

An Occupational Legacy

Malignant Mesothelioma Incidence and Mortality in Wisconsin

Carrie D. Tomasallo, PhD, MPH, Krista Y. Christensen, PhD, MPH, Michelle Raymond, MS, Paul D. Creswell, PhD, Henry A. Anderson, MD, and Jon G. Meiman, MD

Objectives: The aim of the study was to describe mesothelioma occurrence in Wisconsin from 1997 to 2013 by usual industry and occupation (I&O), including occupations generally considered low risk. **Methods:** Population-based rates and standardized incidence and mortality ratios were calculated. Two case-control analyses were designed to compare mesothelioma incidence and mortality in specific I&O groups with occurrence of (1) brain and central nervous system cancers and (2) other causes of death, using logistic regression. **Results:** Mesothelioma incidence and mortality were elevated in Wisconsin (SIR_{adj} = 1.20 [1.13 to 1.28]; SMR_{adj} = 1.30 [1.22 to 1.38]). Certain industry (construction, manufacturing) and occupation (construction and extraction) groups were associated with increased odds of mesothelioma, with some evidence of increased risk among teachers. **Conclusions:** Forty years after the Occupational and Safety Health Act, mesothelioma incidence and mortality remain elevated in Wisconsin, with increased risk continuing for certain I&O groups.

Keywords: asbestos exposure, cancer epidemiology, cancer registry, death certificates, incidence, mesothelioma, mortality

BACKGROUND

Malignant mesothelioma is a rare tumor with high case fatality that is associated with identifiable occupational or environmental exposure to asbestos or other elongated mineral particles. The latency period between asbestos exposure and development of mesothelioma is on the order of decades with peak incidence among persons greater than 65 years of age.¹ In the occupational setting, the risk of mesothelioma may be upward of 10% over the lifetime in heavily exposed asbestos workers.² Currently, the National Cancer Institute's Surveillance, Epidemiology, and End Results (SEER) program estimates there are about 3200 incident cases of

mesothelioma per year in the United States.¹ However, previous surveillance indicates that mesothelioma incidence rate per million residents over 15 years in Wisconsin is elevated compared with the national rate (ie, 16.1 vs 12.5, respectively, in 2010).³ Other evidence shows that Wisconsin experienced an increasing prevalence of mesothelioma deaths from 1960 to 2000 with static rates over the past decade.³

Although the majority of mesothelioma investigations have centered on industries and occupations with known exposure to asbestos, concern has grown regarding low-level occupational and environmental exposures. Despite a steady decline in exposure in the construction and manufacturing industries,⁴ studies indicate that even low-level asbestos exposure increases the risk for malignant mesothelioma.^{5,6} Ongoing surveillance is required to identify hazards within industries and occupations generally considered to be low risk, and environmental sources of exposure such as residence near sources of asbestos containing fugitive emissions and the widespread use of asbestos in building materials which are still in place.⁷ For example, school buildings built before the 1980s are likely to still contain some form of asbestos and teachers may be more likely to be exposed than other occupations,⁸ despite the US Environmental Protection Agency Asbestos Hazard Emergency Response Act (AHERA) program and school management plans.⁹ National surveillance data have shown that the elementary and secondary schools industry was one of the most frequently recorded industries for mesothelioma deaths, and elementary school teachers were one of the occupations with significantly elevated mesothelioma mortality (PMR = 2.1).¹⁰

Objectives

This study builds upon the previous work to describe the most current information on mesothelioma incidence and death in Wisconsin from 1997 to 2013, and the association between mesothelioma and usual industry and occupation (I&O). In addition, it explores the occurrence of mesothelioma for individuals who worked in occupations and industries which are not generally associated with asbestos exposure or mesothelioma using a case control study design. The advantages and shortcomings of using death certificate and cancer registry data for mesothelioma surveillance are discussed.

METHODS

Data Sources

Wisconsin mesothelioma cases were identified through the Wisconsin Cancer Registry System (WCRS) by ICD-O histology code 9050 to 9053. Mesothelioma decedents at least 15 years of age were identified using Wisconsin Vital Records death certificates with an underlying or contributing cause of death ICD-9 code 158, 163, and 164 for deaths from mesothelioma of the peritoneum, pleura, and heart from 1997 to 1998. ICD-10 codes C45 were used to identify deaths from mesothelioma of the pleura, peritoneum, heart and other or unspecified sites from 1999 to 2013.

National mesothelioma incidence data were obtained from the Centers for Disease Control and Prevention (CDC) National

From the Wisconsin Department of Health Services, Division of Public Health, Bureau of Environmental and Occupational Health, Madison, WI (Dr Tomasallo, Dr Christensen, Ms Raymond, Dr Creswell, Dr Anderson, and Dr Meiman); Department of Ophthalmology and Visual Sciences, University of Wisconsin-Madison, Madison, WI (Dr Christensen); Department of Population Health Sciences, University of Wisconsin-Madison, Madison, WI (Ms Raymond, Dr Creswell, and Dr Anderson).

Centers for Disease Control and Prevention, National Institute for Occupational Safety and Health, Wisconsin Fundamental-Plus Occupational Health Surveillance project Grant no. 5U60OH010898-03. Centers for Disease Control and Prevention, National Center for Environmental Health, Enhancing Innovation and Capabilities of the Environmental Public Health Tracking Network in Wisconsin project Grant No. 6 N01EH001342-01-01. US Environmental Protection Agency Great Lakes National Program Office, Great Lakes Restoration Initiative Grant No. GL-00E01285.

