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A Population-Based Feasibility Study of Occupation and Thoracic Malignancies in New Mexico

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Abstract

Background

Occupational exposures in mining and oil/gas extraction are known risk factors for thoracic malignancies (TMs). Given the relatively high proportion of these industries in New Mexico (NM), we conducted a feasibility study of adult lifetime occupational history among TM cases. We hypothesized a higher proportion of occupational TM in NM relative to the estimated national average of 10-14%.

Methods

We identified incident TM cases through the population-based New Mexico Tumor Registry (NMTR), from 2017- 2018. Cases completed a telephone interview. An adjudication panel reviewed case histories and classified cancers as probable, possible, or non-occupational related, taking into account the presence, duration, and latency of exposures. We characterized recruitment and describe job titles and exposures among those with occupational TMs. We also compared the distributions of industry between those with and without occupational TM.

Results

The NMTR identified 400 eligible TM cases, 290 of which were available to be recruited (n=285 lung/bronchial cancer; n=5 mesotheliomas). Of the latter, 60% refused and 18% were deceased, 9% had invalid addresses, 11% were unable to be reached by telephone, and 3% were too ill to participate. The 43 cases who completed an interview held 236 jobs. A total of 33% of cases were classified as probable occupational TM and 5% as possible occupational TM.

Conclusions

High rates of early mortality and refusals were significant barriers to study participation. Nonetheless, the proportion of probable occupational TMs greatly exceeded the estimated national average, highlighting the need for further study of occupational TM in the state.

Key Words: occupational lung disease, occupation, lung cancer, mesothelioma, asbestos, silica, tumor registry, feasibility, carcinogen, mining,

Introduction

Lung cancer and mesothelioma are the most common thoracic malignancies (TMs). Lung cancer is the second most common cancer in the United States (US) and in New Mexico (NM) and the leading cause of cancer death (1). Mesothelioma is relatively rare but has a specific association with occupational exposure to asbestos. For this paper, lung cancer and pleural mesotheliomas are combined as TMs. Despite some treatment advances (2,3), five-year relative survival is less than 20% for all TM (4).

The strongest risk factor for lung cancer is cigarette smoking (5). Other established risk factors for TMs include exposure to asbestos, uranium, radon gas, and other cancer-causing agents in the workplace, radiation therapy to the lungs, and a family history of lung cancer (6-8). The importance of occupation in TMs is emphasized by the Global Burden of Disease (GBD) report indicating that the two main cancers caused by occupational exposures worldwide were lung cancer (274,000 deaths annually) and mesothelioma (27,000 deaths annually) (9). Various estimates attributing occupation to lung cancer include: a 1981 US estimate of 15% for men and 5% for women, or 10% overall

(10), a 1987 NM estimate of 14% in men (11); and, a 2003 US estimate for deaths of 8.0%-19.2% for men and 2% for females, or 6.3%-13.0% overall (12,13). Thus we estimated that overall in the US, 10%-14% of TMs could be attributable to occupation.

Historic and current occupational exposures are of particular interest in NM. Mining, in particular uranium mining, was a major operation in NM from 1950-1970. Mining is still an important industry in this region: between 2011 and 2015, the NM mining industry saw a 20% increase in employment for all types of mining (14). NM also has significant employment in the Mining, Quarrying, and Oil and Gas Extraction industry relative to other parts of the Southwest (15). These industries have a greater share of local employment in NM than in the US overall (16). Additionally, NM was the ninth highest natural gas producer in the US in 2018, producing 1.49 million cubic feet of natural gas (17).

Given the historic and current extraction activities in NM, we hypothesized that NM would have a higher proportion of occupational TMs than the estimated national average of 10%-14%. As an initial step in estimating this occupational TM

cancer burden in NM, we conducted a feasibility study to obtain adult lifetime occupational histories for TM cases.

Methods

Recruitment and Data Collection

This feasibility study was approved (#16-306) by the Human Research Review Committee at the University of New Mexico and cases provided signed, informed consent. We identified incident TM cases from February 1, 2017 to February 2, 2018 via the population-based New Mexico Tumor Registry (NMTR), a founding member of the National Cancer Institute's (NCI) Surveillance Epidemiology and End Results (SEER) Program. Cases were identified by two methods: (1) rapid case ascertainment (RCA) via electronic pathology reports and (2) usual case ascertainment (UCA) via tumor registrars manually collecting data from around the state. Contact with eligible cases involved a three-step process. In step 1, the NMTR contacted treating physicians explaining the study and advising them of their patient's eligibility allowing the physician to state any objection to patient contact. In step 2, the NMTR contacted the patient (letter and study brochure in English and Spanish) informing them about the study and allowing them to opt-out from further contact. In the special case of no physician of record, patients were contacted after a three month wait period. Patients who refused participation or were deceased were ineligible for study contact. In step 3, for the remainder, contact information was released to study personnel.

