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Industry, occupation, and exposure history of mesothelioma patients in the U.S. National Mesothelioma Virtual Bank, 2006–2022

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ABSTRACT

Background: Malignant mesothelioma is associated with environmental and occupational exposure to certain mineral fibers, especially asbestos. This study aims to examine work histories of mesothelioma patients and their survival time.

Method: Using the NIOSH Industry and Occupation Computerized Coding System, we mapped occupations and industries recorded for 748 of 1444 patients in the U.S. National Mesothelioma Virtual Bank (NMVB) during the period 2006–2022. Descriptive and survival analyses were conducted.

Results: Among the 1023 industries recorded for those having mesothelioma, the most frequent cases were found for those in manufacturing (n = 225, 22.0%), construction (138, 13.5%), and education services (66, 6.5%); among the 924 occupation records, the most frequent cases were found for those in construction and extraction (174, 18.8%), production (145, 15.7%), and management (84, 9.1%). Males (583) or persons aged >40 years (658) at the time of diagnosis tended to have worked in industries traditionally associated with mesothelioma (e.g., construction), while females (163) or persons aged 20–40 years (27) tended to have worked in industries not traditionally associated with mesothelioma (e.g., health care). Asbestos, unknown substances, and chemical solvents were the most frequently reported exposure, with females most often reporting an unknown substance. A multi-variable Cox Hazard Regression analysis showed that significant prognostic factors associated with decreased survival in mesothelioma cases are sex (male) and work experience in utility-related industry, while factor associated with increased survival are epithelial or epithelioid histological type, prior history of surgery and immunotherapy, and industry experience in accommodation and food services.

Conclusion: The NMVB has the potential of serving as a sentinel surveillance mechanism for identifying industries and occupations not traditionally associated with mesothelioma. Results indicate the importance of considering all potential sources of asbestos exposures including occupational, environmental, and extra-occupational exposures when evaluating mesothelioma patients and advising family members.

1. Introduction

Mesothelioma is a mesothelial derived cancer arising in the lining tissue of the pleural and peritoneal surfaces. Pleural mesothelioma is the most common form of mesothelioma, accounting for 65–70% of reported cases, while peritoneal mesothelioma accounts for 30% (van Gerwen et al., 2020). Histologically, epithelial, sarcomatoid, and biphasic are the three identifiable subtypes of malignant mesothelioma. The median survival time is around 9 months from the time of diagnosis (van Kooten et al., 2022).

Inhalation of asbestos fibers is the leading cause of mesothelioma (Oberdörster and Graham, 2018; Sekido, 2013). Asbestos fibers are composed of silicate minerals, including the serpentine mineral chrysotile, the amphibole minerals actinolite, amosite, anthophyllite, crocidolite, and tremolite (Sekido, 2013). Other mineral fibers with morphologic characteristics similar to asbestos fibers (e.g., erionite,

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Caledonian antigorite, fluoro-edenite) can also induce mesothelioma (Roggli, 2018). Asbestos and related mineral fibers directly interfere with the cell spindle during human mesothelial cell division, leading to mutations and increased pathogenicity (Sekido, 2013). DeBono et al. (2021) concluded the average latency time between exposure to harmful substances and mesothelioma occurrence is 40 years, and Spinazzè et al. (2022) found a 50-year average latency among 24–94 years old patients. Workers exposed to asbestos fibers are at increased risk for mesothelioma and asbestosis (DeBono et al., 2021).

Multiple studies have analyzed mesothelioma patients' employment history. For example, the Canadian Occupational Disease Surveillance System (DeBono et al., 2021) found that employment in asbestos mines, primary metal industries, boiler and plate works, non-metallic mineral products industries, chemical and chemical product industries, general and special-trade contract construction, and the electric power, gas, and water utility industries is strongly associated with an elevated rate of mesothelioma. Using data from one of the 21 Regional Mesothelioma Operational Centers in Italy, Mangone et al. (2021) found that the most recorded exposure to asbestos was for those employed in construction, railways, refineries, and cement industries. An incidence analysis among European countries (Hemminki et al., 2021) using the NORDCAN database (cancer statistics for Nordic countries) reported a high mesothelioma incidence rate among older patients and projected it to the peak period of asbestos use in industry (1960–1975). Locher et al. (2022) conducted a work history analysis of mesothelioma patients in Switzerland by using Silag, Swiss National Cohort, and National Institute for Cancer Epidemiology and Registration databases, and found that mechanical/electrical/precision engineering, wood processing, railway work, construction, and metal processing were the main industries associated with mesothelioma. A Korean study of an employment insurance database (Kim, 2021) identified the longest ever-worked industries and reported that manufacturing was the industry most commonly associated with mesothelioma. A U.S. mesothelioma mortality analysis (Mazurek et al., 2017) showed that the industries of ship and boat building, petroleum refining, and miscellaneous chemicals production industries had the highest proportionate mortality ratio. Although these studies vary in data resources and populations, they identified similar groups of high-risk industries, which also align well with our understanding of traditional workplace exposure to asbestos and other miscellaneous chemicals (e.g., crocidolite, amosite, and chrysotile) in relation to mesothelioma occurrence.

Findings related to patients' occupation histories are available in addition to findings about mesothelioma patients' industry histories. For example, DeBono et al. (2021) estimated high rates of mesothelioma for certain occupations in construction: forepersons, carpenters, brick and stone masons, plasterers, painters, insulators, and pipefitters. Strong positive associations of a mesothelioma diagnosis with the occupations of managers and administrators, metal machining forepersons, welders and flame cutters, boilermakers and structural metalworkers, and mechanics and repairs were also found (DeBono et al., 2021). A statistical analysis by Rezvani et al. (2020), which included sex, age, occupation, living geolocation, mesothelioma diagnosis time, smoking history, and family mesothelioma history, showed significant association between mesothelioma and occupations for housekeepers and oil company workers. A U.S. mesothelioma mortality analysis (Mazurek et al., 2017) found that insulation workers, chemical technicians, and pipelayers, plumbers, pipefitters, and steamfitters had the highest proportionate mortality ratios. Lastly, a UK-national study (Senek et al., 2022) identified builders, electricians, carpenters, laggers (insulation installers) and plumbers as occupations directly exposed to handling asbestos, while other occupations such as teachers, doctors, nurses, and administrative staff had indirect exposure from contaminated work environments.