HAA has served as a consultant to government and international agencies on asbestos health effects, and has been a consultant and witness on plaintiff's litigation concerning asbestos and disease.

The authors report no conflicts of interest.

Supplemental digital contents are available for this article. Direct URL citation appears in the printed text and is provided in the HTML and PDF versions of this article on the journal's Web site (www.joem.org).

Address correspondence to: Carrie D. Tomasallo, PhD, MPH, Wisconsin Department of Health Services, 1 W. Wilson Street—Rm 150, Madison, WI 53703 (carrie.tomasallo@wisconsin.gov).

Copyright © 2018 American College of Occupational and Environmental Medicine

DOI: 10.1097/JOM.0000000000001461

Program of Cancer Registries and the National Cancer Institute (NCI) Surveillance, Epidemiology, and End Results (SEER) program.¹¹ National mesothelioma death data were obtained from the CDC National Center for Health Statistics (NCHS) Multiple Cause of Death Mortality files.¹² National population estimates for the denominators of incidence and mortality rates were obtained from the CDC NCHS National Vital Statistics System bridged-rate population estimates of the resident population of the United States.¹³

WCRS electronic files included literal text fields of I&O reported as the longest held job at the time of diagnosis for approximately half of the records. Wisconsin electronic death certificate records from 1997 to 1999 had been previously coded with 1990 Census I&O codes. Records from 2000 to 2012 records did not contain text fields or Census I&O codes, and we abstracted the literal “usual industry and occupation” for mesothelioma cases and associated controls from archived death certificates. Electronic death certificate records from 2013 contained literal I&O.

Study Design

We used two different control populations to assess mesothelioma rates for I&O groups. In both instances, controls were frequency matched to mesothelioma deaths and cases based upon distribution of age, race, and sex. First, the cancer control series included malignant brain and central nervous system (CNS) cancer cases. We chose brain and CNS cancer as a control group because it has a similar incidence and case fatality rate as mesothelioma but no known association with asbestos exposure. Controls were identified through the WCRS by ICD-10 histology codes C700 to C716 (meninges, brain, spinal cord, and ventricle), C722 to C725 (cranial nerves), C728 to C729 (other nervous system), C751 to C752 (pituitary gland and craniopharyngeal duct), and C753 (pineal gland). Second, the population control series included a random sample of all deaths, excluding those with an asbestosis or mesothelioma cause of death, to provide an unbiased comparison with respect to I&O and exposures.

Industry and Occupation Coding

We used the National Institute of Occupational Safety and Health (NIOSH) Industry and Occupation Computerized Coding System tool (NIOCCS) to translate I&O text to standardized I&O codes and crosswalk codes between Census I&O classification schemes. NIOCCS was used to crosswalk the 1990 Census I&O codes from 1997 to 1999 death certificate records and code literal I&O from the 2000 to 2012 death certificates to the 2002 Census I&O classification scheme. The 2002 Census I&O codes were categorized into industry and occupation groups, excluding military, using 2007 National Health Interview Survey (NHIS) simple I&O recodes. We linked the WCRS data to death certificate data from Vital Records to supplement I&O from the cancer registry with usual I&O from the death certificate. We used a tiered matching system based on first and last names and date of birth. Of 1083 mesothelioma deaths, 42 were missing a death certificate or could not be translated to Census I&O codes; among controls, 8 could not be translated. Following the linkage of WCRS to death certificate data, approximately 18% and 26% of 1246 incident mesothelioma cases were still missing literal industry or occupation, similar to the proportion missing among controls (20% and 26%, respectively).

Data Analysis

Annual age-standardized incidence and mortality rates were calculated from 1997 to 2013. Standardized incidence ratios (SIRs) and standardized mortality ratios (SMRs) were calculated for the years 2000 to 2013 (age-adjusted and age–sex–race-adjusted) for comparison to the United States (excluding Puerto Rico). Confidence intervals (CIs) following the gamma distribution were

computed to assess statistical significance. SIRs were not calculated from 1997 to 1999 due to differences in SEER registry coverage. National mesothelioma case estimates between 1 and 16 are suppressed, and we imputed the number of events proportionate to the population size for the stratum of interest following a Poisson distribution constrained by an upper bound of 16. Results incorporating imputed event counts are included in Table S2, Supplemental Digital Content 2, <http://links.lww.com/JOEM/A481>. A small number of mesothelioma cases did not have race available in the WCRS record and the total numbers of observed cases is lower in the age–sex–race-adjusted calculations.

We used descriptive analyses to compare cases and controls by demographic and occupational factors. Logistic regression models were used to estimate odds ratios for mesothelioma incidence and mortality while adjusting for the frequency-matched characteristics of age, race, and sex, industry and occupation as described above, year of death or cancer diagnosis (for analyses of mortality and incidence data, respectively), race/ethnicity, and educational attainment (available in mortality data only). For computation of odds ratios, the reference group was selected as the industry or occupation group with both sufficient sample size for model stability, and lowest prevalence of mesothelioma deaths or cases. As a subanalysis, we also identified the subset of individuals with occupation codes specific to teaching and compared their incidence and mortality to all others in the ‘Professional and Management occupations’ group and to all other occupations. In addition, the more specific subset of ‘Elementary and Middle School teachers’ were also compared to those in the ‘professional and related occupations’ group (to reduce potential residual confounding) and to all other occupations. For both case-control analyses, results are shown only for those I&O groups with sufficient cell size (ie, ≥ 5) for purposes of confidentiality and reliability of the estimate. All statistical analyses were generated using SAS/STAT software, version 9.4 for Windows (SAS Institute Inc., Cary, NC). This study was given a nonresearch determination by the Wisconsin Department of Health Services Human Subjects Protection Committee and classified as a public health surveillance activity.

