ray diffraction. The results from the samples were used to calculate a single average concentration for the shift for each participant.

Historical exposure data were obtained from the Mine Data Retrieval System maintained by MSHA and the internal databases of two currently operating taconite mining companies. A total of 682 EMP samples and 3370 silica samples were used

to create the historical reconstruction. By combining comprehensive present-day exposure levels with the historical data, we generated a master database to estimate an SEG-specific exposure. Historical samples were infrequent prior to the mid-1970s, and unavailable or sparse for many of the SEGs. Thus, using a time-varying linear regression model, annual average exposures were estimated for each combination of SEG, year and mine. The final exposure matrix included exposure estimates for each of the 7 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 standardised 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 SEGs 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. Annual and company-specific EMP and silica concentrations were assigned for each SEG. Every individual worker's employment history included a unique exposure concentration for every combination of year, mine and SEG. This concentration was summed to give individual cumulative EMP exposure in  $(\text{EMP}/\text{cc}) \times \text{years}$ , and a cumulative silica exposure measured in  $(\text{mg}/\text{m}^3) \times \text{years}$ .

Many of the workers had employment history in the mining industry before taconite mining began in the 1950s and 1960s. The transition from haematite 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 haematite SEG for which EMP and silica exposure estimates were not available.

It is possible that commercial asbestos was used throughout the operations 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 based on the jobs that formed the SEG. The major scenarios of commercial asbestos exposure were associated with maintenance of building structures and the equipment where asbestos was integrated for insulation and heat resistance. 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 ORs and 95% CIs 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 HRs. In the final models, risk estimates were adjusted for sex, haematite 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 characterised 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 separate models as categorical (split by quartile) and continuous variables. Analyses were repeated restricting the cases to only those identified by a 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 V9.2.

### RESULTS

Follow-up of the 46 170 workers identified 1725 cases corresponding to 3450 controls, 13 565 (29%) deceased and 683 (1.5%) lost to follow-up. After work history abstraction, three cases along with their six corresponding controls and four additional controls were excluded due to poor data quality, for example, 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 for employment with no evidence of actual employment in the taconite mining industry. The final analysis included 1706 lung cancer cases and 3381 controls. Of the 1706 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 years (ranging from less than 1 to 30.7) and 8.5 years (ranging from less than 1 to 30.3), respectively. The total cumulative exposure of EMPs and silica was higher in the controls than in the cases ( $1.7 (\text{EMP}/\text{cc}) \times \text{years}$  and  $0.31 (\text{mg}/\text{m}^3) \times \text{years}$  for controls and  $1.5 (\text{EMP}/\text{cc}) \times \text{years}$  and  $0.28 (\text{mg}/\text{m}^3) \times \text{years}$  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.

Total duration of employment in taconite mining did not appear to increase the risk of lung cancer (OR=0.99, 95% CI 0.96 to 1.01). An inverse association between risk and exposure was observed across quartiles for EMP and silica exposure; however, none of the quartiles exhibited a significant increase in risk. As compared with quartile 1 exposure levels, those with no taconite exposure showed a lower risk of lung cancer (EMP OR=0.81, 95% CI 0.67 to 0.98; silica OR=0.81, 95% CI 0.68 to 0.98). ORs and 95% CIs for the analysis by employment duration 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 ([table 3](#)).

A total of 973 lung cancer cases were identified by MCSS and were included in the subanalysis 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 carcinomas; 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 1** Characteristics of cases and controls