Biological sex is the most common variable taken into consideration when comparing different kinds of exposure, given common differential distributions across occupations between genders. An Italian PRIMATE study (Spinazzè et al., 2022) reported that women are more likely to be exposed to para-occupational, home-related, environmental asbestos than men, while men are more likely to be associated with direct occupational exposure to asbestos. A small sample of semi-structured interviews showed that none of the female mesothelioma patients had worked in traditional high-risk asbestos-related industries (Ejegi-Memeh et al., 2021). A U.K. study (Senek et al., 2022) showed gender differences in reported exposure to asbestos: 76.4% of males and 28.9% of females reported work exposure; 18.6% of females and 3.9% of males reported indirect exposure history through their partners (e.g., doing their partner's laundry). A Korean study (Kim, 2021) showed that male mesothelioma patients predominated in the industries of construction, transportation, and warehousing, while female patients predominated in the health and welfare business and food and lodging business. A U.S. mesothelioma mortality analysis focusing on women (Mazurek et al., 2022) reported that healthcare and social assistance, education services, and manufacturing were the top three industries with the most death from mesothelioma; homemakers, elementary and middle school teachers, and registered nurses were the top three occupations with most mesothelioma deaths among women. According to Lombardy and Piedmont malignant mesothelioma registries, the construction industry was the most common industry among male patients, while the production of textiles and cloths ranked first among female patients (Consonni et al., 2019).

Though, as shown, existing studies have discussed the prevalent industries and occupations of mesothelioma patients, and the sex-differentiated exposure, but few have covered lifetime work history, age group difference, associated patients' clinical history (e.g., treatment), or have discussed the survival status among mesothelioma patients. These knowledge gaps are addressed in this report.

Since 2006, the National Mesothelioma Virtual Bank (NMVB) has been collecting U.S. mesothelioma patients' industry, occupation, and exposure history, which can be a valuable resource for observation studies about high-risk industries and jobs that may put workers at risk for mesothelioma (Cummings et al., 2020). With NMVB data, Amin et al. (2018) has analyzed demographic and clinical factors influencing mesothelioma patients' survival, but that study did not consider occupational exposure as a potential factor. In this paper, our study aims to standardize NMVB patients' work history information, describe the natural history of patient cohorts' occupations, and compare the work history differences between males and females. Combining work history information with the demographic information, exposure history, and treatment, we conducted a survival analysis to explore the research question: Is a particular patient's industry group a risk factor impacting mesothelioma patients' survival time?

2. Materials and methods

The NMVB's records of patients' self-reported work histories in a free-text format were used as the data source for this study. NMVB data collection and research have been approved by the University of Pittsburgh Institutional Review Board: National Mesothelioma Virtual Bank for Translational Research (CR19110265-009). The NMVB Health Assessment Questionnaire work history and exposure section is available in Appendix 1. There are free-text questions like working history with duties and dates (Question 16 b), and multiple-choice questions such as exposure history (Question 17) "Have you ever regularly worked with, or been exposed to, any of the following for greater than a 6 months time period? (Please circle one)." Patients can report multiple records on their work history and exposure history. The NMVB database is available on its website by applying for access through the "How to Apply for Biospecimens and Data" (National Mesothelioma Virtual Bank,).

Since 2006, the NMVB has collected data from 6 institutions for 1444 mesothelioma patients (by January 25, 2022), including malignant, benign, consult only, and slide review only mesothelioma. Among them,

748 patients reported 1091 work history records (Fig. 1), as patients may report multiple job instances: 1 patient reported 7 jobs, 2 patients 5 jobs, 10 patients 4 jobs, 28 patients 3 jobs, 103 patients 2 jobs, and 499 patients 1 job.

To map these free-text records to standard codes, we used the NIOSH Industry and Occupation Computerized Coding System (NIOCCS) Version 4 (https://csams.cdc.gov/nioccs). NIOCCS is an industry and occupation auto-coder built on machine learning methods. For each free-text description of work history, the output of the NIOCCS auto-coder is a North American Industry Classification System (NAICS) code (2012) and a Standard Occupational Classification (SOC) code (2010) for industry and occupation history record, respectively (NAICS Association, 2022; U.S. Bureau of Labor Statistics, 2010). Among the 1091 work history records (industry title and occupation title), 1023 records have been assigned NAICS codes and 924 have been assigned SOC codes (Fig. 1), namely 826 records have been assigned both NAICS and SOC codes.

We examined the distributions of sex, race, ethnicity, age, exposures (not workplace specific), and years from first positive mesothelioma tissue diagnosis to last contact or death. After the NAICS (Appendix 2) and SOC (Appendix 3) sectors grouping (first two digits) (NAICS Association, 2022; U.S. Bureau of Labor Statistics, 2010), we summarized the 10 most frequent industries and occupations, with major sub-groups based on the first three digits of the code. The NMVB database also includes patients' self-reported asbestos exposure for more than 6 months. Although the question (Question 17) does not explicitly distinguish work-related asbestos exposure with non-work-related exposure, most noticeable asbestos exposures (by patients) should be job-related as patients were less likely to aware about a long-time asbestos exposure from other contact rather than from their work. We conducted a prevalence ratio (Equation (1)) analysis focusing on asbestos and industries was conducted in order to study their correlations.

$$Prevelance\ Ratio\ for\ industry\ A = \frac{No.\ patients\ (asbestos\ exposed\ \&\ industry\ A)}{No.\ patients\ (industry\ A\ )} \div \frac{No.\ patients\ (asbestos\ exposed\ \&\ not\ industry\ A)}{No.\ patients\ (not\ industry\ A\ )}$$

Equation 1

Patients without a recorded survival time (years from initial positive diagnosis to last contact/death) or vital status were excluded from survival analysis (referred to as "unselected group"). First, we applied a Chi-square test to identify various demographic differences between the selected and unselected groups (the latter being those in the database but not in survival analysis). Then, for survival analysis, we created dummy variables for the (1) industries, (2) exposure, and (3) therapy history reported by each patient. Survival analysis was conducted in R version 4.1.3 (2022). We conducted Kaplan Meier (KM) analysis and univariable Cox Proportional-Hazard (PH) regression for each variable, and multi-variable Cox PH regression for different industry categories while considering demographic factors, histological type, anatomic site, and treatment. We did not include occupation in the survival analysis, because occupation could be highly correlated to industry and using the combination of industry and occupation as a category would need a much larger sample size.