RESULTS

State-Based Surveillance

From 1997 to 2013, there were 1083 deaths attributed to mesothelioma among Wisconsin residents, with 1021 coded with mesothelioma as the underlying cause of death. During the same period, there were 1246 incident cases of mesothelioma in Wisconsin. Table 1 shows age-adjusted annual mesothelioma death and incidence rates per million Wisconsin residents from 1997 to 2013. Death rates were notably lower during 1997 and 1998 due to lack of a mesothelioma-specific code; death rates from the years 1999 to 2013 are higher but without a noticeable trend (range from 11.47 deaths/million in 1999 to 17.37 deaths/million in 2006). For incidence rates, there was again no clear temporal trend, with incidence ranging from a low of 10.95 cases/million (2012) to 19.50 (2001).

The majority of mesothelioma deaths occurred in those aged 60 to 79 years (58.1%), followed by those aged 80 years and older (29.8%); 12.0% occurred in those aged 15 to 59 years. Nearly all decedents were white (97.8%), with the remainder identified as black (1.9%) or other race (0.3%). Approximately three-quarters (74.8%) of decedents were male. Most decedents had a high school education or less (70.4%), with the remainder split between those with some college (14.3%) and those with a bachelor’s degree or greater (15.3%). At time of death, nearly all were either married (67.4%) or widowed (20.5%). Nearly 80% of death certificates reported other or unspecified site of mesothelioma, whereas the WCRS contained detailed site information. Of incident

TABLE 1. Age-Adjusted Mesothelioma Death* and Incidence Rates/Million Wisconsin Residents Aged ≥15 Years and 95% Confidence Intervals (CIs) by Year, 1997 to 2013

Year	Deaths	Death Rate/million (95% CI)	Cases	Incidence Rate/million (95% CI)
1997	38	9.20 (6.51–12.63)	68	16.36 (12.70–20.75)
1998	39	9.20 (6.54–12.63)	68	15.89 (12.33–20.18)
1999	49	11.47 (8.48–15.24)	56	13.09 (9.88–17.07)
2000	60	13.74 (10.48–17.79)	81	18.70 (14.85–23.34)
2001	73	16.72 (13.10–21.15)	85	19.50 (15.57–24.23)
2002	66	14.79 (11.43–18.99)	77	17.58 (13.87–22.12)
2003	71	15.67 (12.24–19.97)	64	14.14 (10.88–18.26)
2004	69	14.92 (11.60–19.13)	84	18.36 (14.64–22.94)
2005	60	12.90 (9.84–16.90)	73	16.07 (12.59–20.46)
2006	80	17.37 (13.76–21.90)	75	16.00 (12.58–20.36)
2007	66	14.00 (10.81–18.15)	75	15.98 (12.56–20.36)
2008	69	14.43 (11.21–18.63)	69	14.26 (11.08–18.43)
2009	71	14.50 (11.30–18.69)	79	16.57 (13.10–21.02)
2010	66	13.70 (10.58–17.87)	76	15.23 (11.98–19.49)
2011	73	14.30 (11.18–18.47)	72	14.07 (10.99–18.21)
2012	72	13.67 (10.67–17.75)	57	10.95 (8.27–14.78)
2013	61	11.58 (8.83–15.48)	87	16.28 (13.01–20.62)

*Decedents aged ≥15 years for whom the underlying or contributing cause of death ICD-9 codes 158, 163, and 164 for years 1997 to 1998 and ICD-10 code C45 for years 1999 to 2013 were listed on the death certificates.

mesothelioma cases, 82.7% were pleural (C38.4), 9.5% were peritoneal (C48), and 7.8% were categorized as other mesothelioma (all other ICD-10 codes).

When comparing rates by sex, the average incidence in Wisconsin over 2000 to 2013 was (as expected) higher in men compared with women—27.5 and 7.3 cases/million, respectively (Table S1, Supplemental Digital Content 1, <http://links.lww.com/JOM/A480>). For both sexes, rates in Wisconsin were higher compared with sex-specific national rates. There is a suggestion of a slightly higher male:female ratio of incidence rates in the national data, indicating Wisconsin females may have a greater elevation in incidence compared with national rates, compared with Wisconsin men (due to differing potential for exposure, for example).

Table 2 provides standardized mortality ratios (SMRs) and associated 95% confidence intervals (CIs) for mesothelioma as an

underlying or contributing cause of death, by year of death and overall from 2000 to 2013. All annual SMRs were greater than one, indicating more mesothelioma deaths than expected in Wisconsin compared with the United States as a whole. These increases were statistically significant for several individual years and a similar pattern was seen whether adjusting for age only, or for age, sex, and race. The age-adjusted SMR for the overall period 2000 to 2013 was significantly elevated (1.30, 95% CI = 1.22 to 1.38), as was the age–sex–race-adjusted SMR (1.22, 95% CI = 1.14 to 1.30).

