

Occupation and Multiple Myeloma: An Occupation and Industry Analysis

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Background Multiple myeloma (MM) is an incurable plasma cell malignancy with a poorly understood etiology. The purpose of our research was to examine the relationships between lifetime occupations and MM in a relatively large case–control study.

Methods MM cases ($n = 180$) were identified through cancer registries in the Seattle–Puget Sound area and Detroit. Population-based controls ($n = 481$) were identified using random digit dialing and Medicare and Medicaid Services files. In-person interviews were conducted to ascertain occupational histories. Standard occupational classification (SOC) and standard industrial classification (SIC) codes were assigned to each job held by each participant. Unconditional logistic regression was used to generate odds ratios (ORs) and 95% confidence intervals (CIs) for associations between MM and having ever worked in each occupation/industry and according to duration of employment in an occupation/industry.

Results The risk of MM was associated with several manufacturing occupations and industries, including machine operators and tenders, not elsewhere classified (SOC 76) (OR = 1.8, CI = 1.0–3.3); textile, apparel, and furnishing machine operators and tenders (SOC 765) (OR = 6.0, CI = 1.7–21); and machinery manufacturing, except electrical (SIC 35) (OR = 3.3, CI = 1.7–6.7). Several service occupations and industries, such as food and beverage preparation (SOC 521) (OR = 2.0, CI = 1.1–3.8), were also associated with MM. One occupation that has been associated with MM in several previous studies, painters, paperhangers, and plasterers (SOC 644) was associated with a non-significantly elevated risk (OR = 3.6, CI = 0.7–19).

Conclusions We found associations between the risk of MM and employment in several manufacturing and service-related occupations and industries. *Am. J. Ind. Med.* 53:768–779, 2010. © 2010 Wiley-Liss, Inc.

KEY WORDS: multiple myeloma; lymphoma; machinery operators; occupation; painters; service occupations

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INTRODUCTION

Multiple myeloma (MM) is an incurable plasma cell malignancy with a median survival time following diagnosis of only 3 years [Bergsagel and Kuehl, 2005]. The etiology of this disease is poorly understood, but several groups are at increased risk, including males, African Americans, and persons diagnosed with monoclonal gammopathy of undetermined significance (MGUS) [Alexander et al., 2007; Landgren and Weiss, 2009].

Several studies have explored links between occupational risk factors and MM. Agriculture-related jobs have been associated with increased risk in many studies that examined the association [De Roos et al., 2004; Sonoda et al., 2005; Svec et al., 2005; Mester et al., 2006] but attempts to implicate specific etiologic exposures in agriculture have been inconclusive. Employment as a hairdresser also has been related to risk [Guidotti et al., 1982; Spinelli et al., 1984; Miligi et al., 1999], but no association has been found between MM and personal use of hair dyes [Grodstein et al., 1994; Thun et al., 1994; Miligi et al., 2005; Tavani et al., 2005]. Occupation as a chemical worker [Massoudi et al., 1997; Greenberg et al., 2001], rubber worker [Delzell and Monson, 1985; Dost et al., 2007], construction worker [Lee et al., 2003; Mester et al., 2006], painter [Bethwaite et al., 1990; Demers et al., 1993; Lundberg and Milatou-Smith, 1998], and metal worker [Demers et al., 1993; Baysson et al., 2000; Costantini et al., 2001; Lope et al., 2008] have also been linked to MM, as well as employment that involves exposure to wood and paper products [Flodin et al., 1987; Demers et al., 1993; Wong and Harris, 2005; Lope et al., 2008].

Most studies that have investigated whether certain occupations entail increased risk of this cancer have focused on specific occupations or industries and have included few cases (see Alexander et al., 2007 for review). In this relatively large population-based case-control study, we systematically evaluated lifetime occupational histories in relation to the risk of MM.

MATERIALS AND METHODS

Identification of Cases and Controls

MM cases were identified through the Surveillance Epidemiology and End Results (SEER) cancer registries in the Seattle-Puget Sound region of Washington (King and Snohomish counties) and the Detroit metropolitan area of Michigan (Macomb, Oakland, and Wayne counties). Cases eligible to participate in this study: (1) received a diagnosis of MM (ICD-O-2/3 9731:9732) between January 1, 2000 and March 31, 2002; (2) were not previously diagnosed with MM, NHL, or HIV [the latter were excluded based on self-reported HIV status because of the strong association

between the virus and lymphoma development; Noy, 2006]; (3) were between 35 and 74 years old at the time of diagnosis; (4) resided in one of the study areas at the time of diagnosis; and (5) spoke English. Of the 365 cases who appeared to be eligible to participate in this study, 64 (18%) died before they could be contacted, 28 (8%) could not be located, and the physicians of 18 (5%) refused. Of the remaining 255 whom we were able to contact, 74 (29%) refused to participate, leaving a total of 181 cases. Thus, of cases who were alive, able to be contacted, and whose eligibility could be confirmed, 71% (181/255) participated in this study. Of all presumed eligible cases, 50% (181/365) agreed to participate. Case participation was not associated with age, sex, or study site; information about the race of non-participating cases was not available.