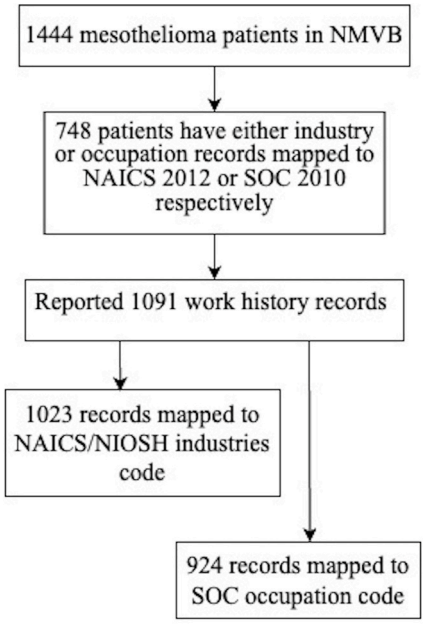

Fig. 1. Data introduction and case inclusion criteria.

3. Results

We firstly report basic statistics of demographic factors, survival time, and substance exposure. Then, we summarize patients' work experience, with subgroup analysis on sex and age groups. Finally, we present results of the univariable and multivariable survival analyses.

3.1. Statistics of demographic factors, survival time, and substance exposure

The summary of patients' backgrounds is shown in Table 1. Most patients are male (78.2%), white (96.0%), or Non-Spanish Non-Hispanic (97.2%), and 64.2% of the patients are in the 61–80 years age group. Our data show that most patients died or were lost to contact within 3 years after the first positive diagnosis of mesothelioma. The top three

Table 1
Summary of patients' demographic information, survival time, and substance exposure (N = 748)[c].

Characteristics	#	%	Characteristics	#	%
Mesothelioma Case			Age Group		
with Available Work History Record	748	51.8%	21–30	12	1.8%
Total	1444		31–40	15	2.2%
Race			41–50	47	6.9%
White	699	96.0%	51–60	117	17.1%
Black	14	1.9%	61–70	248	36.2%
Other	9	1.2%	71–80	192	28.0%
Asian	6	0.8%	81+	54	7.9%
Total[a]	728		Total[a]	685	
Sex			Exposure Substance[b]		
Male	583	78.2%	Asbestos	464	62.0%
Female	163	21.9%	Chemical Solvents	60	8.0%
Total[a]	746		Metal Work	38	5.1%
Ethnicity			Paint	35	4.7%
Non-Spanish Non-Hispanic	724	97.2%	Petroleum	29	3.9%
Hispanic or Latino	21	2.8%	Woodworking	26	3.5%
Total[a]	745		Rubber	15	2.0%
Years from First Positive Mesothelioma			Printing	8	1.1%
Diagnosis to Last Contact or Death			Leather	8	1.1%
<1 year	290	42.5%	Textiles	5	0.7%
1–3 years	228	33.4%	Mining	5	0.7%
3–5 years	74	10.9%	Total number of patients	748	
5–10 years	78	11.4%			
10–20 years	12	1.8%			
Total[a]	682				

[a] Characteristics where numbers do not add up to 748 resulted from missing data for some patients.
[b] Unknown specific substance associated with job duty categories, including metal work, woodworking, printing, and mining.
[c] Categories with frequency less than 5 are not reported here.

known most reported exposure substances are asbestos (62.0%), chemical solvents (8.0%), and metal particles (5.1%). One patient may report more than one exposure substance.

3.2. Statistics of industry and occupation

The top three industries most frequently reported by mesothelioma patients were 1) manufacturing, 2) construction, and 3) education services; the top three most frequently reported occupations were 1) construction and extraction, 2) production, and 3) management (Table 2). The complete list of reported industries and occupations are available in Appendices 4 and 5. Further sub-sector analysis was done based on the first three digits of the NAICS code (major subsectors were presented, selecting from the 3 most major sub-sectors, and discarding the small numbers). Within the manufacturing sector, the major sub-sector was primary metal manufacturing (n = 63, 8.4%). Within the construction sector, the major sub-sector was specialty trade contractors (n = 54, 7.2%). Within the educational services sector, the educational services subsector (n = 66.8.8%) was the only three-digit subgroup. The most frequent occupations in the sub-industries are available in Appendix 6. Occupations reported under each of the top-three industries are distinct across industries (Appendix 7). The top occupation under each industry also accounts for a major part of the corresponding SOC occupation summary.

Considering potential latency impact, we only include jobs that have been started at least 20 years before a mesothelioma diagnosis (Appendix 8). The top five industries were: 1) manufacturing (n = 76; primary metal manufacturing: n = 22; transportation equipment manufacturing: n = 16; chemical manufacturing: n = 10). 2) retail trade (n = 21; motor vehicle and parts dealers: n = 5). 3) construction (n = 18; Specialty Trade Contractors: n = 5). 4) military (n = 12; U.S. navy: n = 8). 5) utilities (n = 11). Frequency of industries and occupations for jobs that have 40-year latency is available in Appendix 9.

Age-group analysis (Table 3) on patients' industry shows that patients 21–40 years old are more likely to work in industries not traditionally associated with mesothelioma risk. As the age of patients rises above 40 years, their reported industries are similar to the top industries listed in Table 2.

Industries and exposures reported by mesothelioma patients by sex are show in Fig. 2. The top three industries for males are manufacturing (n = 201), construction (n = 136) and military (n = 58); for females, the top three industries are educational services (n = 32), health care and social assistance (n = 30), and manufacturing (n = 24). Exposure to asbestos, unknown substances and chemical solvents are the top three exposures in both groups, but interestingly, females reported exposure to unknown substances the most.

Table 4 shows the prevalence ratio of asbestos exposure by industry. Patients who reported work experience in the industries of utilities, construction, manufacturing, administrative and support and waste management and remediation services, public administration, and military have a higher possibility for asbestos exposure. The industries of educational services, healthcare and social assistance, and professional, scientific, and technical services present a lower prevalence of asbestos exposure. A Fisher's test analysis determining the correlation between industry and all exposures is presented in Appendix 10. The most frequent 10 industries and occupations reported along with asbestos are shown in Appendix 11.