When examining cancer incidence, there were 1246 incident cases of mesothelioma in Wisconsin from 1997 to 2013, of which 1054 occurred after 2000. Table 3 shows standardized incidence ratios (SIRs) and associated 95% CIs by year of diagnosis and overall from 2000 to 2013. As noted for mortality, there were several years in which age-adjusted SIRs were significantly elevated above

TABLE 2. Standardized Mortality Ratios (SMRs) and 95% Confidence Intervals (CIs) for Mesothelioma Deaths* in Wisconsin by Year and Overall, 2000 to 2013

Year	Observed Deaths	Age-Adjusted		Age/Sex/Race-Adjusted	
		Expected Deaths	SMR (95% CI)	Expected Deaths	SMR (95% CI)
2000	60	50.44	1.19 (0.91–1.53)	53.39	1.12 (0.86–1.45)
2001	73	49.87	1.46 (1.15–1.84)	53.30	1.37 (1.07–1.72)
2002	66	51.16	1.29 (1.00–1.64)	54.34	1.21 (0.94–1.55)
2003	71	52.11	1.36 (1.06–1.72)	55.17	1.29 (1.01–1.62)
2004	69	52.73	1.31 (1.02–1.66)	56.17	1.23 (0.96–1.55)
2005	60	53.51	1.12 (0.86–1.44)	56.79	1.06 (0.81–1.36)
2006	80	51.15	1.56 (1.24–1.95)	54.24	1.47 (1.17–1.84)
2007	66	51.47	1.28 (0.99–1.63)	54.67	1.21 (0.93–1.54)
2008	69	53.27	1.30 (1.01–1.64)	56.70	1.22 (0.95–1.54)
2009	71	54.06	1.31 (1.03–1.66)	57.80	1.23 (0.96–1.55)
2010	66	53.51	1.23 (0.95–1.57)	57.01	1.16 (0.90–1.47)
2011	73	55.23	1.32 (1.04–1.66)	58.95	1.24 (0.97–1.56)
2012	72	55.86	1.29 (1.01–1.62)	59.45	1.21 (0.95–1.53)
2013	61	51.96	1.17 (0.90–1.51)	55.54	1.10 (0.84–1.41)
2000–2013	957	736.51	1.30 (1.22–1.38)	783.90	1.22 (1.14–1.30)

Bold values indicate statistically significant result.

*Decedents aged ≥15 years for whom the underlying or contributing cause of death ICD-10 code C45 were listed on the death certificates, identified using CDC multiple cause-of-death data for 2000 to 2013.

TABLE 3. Standardized Incidence Ratios (SIRs)* and 95% Confidence Intervals (CIs) for Incident Mesothelioma Cases in Wisconsin by Year, 2000 to 2013

Year	Observed Cases	Age-Adjusted		Age/Sex/Race-Adjusted [†]	
		Expected Cases	SIR (95% CI)	Expected Cases	SIR (95% CI)
2000	81	61.76	1.31 (1.04–1.63)	63.65	1.26 (1.00–1.56)
2001	85	60.83	1.40 (1.12–1.73)	62.27	1.36 (1.09–1.69)
2002	77	62.04	1.24 (0.98–1.55)	64.39	1.18 (0.93–1.48)
2003	64	61.50	1.04 (0.8–1.33)	62.81	1.02 (0.78–1.3)
2004	84	62.56	1.34 (1.07–1.66)	64.46	1.30 (1.04–1.61)
2005	73	64.39	1.13 (0.89–1.43)	66.48	1.10 (0.86–1.38)
2006	75	62.34	1.20 (0.95–1.51)	63.44	1.18 (0.93–1.48)
2007	75	62.04	1.21 (0.95–1.52)	63.98	1.16 (0.91–1.45)
2008	69	63.18	1.09 (0.85–1.38)	65.68	1.05 (0.82–1.33)
2009	79	63.41	1.25 (0.99–1.55)	66.12	1.19 (0.95–1.49)
2010	76	63.79	1.19 (0.94–1.49)	65.26	1.16 (0.92–1.46)
2011	72	64.30	1.12 (0.88–1.41)	66.50	1.05 (0.82–1.33)
2012	57	62.64	0.91 (0.69–1.18)	64.69	0.88 (0.67–1.14)
2013	87	61.85	1.41 (1.13–1.73)	63.72	1.35 (1.08–1.67)
2000–2013	1054	875.94	1.20 (1.13–1.28)	902.90	1.16 (1.09–1.23)

Bold values indicate statistically significant result.

*Calculated without Puerto Rico included, and imputing suppressed cell counts as zero.

[†]Note that six mesothelioma cases did not have information on race, and are therefore not included in the age–sex–race-adjusted calculations.

1.0 (2000, 2001, 2004, 2013), indicating more incident cases of mesothelioma in Wisconsin compared with the SEER sites overall. These differences were attenuated when additionally adjusting for sex and race because a greater number of cell counts were suppressed and imputed to zero for these calculations. The age-adjusted SIR for the overall period 2000 to 2013 was significantly elevated (1.20, 95% CI = 1.13 to 1.28), as was the age–sex–race-adjusted SIR (1.16, 95% CI = 1.09 to 1.23). We also computed SIRs with number of cases imputed where surveillance data were suppressed for reasons of confidentiality. As expected, the overall SIR was slightly lower when adjusted for age only (1.11) or when adjusted for age–sex–race (1.10) compared with the SIRs computed without case counts imputed (see Table S2, Supplemental Digital Content 2, <http://links.lww.com/JOM/A481>).

Case–Control Analysis

Demographic characteristics, along with industry and occupation, were examined among the mesothelioma deaths and incident cases and compared with those of their respective control series. Due to frequency matching by age, sex, and race, none of these characteristics were different from the control series; in addition, there was no difference in distribution of marital status. However, educational attainment was significantly different, with controls having more individuals with higher educational attainment (eg, 18.7% with a bachelor’s degree or greater). To adjust for this difference, educational attainment was included in mortality logistic regression models along with age, sex, race, and year of death. The series of incident mesothelioma cases and matched controls showed essentially the same demographic trends as the mortality series, although educational attainment was not available as part of the cancer registry data.