Controls for this study were the same as those participating in a population-based case-control study of non-Hodgkin lymphoma (NHL) [Chatterjee et al., 2004]. To be eligible for our study of MM, controls (1) could not previously have been diagnosed with MM, plasmacytoma, NHL, or HIV; (2) were between 35 and 74 years old at the time of identification; (3) were residents of the Detroit or Seattle-Puget Sound metropolitan areas between September 1998 and December 2002; and (4) spoke English. Controls were frequency matched on age and sex to the NHL case distribution. Controls <65 years of age were selected using random digit dialing and controls 65–74 years of age were randomly selected from Center for Medicare and Medicaid Services files. A total of 1,133 people from the NHL study were identified as potentially eligible control subjects for our study of MM. Of these, 12 (1%) had died before they could be interviewed and 193 (17%) were not locatable. Of the 928 who could be contacted, 383 (41%) refused to participate and 64 (7%) did not participate for other reasons, leaving 481 (52% of those who were contacted and 42% of all presumed eligible controls) who were included our study of MM. Control participation was not associated with study site or gender, but individuals in the youngest (35–50) and oldest (65–74) age groups were less likely to have participated than those in the middle age group. Similar to the cases, we could not assess associations between race and participation among controls. Informed consent was obtained from each participant preceding the interview and approval was obtained from the Institutional Review Boards at the Karmanos Cancer Center in Detroit and the Fred Hutchinson Cancer Research Center in Seattle.

Exposure Assessment

In-person interviews were conducted using a computer-assisted personal interview (CAPI) program to minimize errors with data entry and to facilitate the interview process. Spouses or other surrogates were not permitted to complete interviews on behalf of study participants but were allowed to

assist in recalling occupational histories, dates, and frequencies of exposures. All jobs held after 1945 for at least 12 months were queried. Participants reported the job start and stop years, titles, and employers for each occupation they held. They were also asked to describe what the employer made or what service was provided, what their main duties were, and how many months of the year and hours per week they worked each job.

We reviewed each job held by each participant, and, blinded to case status, assigned the most appropriate standard occupational classification (SOC) and standard industrial classification (SIC) codes [Office of Management and Budget, 1980, 1987]. These assignments were reviewed by an experienced industrial hygienist (PS) for consistency and accuracy.

Data Analysis

We used SAS software version 9.0 or 9.1 (Cary, NC) for all analyses. Unconditional logistic regression was used to generate odds ratios (ORs) and 95% confidence intervals (CIs) for associations between MM and having ever been employed in each reported occupation/industry, adjusted for gender, age (with indicator variables for categories: 35–50 years (referent), 51–64 years, and 65–74 years), race (only white (referent), any black, any Asian, and other), education (less than 12 years (referent), 12–15 years, and 16 or more years), and SEER site (Seattle and Detroit). Each occupation or industry code was evaluated in a separate regression model and the reference category for each estimate was all other occupation or industry codes combined. Because of the large number of SIC and SOC codes evaluated, we present ORs and 95% CIs for all two-digit codes with at least five exposed participants (cases and controls combined). We also present results for the three-digit codes with at least five exposed participants that were statistically significant ($P < 0.05$). We also decided a priori to present results from three-digit codes that were reported to be significantly associated with incident MM in at least two previous studies that we discovered from reviewing the literature [these were personal service occupations (SOC 525), Guidotti et al., 1982; Miligi et al., 1999; painters, paperhangers, and plasterers (SOC 644), Bethwaite et al., 1990; Demers et al., 1993; metalworking or plastic working machine operators and tenders (SOC 751), Demers et al., 1993; Costantini et al., 2001; Lope et al., 2008; and woodworking machine operators and tenders (SOC 763), Flodin et al., 1987; Demers et al., 1993; Lope et al., 2008].