3.3. Results of survival analysis

Survival analysis was conducted for 693 patients (out of 748 patients with either industry or occupation records) who had survival time and vital status information. Chi-square analysis results among the 1444 patients with a comparison of the demographic variables between selected (n = 693) and unselected (n = 751) groups are available in Appendix 12; these show that only ethnicity and histological type are

Table 2
Most common (top 10) industries (NAICS, 2012) and occupations (SOC, 2010) of 748 mesothelioma patients.[a]

Sector	Subsector	Number (%)	Female	Male
NAICS Sector	**Most Frequent NAICS Subsector**			
31–33 Manufacturing		225 (30.1%)	24	201
	331 Primary Metal Manufacturing	63 (8.4%)	3	60
	336 Transportation Equipment Manufacturing	51 (6.8%)	5	46
23 Construction		138 (18.5%)	1	136
	238 Specialty Trade Contractors	54 (7.2%)	0	54
61 Educational Services		66 (8.8%)	32	34
	611 Educational Services	66 (8.8%)	32	34
62 Health Care and Social Assistance		65 (8.7%)	30	35
	621 Ambulatory Health Care Services	30 (4.0%)	9	21
	622 Hospital	22 (2.9%)	11	11
54 Professional, Scientific, and Technical Services		64 (8.6%)	16	47
	541 Professional, Scientific, and Technical Services	64 (8.6%)	16	47
96–97 Military		59 (7.9%)	1	58
	969 U.S. Navy	40 (5.4%)	1	39
92 Public Administration		59 (7.9%)	5	54
	922 Justice, Public Order, and Safety Activities	23 (3.1%)	1	22
81 Other Services (except Public Administration)		59 (7.9%)	19	40
	811 Retail and Maintenance	38 (5.1%)	5	33
48–49 Transportation and Warehousing		53 (7.1%)	3	50
	484 Truck Transportation	17 (2.3%)	0	17
	482 Rail Transportation	10 (1.3%)	0	10
	488 Support Activities for Transportation	10 (1.3%)	0	10
44–45 Retail Trade		48 (6.4%)	21	27
	441 Motor Vehicle and Parts Dealers	10 (1.3%)	3	7
	445 Food and Beverage Stores	9 (1.2%)	6	3
SOC Sector	**Most frequent SOC Subsector**			
47 Construction and Extraction Occupations		174 (23.3%)	3	170
	47-2 Construction Trades Workers	152 (20.3%)	2	149
51 Production Occupations		145 (19.4%)	21	124
	51-9 Other Production Occupations	56 (7.5%)	10	46
	51-4 Metal Workers and Plastic Workers	38 (5.1%)	2	36
11 Management Occupations		84 (11.2%)	18	66
		57 (7.6%)	16	41

(continued on next page)

Table 2 (*continued*)

Sector	Subsector	Number (%)	Female	Male
	11-9 Other Management Occupations			
	11-1 Top Executives	13 (1.7%)	1	12
49 Installation, Maintenance, and Repair Occupations		67 (9.0%)	2	65
	49-3 Vehicle and Mobile Equipment Mechanics, Installers	30 (4.0%)	0	30
	49-9 Other Installation, Maintenance, and Repair Occupations	30 (4.0%)	1	29
53 Transportation and Material Moving Occupations		66 (8.8%)	8	58
	53-7 Material Moving Workers	29 (3.9%)	5	24
	53-3 Motor Vehicle Operators	26 (3.5%)	2	24
43 Office and Administrative Support Occupations		54 (7.2%)	39	15
	43-9 Other Office and Administrative Support Occupations	14 (1.9%)	11	3
	43-5 Material Recording, Scheduling, Dispatching, and Distributing Workers	12 (1.6%)	4	8
	43-6 Secretaries and Administrative Assistants	12 (1.6%)	11	1
25 Educational Instruction and Library Occupations		47 (6.3%)	23	24
	25-2 Special Education Teachers	30 (4.0%)	17	13
41 Sales and Related Occupations		41 (5.5%)	15	26
	41-2 Retail Sales Workers	15 (2.0%)	6	9
	41-1 Supervisors of Sales Workers	10 (1.3%)	4	6
17 Architecture and Engineering Occupations		39 (5.2%)	1	38
	17-2 Engineers	31 (4.1%)	1	30
29 Healthcare Practitioners and Technical Occupations		36 (4.8%)	11	25
	29-1 Healthcare Diagnosing or Treating Practitioners	26 (3.5%)	6	20
	29-2 Health Technologists and Technicians	10 (1.3%)	5	5

[a] Count represents all jobs reported by the 748 mesothelioma patients. If one patient works at 3 different jobs, then the patient would be counted 3 times.

not significantly different between the two groups.

3.3.1. *Univariable Cox Hazard Regression*

Table 5 shows the results of a univariable Cox Hazard Regression analysis. Predictors of lower survival probability among mesothelioma patients are the following: age greater than 50, male, anatomic site of pleura, therapy history of talc pleurodesis, industry experience in construction, and exposure history to asbestos. In contrast, predictors of higher survival probability include histological type of epithelial or epithelioid, prior therapy with chemotherapy, surgery and immunotherapy, and industry experience in retail trade, health care and social assistance, and accommodation and food services.

Table 3
Top 10 industries in age ranges.

Industry	No.	Industry	No.
Age group (21–30)		**Age group (31–40)**	
Health Care and Social Assistance	4	Health Care and Social Assistance	5
Educational Services	2	Manufacturing	4
Accommodation and Food Services	1	Educational Services	3
Finance and Insurance	1	Public Administration	2
Other Services (except Public Administration)	1	Military	2
		Mining, Quarrying, and Oil and Gas Extraction	1
		Accommodation and Food Services	1
		Agriculture, Forestry, Fishing and Hunting	1
		Finance and Insurance	1
		Information	1
Age group (41–50)		**Age group (51–60)**	
Health Care and Social Assistance	12	Manufacturing	32
Manufacturing	10	Construction	20
Retail Trade	10	Other Services (except Public Administration)	16
Other Services (except Public Administration)	7	Professional, Scientific, and Technical Services	15
Transportation and Warehousing	5	Educational Services	11
Construction	5	Health Care and Social Assistance	11
Accommodation and Food Services	4	Retail Trade	10
Professional, Scientific, and Technical Services	3	Public Administration	10
Educational Services	3	Transportation and Warehousing	8
Finance and Insurance	3	Administrative and Support and Waste Management and Remediation Services	6
Age group (61–70)		**Age group (71–80)**	
Manufacturing	77	Manufacturing	71
Construction	45	Construction	47
Military	30	Transportation and Warehousing	19
Health Care and Social Assistance	24	Educational Services	18
Educational Services	23	Public Administration	15
Public Administration	21	Military	13
Retail Trade	20	Professional, Scientific, and Technical Services	12
Professional, Scientific, and Technical Services	20	Other Services (except Public Administration)	10
Other Services (except Public Administration)	18	Finance and Insurance	7
Transportation and Warehousing	15	Health Care and Social Assistance	7
Age group (81+)			
Manufacturing	18		
Construction	11		
Military	7		
Professional, Scientific, and Technical Services	6		
Educational Services	4		
Transportation and Warehousing	3		
Administrative and Support and Waste Management and Remediation Services	2		
Other Services (except Public Administration)	2		
Mining, Quarrying, and Oil and Gas Extraction	2		
Public Administration	2		