With respect to industry and occupation, there were significant differences in distribution between cases and controls. Table 4 shows the results of the multivariate logistic regression models containing the aforementioned variables, as well as (in separate models) industry and occupation groups. In both the mortality and incidence models, the industry groups associated with elevated risk were construction (ORs ranging 2.5 to 3.0) and manufacturing (ORs ranging 1.5 to 1.7), whereas for occupation, the only group associated with elevated risk was construction and extraction (ORs

ranging 2.8 to 3.1). There was no significant difference in odds of mesothelioma death or incidence for those in the educational services industry group or the professional and related occupation group (which includes teachers).

Table 5 shows the results of an analogous case–control analysis, using more detailed industry and occupation groupings for mortality data. Similar findings were seen for incidence data, although fewer occupation groups were significantly associated with diagnosis. Only those groupings with statistically significant associations are shown but complete results are included in Table S3, Supplemental Digital Content 3, <http://links.lww.com/JOM/A482> (for mortality) and Table S4, Supplemental Digital Content 4, <http://links.lww.com/JOM/A483> (for incidence). Similar to the results shown above for the more general occupation groups, manufacturing and construction-related groupings remained significantly associated with increased odds of mesothelioma, with the addition of paper manufacturing. In addition, the more specific occupation group of primary, secondary, and special education school teachers showed an elevated risk of death with an odds ratio of 2.10 (95% CI = 1.05 to 4.26).

To more closely examine potential risk of mesothelioma mortality and incidence associated with working in the education field, we also performed a subanalysis to look at more detailed occupation amongst those in the “professional and related occupations” group, which includes the subset of specific teaching-related occupations. Compared with the overall “professional and related occupations” group, we found a nonsignificant increased risk of mortality for the subset of “primary, secondary, and special education teachers” (OR = 1.91, 95% CI = 0.89 to 4.11) as well as a nonsignificant increased risk of mesothelioma incidence in the WCRS data (OR = 1.48, 95% CI = 0.77 to 2.85). When comparing these teachers to all other occupations, we observed a similar nonsignificant increased risk of mesothelioma mortality (OR = 1.79, 95% CI = 0.97 to 3.32) and incidence (OR = 1.14, 95% CI = 0.66 to 1.98). To be consistent with previous studies, we also compared the smaller subset of “elementary and middle school teachers” to those in the ‘professional and related occupations’ group and to all other occupations and found a significant increased risk of mesothelioma mortality (OR = 3.50, 95% CI = 1.46 to 8.38 and OR = 2.53, 95% CI = 1.26 to 5.09,

TABLE 4. Adjusted Odds Ratios (ORs) and 95% Confidence Intervals (CIs) for Association Between Mesothelioma Death or Incidence and Industry or Occupation Group

Industry or Occupation Group	Death*	Incidence†
	OR (95% CI)	OR (95% CI)
<i>Industry Group – Reference is Wholesale + Retail Trade</i>		
Agriculture/Forestry/Fishing + Mining + Utilities	1.05 (0.68–1.64)	0.98 (0.62–1.55)
Construction	3.02 (2.01–4.55)	2.51 (1.67–3.77)
Educational Services	1.14 (0.70–1.85)	0.88 (0.55–1.39)
Health Care and Social Assistance	1.40 (0.85–2.32)	1.08 (0.65–1.77)
Information, Finance, and Management	1.16 (0.75–1.80)	0.98 (0.64–1.52)
Manufacturing	1.71 (1.22–2.41)	1.48 (1.04–2.09)
Other Services	1.28 (0.82–1.99)	1.14 (0.73–1.79)
Public Administration	1.06 (0.64–1.74)	0.84 (0.49–1.43)
Transportation + Warehousing	0.98 (0.59–1.61)	0.74 (0.44–1.22)
<i>Occupation Group – Reference is Transportation and Material Moving</i>		
Construction and Extraction	2.83 (1.86–4.31)	3.06 (1.99–4.72)
Farming, Forestry, and Fishing	0.49 (0.10–1.87)	0.64 (0.13–2.75)
Installation, Maintenance, and Repair	1.24 (0.74–2.07)	1.21 (0.71–2.04)
Management, Business, and Financial Operations	0.78 (0.53–1.14)	0.91 (0.62–1.36)
Office and Administrative Support	0.71 (0.44–1.13)	0.73 (0.44–1.19)
Production	1.15 (0.79–1.68)	1.23 (0.82–1.83)
Professional and related occupations	1.05 (0.68–1.64)	0.86 (0.57–1.30)
Sales and Related	0.86 (0.54–1.36)	0.82 (0.51–1.30)
Service occupations	0.82 (0.53–1.28)	1.01 (0.64–1.59)

*Effect estimates for age, race, and sex are not shown because these factors were used for frequency matching of cases and controls. Bold values indicate statistically significant result. For year of death, 2006 showed elevated ORs compared with 1997 (OR = 1.9).

†Effect estimates for age, race, and sex are not shown because these factors were used for frequency matching of cases and controls. Bold values indicates statistically significant result. For year of diagnosis, 1998, 2000, 2001, and 2004 showed elevated ORs compared with 1997 (ranging from 1.8 to 2.5).

respectively), and a nonsignificant increased risk of mesothelioma incidence (OR = 1.64, 95% CI = 0.74 to 3.65 and OR = 1.20, 95% CI = 0.62 to 2.33, respectively).