All potential cases in step 3 were mailed documents in both English and Spanish including: an introductory letter, a flyer about benefits counseling, a Frequently Asked Questions sheet, two copies of a Residence and Work History worksheet, a Life Events Calendar, showcards, and two copies of the

consent form. One consent form was for the case to sign and keep and the other was signed and returned to the study, along with one copy of the Residence and Work History worksheet. Showcards functioned as a visual aid by listing possible answers to interview questions. The Life Events Calendar functioned as a memory aid to anchor major life events like marriages, births, deaths, relocations, job changes, and other historical events. The Residence and Work History Worksheet gave the cases a time frame to date their paid jobs and occupations, held for at least 6 months, during their adult life and was used for reference during the interview. Work did not have to occur in the state of NM. Study interviewers contacted cases by telephone to answer questions. Those who expressed a willingness to participate were asked to complete and return the worksheets/consent form and to schedule an interview.

Consenting cases completed the same structured telephone interview with an embedded script that obtained information on demographics, lifestyle factors, medical history, reproductive history (women only) and adult lifetime occupational history. For each and every job held for six months or longer from age 18 years onwards, the cases provided job title, city and country of job location, job status (full-time/part-time), job duties, exposure information on relevant agents (18) (a list of more than 30 relevant exposures was provided to cases) including the duration of each exposure, and age at start and end of the job. All cases were asked all job-related questions providing a detailed and specific work history for each individual. Data were recorded in Research Electronic Data Capture (REDCap) database (19). Cases received a small merchandise card in appreciation. All potential cases and surviving family members were given an optional referral to a benefits counselor regardless of their self-reported exposures or

determination by the Data Adjudication Committee (DAC).

Determination of Occupational TM

De-identified occupational history summaries were reviewed by the DAC to determine if each case was attributable to occupational exposures, as summarized below. The DAC was composed of three voting members: a pulmonologist with expertise in occupational pulmonary diseases associated with the coal and uranium mining industries; a preventive medicine specialist with expertise in occupational health who works in the Center for Occupational Environmental Health Promotion; and, an attorney with expertise in the medicolegal definitions for causation in the occupational setting. A non-voting member (CRP) served as the committee Chair to tally votes and mediate further discussion if necessary.

This expert panel independently reviewed the de-identified individual job histories for each case, and considered exposures that had a latency of at least 10 years, exposure durations of at least one year, and exposure intensity through self-reported frequency of exposure on the job. To aid in assessment, each panel member was provided a summary table of the known strength of the association between relevant exposures and TM occurrence (available upon request) (20-27). After independent review, the panel would meet to discuss and vote on classification. If all three DAC members found sufficient evidence for relevant occupational exposure, the case was classified as a probable occupational TM. If at least one DAC member found insufficient evidence for relevant occupational exposure, the case was classified as a possible occupational TM. If all DAC members found insufficient evidence for relevant occupational exposure, the case was classified as non-occupational TM. Smoking history for each case was provided to the DAC, but occupational

cancer was decided independent of smoking, except in the case of asbestos exposure where a synergistic relationship is well supported by the published literature (28). Because of the participant burden and the high likelihood of misclassification, we did not collect information on environmental tobacco smoke or biomass/coal smoke for each job reported in this study. A letter was sent to each case with the DAC's determination.

Analysis

After the determination of occupational TM status by the DAC, each job title for each case was coded to an industry using the NIOSH Industry and Occupation Computerized Coding System (NIOCCS) (29). Each job title was submitted, and using the "Census 2010/NAICS 2007/SOC 2010" coding scheme, the most appropriate 2010 Industry Census Code provided by the industry and occupation output was selected. If the industry was unclear based on the job title alone, the work history was reviewed for the company name, job duties, or other relevant notes. In these situations, once an industry was selected, the industry was independently verified by another study team member. The possible 269 industry categories in the 2010 census system were further summarized into 20 North American Industry Classification System (NAICS) sectors (30).