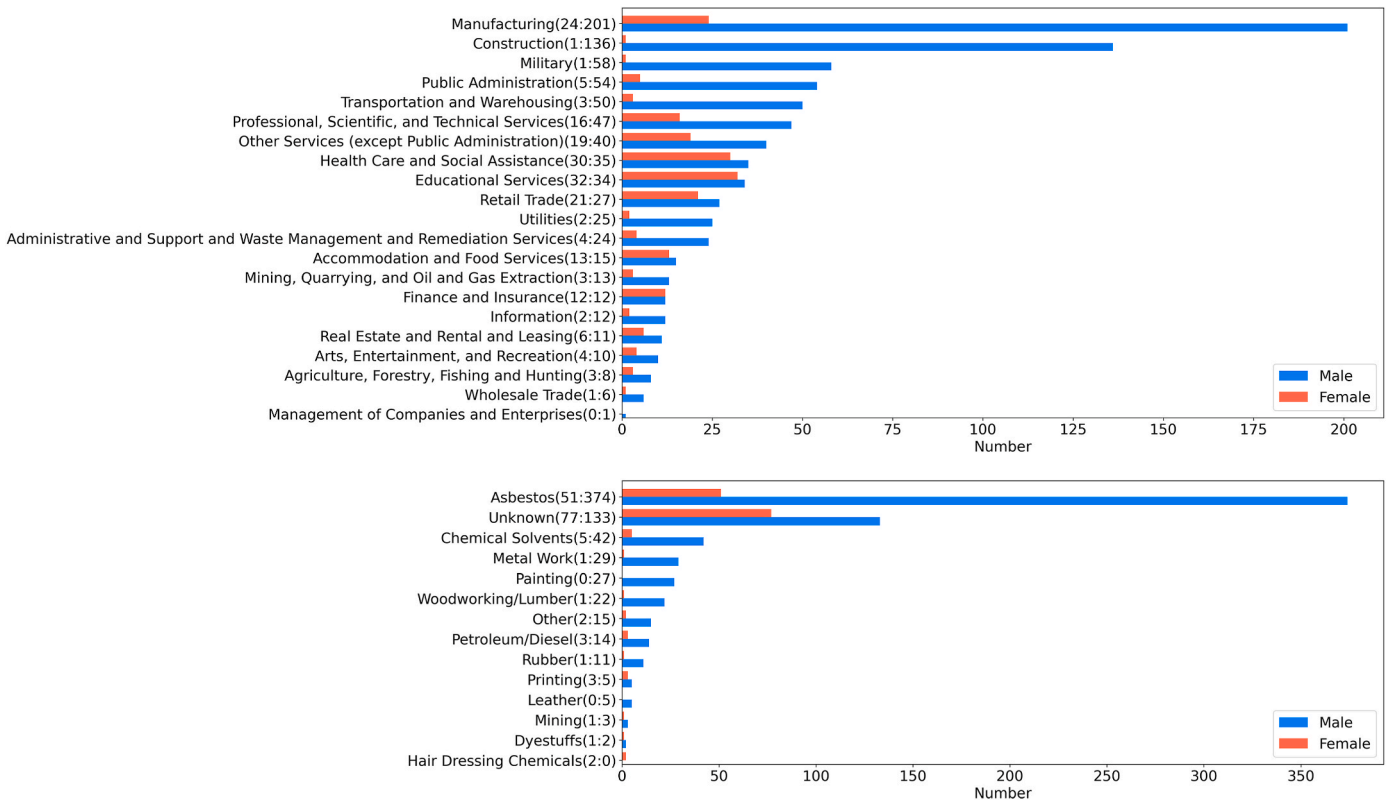

Fig. 2. Reported industries (upper) and exposure (lower) by sex (Female: Male).

Table 4
Prevalence ratio of asbestos exposure, by industry.

Industry	Asbestos Exposure	
	Prevalence Ratio (95% CI)	P-value
Agriculture, Forestry, Fishing and Hunting	0.88 (0.51–1.51)	0.650
Mining, Quarrying, and Oil and Gas Extraction	0.91 (0.59–1,40)	0.666
Utilities	**1.46 (1.26–1,69)**	**<0.001**
Construction	**1.46 (1.32–1.61)**	**<0.001**
Manufacturing	**1.33 (1.20–1.48)**	**<0.001**
Wholesale Trade	0.92 (0.48–1.75)	0.813
Retail Trade	0.97 (0.77–1.23)	0.827
Transportation and Warehousing	1.17 (0.98–1.40)	0.086
Information	1.16 (0.83–1.62)	0.409
Finance and Insurance	0.73 (0.47–1.14)	0.165
Real Estate and Rental and Leasing	0.85 (0.54–1.34)	0.492
Professional, Scientific, and Technical Services	**0.69 (0.52–0.91)**	**0.009**
Administrative and Support and Waste Management and Remediation Services	**1.40 (1.20–1.65)**	**<0.001**
Educational Services	**0.64 (0.48–0.86)**	**0.003**
Health Care and Social Assistance	**0.60 (0.44–0.82)**	**0.001**
Arts, Entertainment, and Recreation	1.16 (0.83–1.63)	0.391
Accommodation and Food Services	0.68 (0.44–1.05)	0.083
Other Services (except Public Administration)	1.16 (0.98–1.38)	0.088
Public Administration	**1.19 (1.01–1.41)**	**0.038**
Military	**1.47 (1.32–1.65)**	**<0.001**

3.3.2. *Univariable Kaplan Meier analysis*

Appendix 13 shows the non-parametric univariable Kaplan Meier analysis and log rank tests (only presents significant result, p-value<0.05). Overall, patients in the 21–30 and 31–40 age groups have a higher survival probability than older patients; females have a higher survival probability than males; and race and ethnicity are not significant enough to see a trend ($p > 0.05$). Patients who have recorded peritoneum as the anatomic site of their lesion have a higher survival rate than those whose lesion was in the pleura. Patients who recorded epithelial or epithelioid as the histological type of their mesotheliomas have a higher survival rate than those who reported having biphasic and sarcomatoid mesotheliomas. When it comes to therapies, patients who have undergone chemotherapy, immunotherapy, or surgery have a higher survival probability than those who have not, while patients who have had talc pleurodesis as therapy present a lower survival probability than those who have not. Within each industry, the patients working in accommodation and food services, health care and social assistance, and the retail trade have a higher survival probability than those who did not. Patients reporting having worked in the construction industry had a lower survival probability than patients did not. In the category of exposure to substance, patients exposed to asbestos have a lower survival probability than those who did not.