DISCUSSION

We used cancer registry and death record data to describe trends in mesothelioma incidence and mortality in Wisconsin from 2000 to 2013. Elevated SIRs and SMRs both overall and for several individual years indicate higher than expected occurrence in Wisconsin compared with the nation as a whole. This is in accordance with previously identified regional variation in mesothelioma incidence and mortality in the United States.^{1,14} This increased occurrence may be due to a higher prevalence of

occupations and industries where asbestos exposure is possible, including construction, extraction, and shipbuilding, as well as occupations and industries not previously identified as high risk, such as paper manufacturing. This analysis also identified occupations generally considered to be lower risk which could be due to para-occupational or environmental exposures such as from buildings with asbestos-containing materials (such as thermal insulation) in poor repair. Finally, we show that use of cancer registry data provides similar estimates of mesothelioma occurrence as death records and demonstrate the utility and feasibility of jointly analyzing the two data sources. Future analyses that combine these data may provide improved risk characterization than either alone.

TABLE 5. Detailed Industry and Occupation Groups* With Significantly Elevated Adjusted Odds Ratios† (ORs) and 95% Confidence Intervals (CIs) for Mesothelioma Death

Industry or Occupation Group	Total (n)	Cases (n)	OR (95% CI)
<i>Industry Group – Reference is Public Administration</i>			
Chemical manufacturing	20	15	3.92 (1.36–13.07)
Construction	240	160	2.93 (1.79–4.84)
Utilities	50	33	2.66 (1.30–5.58)
Fabricated metal product manufacturing	34	23	2.65 (1.17–6.30)
Paper manufacturing	59	37	2.38 (1.22–4.73)
<i>Occupation Group – Reference is Other Management Occupations</i>			
Construction trades workers	215	157	4.20 (2.78–6.42)
Operations specialties managers	35	21	2.37 (1.13–5.12)
Primary, secondary, and special education school teachers	49	28	2.10 (1.05–4.26)
Engineers	51	28	2.02 (1.07–3.86)
Other installation, maintenance, and repair occupations	52	29	1.92 (1.03–3.62)
Metal workers and plastic workers	115	62	1.77 (1.11–2.85)

*Limited to those industries and occupation groups with at least five mesothelioma cases and five controls.

†Model adjusted for frequency matched characteristics of age, race and sex, in addition to ethnicity, year of death, industry or occupation group, and educational attainment.

Overall, our case-control analyses indicate that mesothelioma mortality in Wisconsin is highest in the construction and manufacturing industries. Detailed analysis of industry and occupation showed chemical manufacturing and utilities industries, as well as construction trade workers and engineers, to be at highest risk. These findings are consistent with those from national surveillance data.^{10,14} Of note, we also found a significantly increased risk of mesothelioma in paper manufacturing. Although asbestos exposure is not typically considered a significant hazard in this industry, long-term cohort studies have demonstrated an increased risk of pleural cancers in paper mill workers.^{15,16} Exposure measurements have frequently detected asbestos in milling plants because of use in the brakes of rolling machines and to insulate processing equipment.¹⁷ Maintenance workers are likely at highest risk for developing mesothelioma.¹⁸ Given that Wisconsin has one of the largest paper manufacturing industries in the United States, employing over 56,000 workers in 1988 and 30,000 workers currently,^{19,20} increased attention to low-level exposures in this industry is warranted given the risks demonstrated in this analysis.

We also found evidence for increased risk of mortality among primary, secondary, and special education schoolteachers compared with individuals working in “other management occupations.” Furthermore, we found a nonsignificant increased risk of mesothelioma incidence and mortality among the subset of primary, secondary, and special education teachers when compared with others in the broader “professional and management occupations” group and when compared with all other occupations as well as increased risk of mortality for the subset of elementary and middle school teachers. Para-occupational, or take-home exposures, may be responsible in part for the observed risk. A 2004 study by Wisconsin Department of Health Services (WI DHS) investigated potential exposure to asbestos-contaminated vermiculite as part of the Agency for Toxic Substances and Disease Registry (ATSDR) Pilot Mesothelioma Surveillance Program.²¹ The source of exposure was identified as Libby amphibole asbestos mined from Libby, MT, and shipped to processing facilities across the nation, including several receiving and exfoliation sites in the Milwaukee area. The study found that many of the communities receiving Libby amphibole asbestos—including those in Wisconsin—had statistically significantly increased rates of disease.

For teachers, incidental asbestos exposure within the school environment may also be a contributing factor in the elevated rates we found in this study. A previous Wisconsin case-series analysis conducted by Anderson et al suggested that working as a school teacher or in the school setting was an underappreciated source of asbestos exposure with subsequent increased risk of mesothelioma.⁸ In addition, a death certificate review of Wisconsin mesothelioma deaths from 1959 to 1989^{8,22} documented the occurrence of mesotheliomas among maintenance workers and teachers in Wisconsin schools. Among the maintenance workers, 34% (10 out of 29 workers) were likely exposed to asbestos only through their work in the school setting; notably, this was the case for 75% (9 out of 12) of the teachers. Other investigations have also indicated increased risk. Cocco and Dosemeci performed a death certificate review for individuals with peritoneal cancer and found the odds ratio among women was nonsignificantly elevated for elementary school teachers (occupation) and for the industry group including elementary and secondary schools.²³ Lilienfeld presented four cases of malignant mesothelioma occurring among school teachers whose only documented exposure to asbestos was the schools in which they taught.²⁴ In contrast, two studies conducted in Europe did not find associations between education-related occupations and increased occurrence of mesothelioma.^{25,26} Although our data sources do not provide specific occupational history to discern other potential sources of asbestos exposure, future research should investigate this finding further given that teachers comprise one of the largest

professional occupation groups in Wisconsin, approximately 5% of the workforce or 164,000 teachers.^{20,27}