	Cases (n=1706) n (%)	Controls (n=3381) 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)
Haematite only	738 (43.26)	1532 (45.28)
Taconite and haematite	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)
	<b>Mean (SD)</b>	<b>Mean (SD)</b>
Birth year	1930 (7.92)	1930 (7.90)
Years of employment		
Taconite	7.67 (8.22)	8.52 (8.57)
Haematite	3.57 (5.34)	3.67 (5.58)
Years of taconite employment by zone		
Zone 1	7.38 (5.97)	7.60 (5.76)
Zone 2	5.41 (7.88)	7.11 (8.48)
Zone 4	8.81 (9.74)	9.27 (10.26)
(EMP/cc)×years		
Total*	1.48 (2.17)	1.68 (2.31)
Zone 1	0.52 (1.00)	0.52 (0.94)
Zone 2	1.17 (1.75)	1.54 (1.94)
Zone 4	2.51 (2.74)	2.61 (2.85)
Silica (mg/m <sup>3</sup> )×years		
Total*	0.28 (0.31)	0.31 (0.31)
Years of employment by department		
Mining	1.28 (3.50)	1.36 (3.79)
Crushing	0.16 (0.92)	0.20 (1.00)
Concentrating	0.20 (1.18)	0.22 (1.23)
Pelletising	0.25 (1.64)	0.24 (1.56)
Shop mobile	2.59 (5.50)	2.98 (5.79)
Shop stationary	0.68 (2.76)	0.71 (2.59)
Office	0.30 (1.93)	0.65 (2.97)
Missing/unknown	0.48 (2.17)	0.46 (2.36)
General mine	0.69 (2.56)	0.47 (2.02)
General plant	0.38 (1.85)	0.44 (2.22)
General shop	0.68 (2.53)	0.79 (2.73)

\*Mean cumulative exposure.  
EMP, elongate mineral particle.

**Table 2** Risk of lung cancer by employment duration, cumulative elongate mineral particle (EMP), and cumulative silica exposure

Years of employment	OR	95% CI
Total		
Taconite years*	0.99	0.96 to 1.01
Haematite years†	0.99	0.98 to 1.01
By department‡		
Mining	0.99	0.97 to 1.01
Crushing	0.96	0.88 to 1.05
Concentrating	0.99	0.93 to 1.06
Pelletising	1.02	0.97 to 1.07
Shop mobile	0.99	0.98 to 1.01
Shop stationary	1.01	0.98 to 1.05
Office	0.95	0.92 to 0.99
EMP exposure ((EMP/cc)×years*)		
By quartiles (lower cut point)		
Unexposed§	0.81	0.67 to 0.98
Q1 (0)	1	
Q2 (0.1298)	1.00	0.79 to 1.25
Q3 (0.4527)	0.98	0.77 to 1.24
Q4 (2.353)	0.82	0.57 to 1.19
Silica exposure ((mg/m <sup>3</sup> )×years¶)		
By quartiles (lower cut point)		
Unexposed§	0.81	0.68 to 0.98
Q1 (0)	1	
Q2 (0.0373)	1.04	0.84 to 1.29
Q3 (0.2064)	0.95	0.74 to 1.22
Q4 (0.5189)	0.97	0.70 to 1.35

\*Adjusted for haematite exposure, silica exposure, asbestos exposure and sex.

†Adjusted for taconite exposure, silica exposure, asbestos exposure and sex.

‡Adjusted for years in unknown similarly exposed groups (SEGs), haematite, general mine, general plant, general shop, sex and asbestos.

§Worked only in haematite production and did not have taconite exposure.

¶Adjusted for taconite exposure, haematite exposure, asbestos exposure and sex.

did have a carcinogenic effect, they 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<sup>25</sup> in this taconite workers cohort. Specifically, SMRs and SIRs 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

## 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. Owing 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.<sup>28 29</sup> This would suggest that if non-asbestiform EMPs

**Table 3** Risk of lung cancer by employment duration and cumulative elongate mineral particle (EMP) exposure in each zone of the iron range

	OR	95% CI
Taconite years by zone*		
Zone 1	1.01	0.97 to 1.04
Zone 2	0.99	0.96 to 1.02
Zone 4	0.99	0.96 to 1.01
(EMP/cc)×years by zone*		
Zone 1	1.00	0.87 to 1.16
Zone 2	0.94	0.85 to 1.02
Zone 4	0.95	0.89 to 1.01

\*Adjusted for haematite exposure, silica exposure, asbestos exposure, exposure in other zones and sex.