3.3.3. *Multi-variable Cox Hazard Regression*

With demographic variables (i.e., sex, age, race, ethnicity), mesothelioma histological type, anatomic site, treatment, and industry experience, we further conducted a multi-variable Cox HR analysis (Fig. 3). Results show that significant prognostic factors associated with decreased survival in mesothelioma cases in this NMVB cohort are sex (male) and work experience in utility-related industry (NAICS 22). The significant prognostic factor associated with increased survival are epithelial or epithelioid histological type, prior history of surgery and immunotherapy, accommodation and food services (NAICS 72), or industry experience in wholesale trade (NAICS 42). Note that the wholesale trade has only 7 instances, the finding about it may not be stable.

4. Discussion

Asbestos' applications, like fireproofing and insulation, made it important to the industries of construction, manufacturing, power plants, chemical products, and even the U.S. military (Frank, 2006). The use of asbestos increased in the latter 19th century, especially in commercial settings, and came to its peak in 1975 worldwide (Ejegi-Memeh

Table 5
Univariable cox proportional-hazard regression analysis.

Variable	Hazard Ratio	95% confidence interval	p-value for trend[a]
Age Range (n=641)			
21–30	1	REF	
31–40	0.62	0.19–2.03	0.4
41–50	1.96	0.82–4.68	0.13
51–60	2.49	1.09–5.68	**0.031**
61–70	3.48	1.54–7.87	**0.003**
71–80	4.65	2.05–10.6	**<0.001**
81+	7.45	3.16–17.5	**<0.001**
Sex (n=691)			
Female (n = 148)	1.00	REF	REF
Male (n = 543)	1.94	1.555–2.426	**<0.001**
Ethnicity (n=654)			
Hispanic or Latino (n = 17)	1.00	REF	REF
Non-Spanish Non-Hispanic (n = 637)	1.37	0.7528–2.488	0.304
Race (n=678)			
Asian (n = 5)	1.00	REF	REF
Black (n = 12)	0.80	0.2347–2.740	0.725
Other (n = 8)	0.99	0.2669–3.706	0.993
White (n = 653)	1.73	0.6471–4.639	0.274
Histological Type (n=534)			
Biphasic (n = 88)	1.00	REF	REF
Epithelial or epithelioid (n = 409)	0.41	0.3220–0.5293	**<0.001**
Sarcomatoid (n = 37)	1.06	0.7117–1.5676	0.786
Anatomic Site (n=337)			
Peritoneum (n = 44)	1.00	REF	REF
Pleura (n = 293)	2.44	1.658–3.582	**<0.001**
Therapy (therapy itself =0 is the REF) (n=693)			
Chemotherapy (458: 235)	0.64	0.5356–0.761	**<0.001**
Surgery (477: 216)	0.55	0.463–0.6641	**<0.001**
Radiation therapy (136: 557)	0.92	0.7486–1.128	0.418
Immunotherapy (49: 644)	0.47	0.3183–0.6819	**<0.001**
Photodynamic (76: 617)	0.92	0.709–1.192	0.526
Talc Pleurodesis (23: 670)	1.70	1.106–2.6	**0.01**
Exposure (exposure itself =0 is the REF) (n=693)			
Asbestos (426: 267)	1.50	1.236–1.76	**<0.001**
Unknown (97: 596)	0.88	0.6867–1.122	0.298
Chemical Solvents (47: 646)	1.10	0.7824–1.513	0.616
Woodworking (23: 670)	0.78	0.4586–1.326	0.358
Rubber (12: 681)	0.78	0.4044–1.511	0.464
Leather (5: 688)	1.10	0.3447–3.34	0.903
Petroleum (17: 676)	0.69	0.3686–1.288	0.243
Painting (27: 666)	1.30	0.8275–1.984	0.267
Metal Work (30: 663)	1.20	0.8304–1.856	0.292
Printing (8: 685)	0.55	0.2267–1.323	0.181
Industry (industry itself=0 is the REF for each) (n=693)			
Format: Industry (n1:n0) (n1 = YES, n0 = NO)			
Agriculture, Forestry, Fishing and Hunting (9: 684)	0.66	0.3114–1.384	0.269
Mining, Quarrying, and Oil and Gas Extraction (15: 678)	1.00	0.5845–1.839	0.902
Utilities (24: 669)	1.10	0.6431–1.74	0.825
Construction (113: 580)	1.30	1.042–1.606	**0.020**
Manufacturing (188: 505)	1.20	0.992–1.431	0.061
Wholesale Trade (7: 686)	0.34	0.1107–1.071	0.066
Retail Trade (40: 653)	0.57	0.3816–0.8659	**0.008**
Transportation and Warehousing (46: 647)	1.00	0.7429–1.437	0.847
Information (14: 679)	0.86	0.4729–1.562	0.619
Finance and Insurance (20: 673)	0.67	0.3915–1.132	0.133
Real Estate and Rental and Leasing (12: 681)	0.74	0.3819–1.427	0.367
Professional, Scientific, and Technical Services (53: 640)	0.75	0.5406–1.03	0.075
Administrative and Support and Waste Management and Remediation Services (23: 670)	0.99	0.6116–1.608	0.973
Educational Services (57: 636)	1.00	0.7348–1.37	0.984
Health Care and Social Assistance (55: 638)	0.55	0.3945–0.7718	**<0.001**
Arts, Entertainment, and Recreation (10: 683)	0.69	0.3282–1.46	0.334
Accommodation and Food Services (24: 669)	0.58	0.3465–0.9732	**0.039**
Other Services (except Public Administration) (48: 645)	0.81	0.5662–1.157	0.246
Public Administration (52: 641)	1.10	0.7723–1.495	0.670
Military (54: 639)	1.00	0.7532–1.425	0.828

(Categories with less than 5 records are not included in the table. REF is the reference group.)