Results

Of the 400 eligible cases initially identified via the NMTR, 110 (28%) were not released to study personnel for the following reasons: 33 (30%) refused to have their information released to investigators; 47 (43%) were deceased; 23 (21%) had no physician of record and were in the 3-month wait period; four (4%) had an invalid address; two (2%) were subsequently determined to be ineligible, and one case (1%) was determined to have a duplicate record in the NMTR.

The remaining 290 eligible cases were invited to join the study, of which 285 had lung cancer and 5 had mesothelioma. Over-all, refusals (60%) and deaths (18%) were the two major reasons for non-participation in the interview, but cases also had invalid addresses (9%), were unable to be reached by telephone (11%), or were too ill to participate

(3%). Of the 43 cases, 98% agreed to future tumor tissue testing and medical record reviews.

Demographic characteristics of cases are detailed in Table I.

Table I. Demographics of Thoracic Malignancies (TM) cases

Characteristics	Cases, N=43	
Age at diagnosis (years)	N	%
<50	4	9
50-59	2	5
60-69	18	42
≥70	19	44
Sex		
Male	21	49
Female	22	51
Race/ethnicity		
Non-Hispanic white	30	70
Hispanic	9	21
Other/Refused	4	9
Education		
High school or less	10	23
Some college, Bachelor's Degree	23	53
Advanced/Graduate Degree	10	23
Gross household income		
< \$50,000	18	42
\$50,000 - <\$100,000	12	28
>= \$100,000	8	19
Unknown/refused	5	12
Health insurance		
No	2	5
Yes	41	95
Sought compensation/benefits for cancer before study		
No	39	91
Yes	4	9

Among the cases, 51% were women, 70% were Non-Hispanic White, 86% were ≥60 years of age, 19% reported a parent had lung cancer. In terms of insurance and benefits,

95% had some type of health insurance, but only 9% had sought compensation through Social Security Disability, Worker's Compensation, or the Veterans

Administration before the study. Medical Histories of cases are detailed in Table II.

Table II. Medical History of Thoracic Malignancies (TM) cases.

Medical History	Cases, N=43	
	N	%
Ever had a mammogram before cancer diagnosis (women only)		
No	1	5%
Yes	21	95%
Smoked ≥ 100 cigarettes in lifetime?		
No, Never	12	28
Yes, Currently smoke	5	12
Yes, but quit smoking	26	60
Ceremonial smoking in American Indian Ceremonies?		
No	42	98
Yes	1	2
Smoked a pipe regularly?		
No, never	29	67
Yes, but quit smoking	12	28
Don't Know/Missing	2	5
Smokeless tobacco products ≥ 20 times in lifetime?		
No, never	36	84
Yes, currently	1	2
Yes, but quit	3	7
Don't Know/Missing	3	7
E-cigarettes ≥ 20 times in lifetime?		
No, never	30	70
Yes, currently	6	14
Yes, but quit	6	14
Don't know	1	2
BMI (kg/m ²)		
Underweight (<18.5)	1	2
Normal or Healthy Weight (18.5 – 24.9)	21	49
Overweight (25.0 – 29.9)	14	33
Obese (≥ 30)	7	16
First degree family history lung cancer		
Adopted, unknown blood relatives	1	2
No	34	79
Yes	8	19
Father	5	
Mother	3	
Ever diagnosed		
Pulmonary Fibrosis, Yes	2	5
COPD/Emphysema, Yes	11	26
Chronic Bronchitis, Yes	8	19
High Blood Pressure, Yes	19	44
Heart Disease, Yes	4	9

Among the cases, 49% were overweight/obese. Both smoking (72% current/former cigarette smokers) and non-malignant respiratory diseases (40% reporting pulmonary fibrosis, COPD, or chronic bronchitis) were common.

Cases reported 236 jobs representing 20 NAICS sectors, and 14 (33%) were classified as probable and 2 (5%) as possible occupational TM. Among the probable occupational TM cases, 11 (79%) were men, and both the possible occupational TMs

were men. The 14 cases with a probable occupational TM self-reported one or more

of the following occupational exposures: aluminum production (n=1), arsenic (n=1), asbestos (n=7), cadmium (n=1), coal-tar (n=1), diesel (n=7), ether (n=5), nickel (n=2), paint (n=1), radiation (n=1), silica (n=9), and soot (n=2). The joint distribution of these cases by job title and exposure category is shown in Figure 1.