This analysis demonstrates that cancer registry and death records demonstrate comparable trends and can be used to supplement data that is missing or is unavailable in either alone. Similar to previous studies,^{28,29} we found that usual industry and occupation were frequently missing (in approximately 50% of records) from the cancer registry. The recent study by Silver et al did find that although codability varied by cancer type, mesothelioma was one of three malignancies with industry coding rates above 50%.²⁶ The cancer registry did, however, provide detailed information on cancer site (in contrast to death certificates, which most often reported “other” or “unspecified” site of mesothelioma). With respect to I&O coding, there was generally agreement between death certificates and WCRS when coding high-level I&O groups (76% and 71% for industry and occupation, respectively) for decedents with literal text also available from both data sources. In the absence of dedicated mesothelioma registries containing detailed exposure histories, states and national governments often rely upon cancer registry and vital records data to monitor trends and identify high-risk industries and occupations. We demonstrate that these data sources provide comparable standardized rates. This creates an opportunity to perform data linkage; risk factors by pleural and peritoneal mesothelioma, for example, can be examined separately by industry and occupation. Although our sample size was too small in this investigation to perform such statistical analyses, linkage using larger state registries or national surveillance data may reveal important differences in exposure risks, particularly for women. Efforts should be made to improve collection of cancer registry data but can be supplemented with death certificates to gauge exposures.

Limitations

Our analysis of industry and occupation relied upon death certificate coding (primary), supplemented by WCRS case record coding, both of which were based on usual or longest-held job. As such, we were unable to determine occupational exposure to asbestos that may have occurred from other work periods. Similarly, there is no information in either vital statistics or WCRS records that would allow us to identify nonoccupational exposure to asbestos (eg, those occurring during home renovations). This lack of information could lead to exposure misclassification. However, if this occurred nondifferentially between mesothelioma decedents or cases and their respective controls, we would expect any bias introduced to be toward the null and lead to more conservative estimates of effect. Another limitation is the demonstrated potential for miscoding of ICD-9 codes before the unique codes in ICD-10,³⁰ and for underreporting of mesothelioma.³¹ This underreporting and miscoding may have decreased our ability to truly assess the burden of mesothelioma in Wisconsin. Finally, it is possible that the control series of brain/CNS cancers—whereas unlikely to have arisen due to asbestos exposure—could be enriched in occupation or industry groups with coexisting exposure to other carcinogenic substances.³² If this were the case, findings would be biased toward the null; such confounding seems unlikely given the similarity of findings between analyses of deaths and incident cases, however.

In conclusion, this study provides an update of both mesothelioma incidence and mortality in Wisconsin from 1997 to 2013. Findings demonstrate that rates remain elevated in Wisconsin compared with national data. Reasons may include specific and prevalent sources of asbestos exposure due to industrial activity and building stock in the state. When more closely investigating usual industry and occupation, we found that certain groups were at increased risk for mesothelioma, including construction and extraction, and paper manufacturing. Furthermore, we found evidence of increased risk among those employed in the educational field, as was suggested by an earlier investigation of teachers in Wisconsin

schools. Finally, we found that cancer registry and death records contain different levels of completeness depending on the element of interest and can be used to supplement missing data for an individual. We propose that a broader range of industry and occupation groups with elevated risk for mesothelioma but with borderline statistical significance merit further investigation using more detailed work and personal history to document exposure to asbestos.

ACKNOWLEDGMENTS

The authors thank Pamela Schumacher at NIOSH for her assistance in coding literal industry and occupation using the NIOCCS autocoding and computer-assisted software tool.