[a] *p*-value has not been adjusted here. Each patient was compared multiple times for the industry, therapy, and exposure; therefore, type I error may increase.

et al., 2021; Frank, 2006). In the U.S., per capita asbestos consumption came to a peak in 1951, and then decreased gradually until a sharp decrease after 1973 (dos Santos Antao et al., 2009). In our study, most of mesothelioma patients were aged 61–80 years, namely those born in the 1940s–1960s, who started their career life around the asbestos peak consumption period. The industries and occupations reported by mesothelioma patients, including manufacturing, construction, and the military, had large demands for asbestos in the past. Our study shows that patients aged older than 80 and those aged 41–60 reported similar industries, while the younger patients (aged 21–40) have reported industries not traditionally associated with high asbestos demand, for example, healthcare and accommodation.

By 2010, most countries had banned asbestos in all its forms, but due to the past use of asbestos-containing construction materials, it is still present in some buildings and structures (Rezvani et al., 2020). The work of removal or remediation of such material includes the risk of exposure to asbestos (DeBono et al., 2021). Workers employed in non-direct asbestos-using industries, like educational services, might be exposed to asbestos present in their workplaces. People who work without direct use of asbestos can be described as “bystanders” as they are within an asbestos-containing environment (Spinazzè et al., 2022), and they are likely to under report their exposure to asbestos (Rezvani et al., 2020). A regional survey from Italy (Mangone et al., 2021) found that such environmental exposure is the second most likely exposure of asbestos, right after occupational exposure. Thus, the bystander exposure can contribute to our study findings among female subjects: education was the top industry for women.

Extra-occupational exposure consists of familial exposure (e.g., from a cohabitant’s contaminated clothes) and domestic exposure (e.g., repair or removal of asbestos-containing materials in own house) (Spinazzè et al., 2022). Our study suggests that females may experience more extra-occupational exposure than males. From our summary among all examined patients, the top 10 industries and occupations largely overlap with the ones associated with asbestos exposures (Table 2 and Appendix 11). Among mesothelioma cases in these industries, male workers account for a large proportion of the cases, with only a few female instances. Except manufacturing, the most common industries in which females work (i.e., healthcare, educational services) are not at great risk for asbestos exposure, and the most frequent exposure substance reported by female is unknown (Table 5). Moolgavkar et al. (2017) summarized a few studies showing that a significant fraction of female cases has no history of exposure to asbestos. Catelan et al. (2020) found that non-identified asbestos exposure is usually higher among women as well. Female exposure to asbestos may be explained by environmental exposure from their workplaces (e.g., old buildings), meanwhile DeBono et al. (2021) pointed out that the take-home exposure may also be the cause, as males, their partners, are more likely to work in the occupational-exposed industries. As education was the top industry for women, the findings in this group likely combines both bystander and take-home exposures. To reveal the origin of exposure, future studies should consider the patients’ family environments, and try to consider