Figure 1. Relevant Self-Reported Exposures by Job Titles per Industry Sector for the Cases with Occupationally Related Thoracic Malignancies *

North American Industry Classification System (NAICS) sector and Job Titles	Relevant self-reported exposures											
	aluminum production	arsenic	asbestos	cadmium	coal-tar	diesel	ether	nickel	paint	radiation	silica	soot
CONSTRUCTION												
Builder/ Construction Coordinator	X		X		X	X	X		X		X	
Carpenter											X	
Carpet Installer			X									
Remodeling Contractor			X									
Plumber			X								X	X
Construction Workers (2)			X			X					X	
EDUCATIONAL SERVICES												
Teachers (2)							X				X	
HEALTHCARE AND SOCIAL ASSISTANCE												
Volunteer Firefighter						X						X
MANUFACTURING												
Tube Bender			X									
Laser Technician											X	
Sawmill Worker						X						
Jeweler			X								X	
MINING, QUARRYING AND GAS AND OIL EXTRACTION												
Mine Manager- Mining Engineer											X	
Oil Refinery Construction						X		X				
PROFESSIONAL, SCIENTIFIC AND TECHNICAL SERVICES												
Nuclear Weapons Specialist - Senior Technician				X						X		
Consultant for coal mining						X					X	
RETAIL TRADE												
Sales Agent							X					
Gas Station Jockey		X					X	X				
Manager for tire company							X					
TRANSPORTATION AND WAREHOUSING												
Truck Drivers (2)						X						

* Exposures deemed to be causal by the Data Adjudication Committee.

The study population only included those who were diagnosed and captured by the NMTR

from February 1, 2017 to February 2, 2018 (n=400). Case identification at the NMTR, especially for cancers like TMs where there

may not be a pathology report, may be ascertained more than a year after diagnosis. A NMTR query in March 2020 for diagnoses in the same time period noted above yielded

more than double the number of TM cases (n=913). Thus we had the opportunity to compare those identified early (n=400) and

up to two years later (n=513) as well as those released to the study for contact (n=290) with those whose names were not released for study contact (n=110) by selected demographic and histological characteristics (Table III).

Table III. Summary of the characteristics of the lung cancer and mesothelioma cases diagnosed between 2/1/17 - 2/2/18 for the OCTOPUS Study. Data source New Mexico Tumor Registry (NMTR).

	Total (n=913)	identified during the study period	
		No (n=513)	Yes (n=400)
Sex			
Male	467 (51)	271 (53)	196 (49)
Female	446 (49)	242 (47)	204 (51)
Age at diagnosis			
<50	23 (3)	10 (2)	13 (3)
50 – 59	107 (12)	50 (10)	57 (14)
60 – 69	266 (29)	139 (27)	127 (32)
70 – 79	311 (34)	182 (35)	129 (32)
80 – 89	181 (20)	112 (22)	69 (17)
90 – 99	25 (3)	20 (4)	5 (1)
Race, ethnicity			
White, non-Hispanic	638 (70)	379 (74)	259 (65)
White, Hispanic	219 (24)	116 (23)	103 (26)
White, unknown ethnicity	4 (<1)	1 (<1)	3 (1)
Black	18 (2)	9 (2)	9 (2)
Native American (technically not eligible)	4 (<1)	0 (0)	4 (1)
Asian	20 (2)	4 (1)	16 (4)
Other & Unknown	10 (1)	4 (1)	6 (2)
Histology			
Non-Small Cell Carcinoma (Adenocarcinomas, Squamous cell carcinomas, Non-small cell carcinomas, Large cell carcinomas)	606 (66)	311 (61)	295 (74)
Small Cell Carcinoma	84 (9)	41 (8)	43 (11)
Other, malignant	205 (22)	151 (29)	54 (14)
Mesothelioma	15 (2)	8 (2)	7 (1)
Adenocarcinoma or carcinoma in situ	3 (<1)	2 (<1)	1 (<1)
Urban/Rural Residence (RUCA)			
Urban (1-3 codes)	590 (65)	284 (55)	306 (77)
Rural (4-10 codes)	320 (35)	227 (44)	93 (23)
Unknown	3 (<1)	2 (<1)	1 (<1)
Vital Status (on 4-2-2020)			
Alive	285 (31)	147 (29)	138 (35)
Dead	628 (69)	366 (71)	262 (65)
AJCC 7 Stage			
I - II	195 (21)	105 (20)	90 (23)
III – IV	416 (46)	224 (44)	192 (48)
Occult, Unknown & Missing	300 (33)	182 (35)	118 (29)
0, in situ	2 (<1)	2 (<1)	0 (0)

There were differences in age between the 400 cases identified during the study period (50% for those 70 years and older) and the 513 cases identified later (57% for those 70 years and older) ($p<0.05$) and rurality between the 400 cases identified during the study period (23% rural) and the 513 cases identified later (44% rural) ($p<0.001$). Apart from the obvious difference in death as this was a criteria for not releasing contact to the study, a difference in histology was noted for those released to the study (77% non-small cell carcinoma) and those not released (66% non-small cell carcinoma) ($p<0.05$).