**Table 4** Risk of major histological subtypes of lung cancer by cumulative elongate mineral particle (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* (lower cut point)					
Unexposed†	0.65 (0.40 to 1.06)	0.78 (0.50 to 1.22)	0.77 (0.37 to 1.60)	0.93 (0.53 to 1.64)	0.89 (0.33 to 2.43)
Q1 (0)	1	1	1	1	1
Q2 (0.1298)	1.03 (0.58 to 1.82)	0.92 (0.55 to 1.53)	0.99 (0.46 to 2.14)	0.96 (0.49 to 1.90)	0.47 (0.13 to 1.67)
Q3 (0.4527)	1.20 (0.66 to 2.20)	0.79 (0.46 to 1.36)	0.93 (0.41 to 2.06)	0.91 (0.47 to 1.74)	1.01 (0.33 to 3.07)
Q4 (2.353)	1.04 (0.42 to 2.58)	0.54 (0.23 to 1.30)	1.07 (0.31 to 3.70)	1.44 (0.56 to 3.72)	0.11 (0.01 to 1.04)
Silica (mg/m <sup>3</sup> )×years quartiles‡ (lower cut point)					
Unexposed†	0.67 (0.41 to 1.08)	0.78 (0.51 to 1.19)	0.64 (0.30 to 1.34)	1.06 (0.59 to 1.91)	1.24 (0.44 to 3.49)
Q1 (0)	1	1	1	1	1
Q2 (0.0373)	1.11 (0.64 to 1.95)	0.92 (0.57 to 1.48)	0.76 (0.36 to 1.60)	1.15 (0.62 to 2.16)	2.10 (0.73 to 6.05)
Q3 (0.2064)	1.25 (0.71 to 2.18)	0.96 (0.59 to 1.56)	0.71 (0.32 to 1.57)	1.57 (0.79 to 3.10)	0.99 (0.22 to 4.47)
Q4 (0.5189)	1.28 (0.73 to 2.24)	0.96 (0.58 to 1.59)	0.98 (0.43 to 2.25)	1.72 (0.88 to 3.36)	1.90 (0.62 to 5.83)

\*Adjusted for haematite exposure, silica exposure, asbestos exposure and sex.

†Worked only in haematite production and did not have taconite exposure.

‡Adjusted for haematite exposure, EMP exposure, asbestos exposure and sex.

mesothelioma (SMR=2.8, 95% CI 1.9 to 4.0) and lung cancer (SMR=1.2, 95% CI 1.1 to 1.2). Cancer incidence was elevated for mesothelioma (SIR=2.4, 95% CI 1.8 to 3.2) and lung cancer (SIR=1.3, 95% CI 1.2 to 1.4). Results from the current analysis suggest that the increase in risk for mortality and incidence of lung cancer in this study population may not be a function of the duration of employment in the taconite industry or the level of EMP and silica exposures experienced in this industry. However, it is possible that the duration of exposures in this study population were not long enough to cause lung cancer. While there is evidence that workers in this industry can be exposed to EMPs and silica above recommended levels,<sup>2</sup> it is quite possible that the excess lung cancer occurrence is related to non-occupational exposures, specifically smoking.

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-year 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 1397 cases identified through death certificates and their corresponding controls.

The strong association between asbestiform EMP exposure and lung cancer is well documented;<sup>3, 30</sup> however, the carcinogenicity 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,<sup>29</sup> but epidemiology studies have been inconclusive. NIOSH has specifically identified non-asbestiform EMPs as a needed area of research.<sup>3</sup> 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<sup>13</sup> and South Dakota gold miners<sup>16–18</sup> have shown inconclusive evidence of an association between non-asbestiform EMPs and malignant lung disease. Results from some animal studies have suggested that fibre dimension, and not composition, is the major determinant of carcinogenicity for mineral fibres.<sup>3</sup> There remains a need to determine whether non-asbestiform EMPs in different physical forms are also capable of causing disease.<sup>3</sup> 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 modelling 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. Further, selection bias is possible since cancer-specific mortality could not be ascertained prior to 1988.

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. Although standardisation 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. Although we did not have smoking information for the study population, there were data available on the smoking habits from a survey of 1186 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<sup>3</sup>)×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.<sup>31</sup>

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 that exposure to non-asbestiform EMPs and to silica are not risk factors for development of lung cancer in this population of taconite miners.

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**Competing interests** None declared.

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