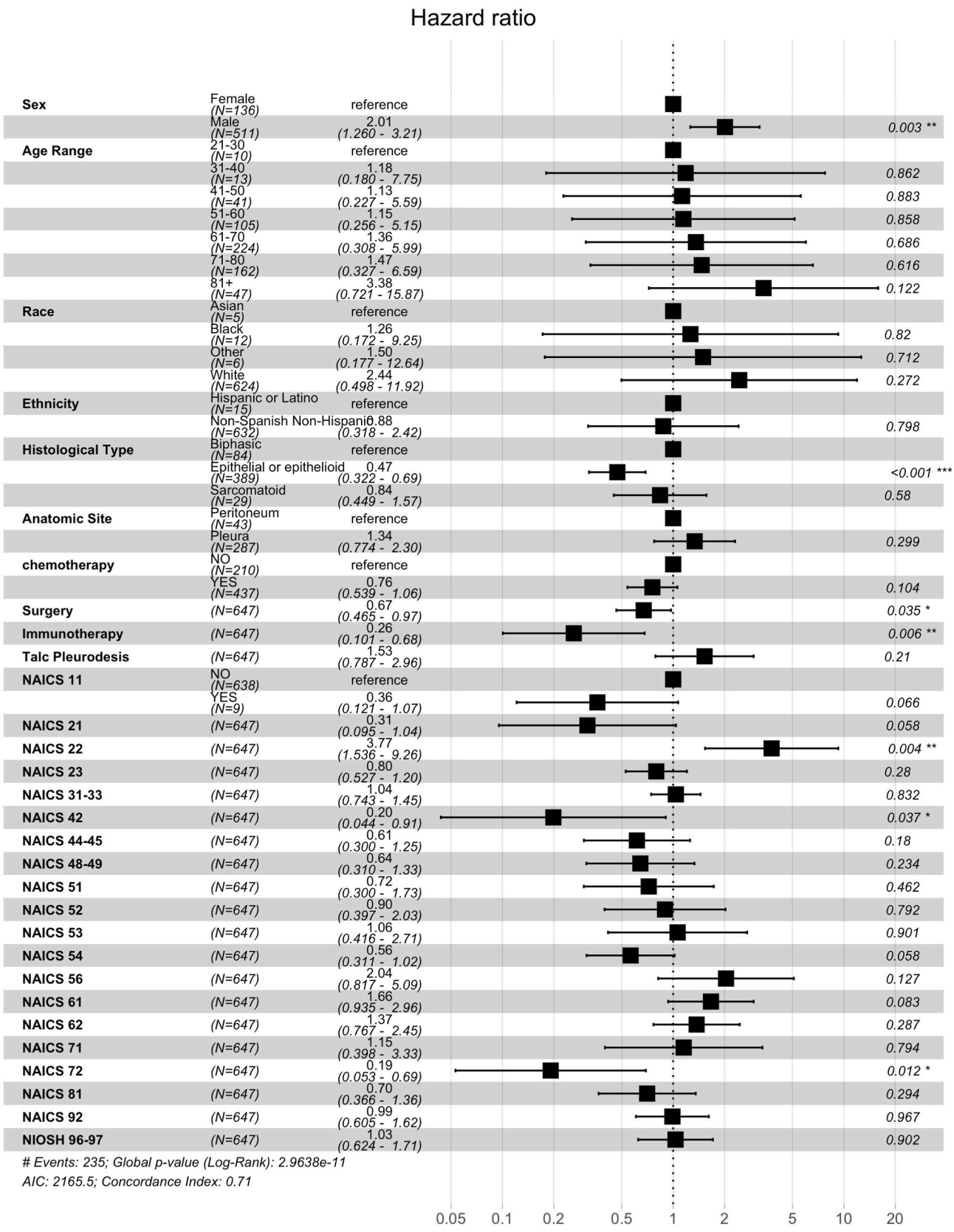

Fig. 3. Multi-variable cox regression analysis (NAICS 11: Agriculture, forestry, fishing and hunting; 21: Mining, quarrying, and oil and gas extraction; 22: Utilities; 23: Construction; 31–33: Manufacturing; 42: Wholesale trade; 44–45: Retail trade; 48–49: Transportation and warehousing; 51: Information; 52: Finance and insurance; 53: Real estate and rental and leasing; 54: Professional, scientific, and technical services; 55: Management of companies and enterprises; 56: Administrative and support and waste management and remediation services; 61: Educational services; 62: Health care and social assistance; 71: Arts, entertainment, and recreation; 72: Accommodation and food services; 81: Other services except public administration; 92: Public administration; NIOSH 96–97: Military).

both non-occupational and occupational exposure histories in mesothelioma cases. Therefore, an addition to the work history questionnaire of the NMVB (Appendix 1) might be to also include the work history of a spouse/partner or household members who has lived with the mesothelioma patient.

Regarding to environment exposure, prevalent industries among mesothelioma patients present a geolocation preference: in Iran, oil industry occupational experience ranked second among mesothelioma patients (Rezvani et al., 2020), and the shipbuilding industry was a prevalent feature in Finland and Sweden (Hemminki et al., 2021). Therefore, geo-preference is one direction to linking work history and mesothelioma. In our study, we were unable to identify the impact of residence on mesothelioma incidence due to the lack of geographic information. Future mesothelioma patient registries should consider including geo-mapping to see possible geography related patterns in their exposure history.

Mesothelioma is an occupational-related disease (DeBono et al., 2021; Spinazzè et al., 2022; Wilk and Krówczynska, 2021; Catelan et al., 2020; Consonni et al., 2020). Our multi-variable Cox Hazard Regression analysis showed work experience can further impact patients' survival time after diagnosis: patients with utility-related industry experience had a shorter survival time compared to patients who did not have this work experience. Patients who had industry experience in accommodation and food services had an increase survival time. Collecting more mesothelioma samples, their work history, the asbestos exposure time and the connection to work history, and patients' social economic status may help study the impact of work history on survival time more thoroughly.

The limitations of this study are as follows: 1) the database used in this study is not randomly sampled from the population, as a patient cohort. Therefore, there may be a selection bias in our data. 2) The work duration was not considered for each reported work history, which means some short exposure histories were included in our analyses. 3) Exposure information was self-reported and can be either occupational or non-occupational or both. Given patients were less possible to identify the exposure (for more than 6 months) outside work experience, we assumed all reported exposure were occupation-related that may be incorrect sometimes. In future study, the link between substance exposure and jobs can be enhanced by explicitly distinguishing whether the substance exposure is work-related or not, as well as include the start and end date for substance exposure in NMVB questionnaire. 4) our analysis included industry-only or occupation-only records, which may cause associations to wash out due to mixing of occupations for industries or mixing of industries for occupations; 5) our analysis did not consider the latency of mesothelioma and how this latency affect young patients. With more data, future analysis may exclude each job exposure record if there is no sufficient year lag between the start year of the job record and the year of the disease diagnosis of the patient (i.e., remove a job instance that is no more than 20 years before a mesothelioma diagnosis). When studying the relationship between a job exposure and a health outcome, we may exclude outcomes that happen within a set time period of the beginning of the job exposure. If a job exposure starts too close to the disease diagnosis, we would recode the outcome as censored at that time point.

Even though asbestos' world-wide production and use are now dropping, considering the long latency of mesothelioma diagnosis from the first exposure and ongoing exposure caused by remaining asbestos materials, the risk for potential mesothelioma will extend for decades (Wilk and Krówczynska, 2021). Environmental exposure, including from asbestos-contaminated buildings and outdoor environmental exposure, like living near asbestos-associated factories (Consonni et al., 2020), could be more important than direct exposure when studying current or future mesothelioma cohorts. On the other hand, with the decline in the use of asbestos, risk factors other than asbestos exposure, like ionizing radiation, a multi-site carcinogen, or age, a corresponding factor with mutation at gene loci, could contribute more to the incidence of mesothelioma than before (Moolgavkar et al., 2017). Germline mutation at the mesothelioma related gene locus may carry a high risk of incidence in the posterity who inherits it (Moolgavkar et al., 2017). Including more carcinogenic features and family hereditary diseases history in the registry may help to discover other unnoticed risk factors and may explain the inducement in young patients.

5. Conclusion

The NMVB patient registry has the potential of serving as a sentinel surveillance mechanism for identifying industries and occupations not previously associated with mesothelioma. The work history questionnaire for mesothelioma patients could benefit from adding information about their work/living environment as well as the work history of spouse/partner so that environmental exposure (in old buildings or at-risk living areas) and non-occupational exposure can be further monitored and studied. More information gathering about geolocation may help in seeking out the geographic characteristics of mesothelioma. Given the decreasing use of asbestos, the impact of exposure might decrease in prominence compared to the past while other mesothelioma risk factors, like hereditary history, may become more prominent.

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Author contribution

Yuhe Gao: Methodology, Software, Data curation, Formal analysis, Writing – original draft, Visualization. Jacek M. Mazurek: Writing – review & editing. Yaming Li: Resources, Writing – review & editing. David Blackley: Writing – review & editing. David N. Weissman: Methodology, Writing – review & editing. Shirley V. Burton: Writing – review & editing. Waqas Amin: Writing – review & editing. Douglas Landsittel: Methodology, Writing – review & editing. Michael J. Becich: Writing – review & editing, Funding acquisition, Supervision. Ye Ye: Conceptualization, Data curation, Methodology, Writing – review & editing, Project administration.

IRB statement

The NMVB data collection and research have been approved by the University of Pittsburgh Institutional Review Board: National Mesothelioma Virtual Bank for Translational Research (CR19110265-009).

Disclaimer

The findings and conclusions in this report are those of the author(s) and do not necessarily represent the official position of the National Institute for Occupational Safety and Health, Centers for Disease Control and Prevention.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Data availability

Data will be made available on request.

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Appendix A. Supplementary data

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