Discussion

This feasibility study was designed to obtain lifetime occupational histories from a population-based sample of TM cases and to determine the proportion of such cases that were likely attributable to occupational exposures. Despite our efforts to recruit these subjects in a timely manner, high rates of early mortality and refusals were significant barriers to study enrollment, indicating that a definitive study is not possible based on these methods. Among those who participated in the study, the proportion of cases with occupational TM (33%) was two to three times higher than prevailing national estimates (10-14%). While this result is intriguing and may warrant further study, we cannot say with certainty if this result is due to the low response percentage and the possible selection bias of having cases that were more likely to have relevant occupational exposures, or if this result truly reflects the occupational exposures in NM.

Recruiting TM cases via a population-based cancer registry is challenging. In total, 25% of eligible cases died before they could be recruited to the study via the NMTR or study personnel. An even higher proportion refused, 52% of eligible cases, in part due to

poor health as cancer progressed and to the burden of treatment concurrent with study participation. Such a high refusal percentage could be a source of selection bias in which various occupations were under- or over-represented, but we had no data to address this bias directly. Additionally, the study only included those who were diagnosed and captured by the NMTR from February 1, 2017 to February 2, 2018 ($n=400$). We noted a substantial difference in rurality between the 400 cases identified for our study (23% rural) and the 513 cases identified later (44% rural). The majority of counties in NM are rural or frontier (26/33) (31). TM cases diagnosed among residents of these areas are less likely to receive health care in facilities that are served by pathology laboratories with electronic reporting; instead cancer registrars visit the facilities to manually abstract medical records leading to a longer reporting timeline. These results imply that rural TM cases were under-represented in our study, and since those with mining and other extraction occupations are more likely to reside and get health care in rural areas, our estimate of 33% occupational TM might be an underestimate.

From the list of more than 30 possible exposures that are known or suspected carcinogens for lung cancer (32), probable occupational TM cases reported exposures to aluminum production, arsenic, asbestos, cadmium, coal-tar, diesel fumes, ether, nickel, paint, radiation, silica, and soot. Limitations of these results include the difficulty of retrospective estimation of the intensity and duration of each of these exposures at each job, and the fact that the study did not have enough cases to conduct an analysis accounting for other exposures such as tobacco use, comorbidities, and socioeconomic factors (33). Further, we did not have information on exposures to indoor

smoke in the home from, for example, wood burning stoves.

The U.S. does not have a comprehensive employment and exposure database or an occupational disease mortality surveillance system that could provide more objective and comprehensive occupational information than self-report. In some countries, researchers can link data from national cancer registries and occupational databases to help confirm associations between occupational exposures and cancers (34). Inclusion of an occupational history in medical records could also provide more objective data, but such practices are currently sporadic and non-uniform. While death certificates often record a decedent's longest or lifetime occupation, no exposure details are included, and access to this minimal data is often restricted in an effort to maintain confidentiality (35). Thus, improvements to the evaluation of occupation and occupational exposures for cancers such as TMs on a population-basis remains a challenge.

Other strengths of our study not indicated above include: our success in ascertaining a detailed adult lifetime occupational history from lung cancer survivors using an English or Spanish interview; inclusion of racial/ethnic minorities; inclusion of both men and women (with 21% of women in our study having a probable occupational TM); no eligibility restriction to a specific industry or exposure; a rigorous procedure via the DAC to establish a probable-occupational, possible-occupational, or non-occupational classification for each case; and offering cases a referral for benefits counseling (65% accepted). The limitations of this study have been discussed above.

This feasibility study suggests that 33% of cases had a probable occupational TM, two to three times the national historical estimate,

highlighting the importance of exposures and jobs in the NM population that can lead to occupational TMs. However, a more definitive study is not feasible based on the methods used in this study as the ability to overcome the above-described methodological and recruitment challenges remains a significant barrier to further population-based studies of occupation-related TM in NM and the US.

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