REFERENCES

- Henley SJ, Larson TC, Wu M, et al. Mesothelioma incidence in 50 states and the District of Columbia, United States, 2003–2008. *Int J Occup Environ Health*. 2013;19:1–10.
- Selikoff IJ, Hammond EC, Seidman H. Latency of asbestos disease among insulation workers in the United States and Canada. *Cancer*. 1980;46:2736–2740.
- Wisconsin Department of Health Services, Division of Public Health, Bureau of Environmental and Occupational Health. Wisconsin Occupational Health Indicator Report: Summary of worker health and safety data for years 2003–2012. 2016.
- Centers for Disease Control and Prevention, National Institute for Occupational Safety and Health. Asbestos Fibers and Other Elongate Mineral Particles: State of the Science and Roadmap for Research, in Current Intelligence Bulletin 62. 2011.
- Iwatsubo Y, Pairon JC, Boutin C, et al. Pleural mesothelioma: dose-response relation at low levels of asbestos exposure in a French population-based case-control study. *Am J Epidemiol*. 1998;148:133–142.
- Lacourt A, Gramond C, Rolland P, et al. Occupational and non-occupational attributable risk of asbestos exposure for malignant pleural mesothelioma. *Thorax*. 2014;69:532–539.
- Landrigan PJ. The third wave of asbestos disease: exposure to asbestos in place. Public health control. Introduction. *Ann N Y Acad Sci*. 1991;643: xv–xvi.
- Anderson HA, Hanrahan LP, Schirmer J, Higgins D, Sarow P. Mesothelioma among employees with likely contact with in-place asbestos-containing building materials. *Ann N Y Acad Sci*. 1991;643:550–572.
- United States Environmental Protection Agency. Asbestos and School Buildings. 2018. Available at: <https://www.epa.gov/asbestos/asbestos-and-school-buildings>. Accessed May 4, 2018.
- Centers for Disease Control and Prevention, National Institute for Occupational Safety and Health. Work-Related Lung Disease Surveillance Report 2007. 2008.
- WONDER Online Database, United States Cancer Statistics: 1999–2013 Incidence. Centers for Disease Control and Prevention and National Cancer Institute. 2016. Available at: <http://wonder.cdc.gov/cancer-v2013.html>. Accessed October 11, 2017.
- WONDER Online Database, Multiple Cause of Death 1999–2016 files. Compiled from data provided by the 57 vital statistics jurisdictions through the Vital Statistics Cooperative Program. Centers for Disease Control and Prevention, National Center for Health Statistics. 2015. Available at: <http://wonder.cdc.gov/mcd-icd10.html>. Accessed December 31, 2017.
- WONDER Online Database, Bridged-Race Population Estimates, United States July 1st resident population by state, county, age, sex, bridged-race, and Hispanic origin. Centers for Disease Control and Prevention, National Center for Health Statistics. Compiled from 1990–1999 bridged-race intercensal population estimates (released on 7/26/2004); revised bridged-race 2000–2009 intercensal population estimates (released on 10/26/2012); and bridged-race Vintage 2015 (2010–2015) postcensal population estimates (released on 6/28/2016). Available at: <http://wonder.cdc.gov/bridged-race-v2015.htm>. Accessed May 19, 2017.
- Mazurek JM, Syamlal G, Wood JM, Hendricks SA, Weston A. Malignant mesothelioma mortality—United States, 1999–2015. *MMWR Morb Mortal Wkly Rep*. 2017;66:214–218.
- Andersson E, Westberg H, Bryngelsson IL, Magnuson A, Persson B. Cancer incidence among Swedish pulp and paper mill workers: a cohort study of sulphate and sulphite mills. *Int Arch Occup Environ Health*. 2013;86:529–540.
- Carel R, Boffetta P, Kauppinen T, et al. Exposure to asbestos and lung and pleural cancer mortality among pulp and paper industry workers. *J Occup Environ Med*. 2002;44:579–584.
- Kauppinen T, Teschke K, Savela A, Kogevinas M, Boffetta P. International data base of exposure measurements in the pulp, paper and paper product industries. *Int Arch Occup Environ Health*. 1997;70:119–127.
- Toren K, Persson B, Wingren G. Health effects of working in pulp and paper mills: malignant diseases. *Am J Ind Med*. 1996;29:123–130.
- Wisconsin Department of Natural Resources. Paper sector. 2018. Available at: <https://dnr.wi.gov/topic/Sectors/Paper.html>. Accessed April 3, 2018.
- Employed labor Force (ELF) Online Database, Employed worker population estimates based on a subset of the Bureau of Labor Statistics (BLS) Current Population Survey (CPS) public access data files, 1980–2016. Centers for Disease Control and Prevention, National Institute for Occupational Safety and Health. 2018. Available at: https://www.cdc.gov/wisards/cps/cps_estimates.aspx. Accessed May 18, 2018.
- Horton DK, Bove F, Kapil V. Select mortality and cancer incidence among residents in various U.S. communities that received asbestos-contaminated vermiculite ore from Libby, Montana. *Inhal Toxicol*. 2008;20:767–775.
- Anderson HA, Hanrahan L, Phillips JL. Malignant mesothelioma in Wisconsin, 1959–1989. *Wis Med J*. 1991;90:479–480.
- Cocco P, Dosemeci M. Peritoneal cancer and occupational exposure to asbestos: results from the application of a job-exposure matrix. *Am J Ind Med*. 1999;35:9–14.
- Lilienfeld DE. Asbestos-associated pleural mesothelioma in school teachers: a discussion of four cases. *Ann N Y Acad Sci*. 1991;643:454–458.
- Carder M, Darnton A, Gittins M, et al. Chest physician-reported, work-related, long-latency respiratory disease in Great Britain. *Eur Respir J*. 2017;50.
- Pukkala E, Martinsen JI, Lyng E, et al. Occupation and cancer – follow-up of 15 million people in five Nordic countries. *Acta Oncologica*. 2009;48:646–790.
- Wisconsin Department of Workforce Development, Bureau of Workforce Information and Technology. May 2016 Wisconsin Occupational Employment and Wage Estimates. 2016. Available at: <http://worknet.wisconsin.gov/worknet/default.aspx>. Accessed January 4, 2018.
- Freeman MB, Pollack LA, Rees JR, et al. Capture and coding of industry and occupation measures: findings from eight National Program of Cancer Registries states. *Am J Ind Med*. 2017;60:689–695.
- Silver SR, Tsai RJ, Morris CR, et al. Codability of industry and occupation information from cancer registry records: differences by patient demographics, casefinding source, payor, and cancer type. *Am J Ind Med*. 2018;61:524–532.
- Davis LK, Martin TR, Kligler B. Use of death certificates for mesothelioma surveillance. *Public Health Rep*. 1992;107:481–483.
- Park EK, Takahashi K, Hoshuyama T, et al. Global magnitude of reported and unreported mesothelioma. *Environ Health Perspect*. 2011;119:514–518.
- Zheng T, Cantor KP, Zhang Y, Keim S, Lynch CF. Occupational risk factors for brain cancer: a population-based case-control study in Iowa. *J Occup Environ Med*. 2001;43:317–324.