Analyses by duration of employment (never, 1–5 years, >5 years; we chose five years as a cut-off because we believed that subjects would have needed to have been exposed to carcinogenic substances for at least five years in order for those substances to have contributed to development of MM. We did not select a cut-off of longer than five

years because such lengthy durations of employment in many of the SICs and SOCs were not reported by sufficient numbers of study subjects to have allowed meaningful analysis) were performed for occupations and industries that were statistically significant or had ORs ≥ 2.0 or ≤ 0.5 in the initial analyses. Tests of trend were conducted using a linear term for the median duration of employment among controls in each duration category. Finally, assuming MM progresses over a number of years and recent exposures may be less relevant than those that took place in the more distant past, we did analyses that separately compared people who held jobs 1–10 years and more than 10 years before diagnosis to people never employed in each occupation/industry. However, since few participants started jobs less than 10 years before their date of entry in the study, results of the lagged analysis were not meaningfully different from the other analyses and are not presented. Because the case-to-control ratios differed between Seattle and Detroit and since we also expected the prevalence of occupations and industries to differ by study site, we were concerned that differential case/control selection by site may have influenced our results. We therefore conducted the ever/never SOC and SIC analyses with stratification by SEER site in order to see where within-site results differed from results in the entire study population. In the results, we note associations that were present in only one site (based on the direction of association rather than statistical significance within each site). Finally, because the distribution of men and women in the occupations and industries might have varied and/or MM etiologies might have differed by gender, we also performed analyses stratified on gender. Again, we note associations in the text of the results that were present in only one gender.

RESULTS

Descriptive statistics of this study population, stratified by study site, are shown in Table I. One case was missing covariate information, so a total of 180 cases were included in analyses. Overall, the distributions of sex, age, education, and race were similar between cases and controls in Seattle. In Detroit, sex and education were similarly distributed between cases and controls but cases were more likely to have been in the middle than the oldest age group and were less likely to have been white than controls.

Occupations

Associations between occupations and the risk of MM are shown in Table II and trends by duration of employment are shown in Table III. Occupation as an engineer (SOC 163) (most were mechanical or electrical engineers) was associated with MM (OR = 3.3, CI = 1.3–8.5) with increasing risk by duration ($P = 0.02$). Work as social, recreation, and

TABLE I. Descriptive Statistics of the Study Population, Stratified by Site

	Seattle		Detroit		Total	
	Cases (n = 58)	Controls (n = 278)	Cases (n = 122)	Controls (n = 203)	Cases (n = 180)	Controls (n = 481)
Male	32 (54%)	144 (52%)	67 (55%)	99 (49%)	99 (55%)	243 (51%)
Female	26 (45%)	134 (48%)	55 (45%)	104 (51%)	81 (45%)	238 (49%)
35–50 years old	10 (17%)	66 (24%)	23 (19%)	44 (22%)	33 (18%)	110 (23%)
51–64 years old	22 (38%)	99 (36%)	55 (45%)	63 (31%)	77 (43%)	162 (34%)
65–74 years old	26 (45%)	113 (41%)	44 (36%)	96 (47%)	70 (39%)	209 (43%)
Only White	52 (90%)	252 (91%)	68 (56%)	147 (72%)	120 (67%)	399 (83%)
Any African American	2 (3.5%)	7 (2.5%)	48 (39%)	54 (27%)	50 (28%)	61 (13%)
Any Asian American	1 (1.7%)	8 (2.9%)	1 (0.8%)	0	2 (1.1%)	8 (1.7%)
Other	3 (5.1%)	11 (4.0%)	5 (4.1%)	2 (1.0%)	8 (4.4%)	13 (2.7%)
<12 years education	7 (12%)	13 (4.7%)	19 (16%)	38 (19%)	26 (14%)	51 (11%)
12–15 years education	27 (47%)	142 (51%)	76 (62%)	107 (53%)	103 (57%)	249 (52%)
16+ years education	24 (41%)	123 (44%)	27 (22%)	58 (29%)	51 (28%)	181 (38%)

TABLE II. Associations Between the Occupation (SOC) and Risk of MM*

Occupation (SOC code)	Controls (n = 481), n (% of controls)	Cases (n = 180), n (% of cases)	OR (95% CI) ^{a,b}
Officials and administrators, other (12)	35 (7.3)	11 (6.1)	0.9 (0.5–2.0)
Officials and administrators, other (13)	32 (6.7)	14 (7.8)	1.5 (0.8–3.0)
Management-related occupations (14)	27 (5.6)	10 (5.6)	1.2 (0.5–2.7)
Engineers, surveyors, and architects (16)	25 (5.2)	12 (6.7)	1.9 (0.9–4.1)
Engineers (163)	12 (2.5)	10 (5.6)	3.3 (1.3–8.5)
Natural scientists (18)	7 (1.5)	2 (1.1)	1.4 (0.3–7.0)
Social, recreation, and religious workers (20)	4 (0.8)	7 (3.9)	5.9 (1.5–22)
Teachers, postsecondary institutions (22)	9 (1.9)	5 (2.8)	1.5 (0.5–5.2)
Teachers, except postsecondary institutions (23)	42 (8.7)	11 (6.1)	0.9 (0.4–1.9)
Librarians, archivists, and curators (25)	5 (1.0)	3 (1.7)	3.3 (0.7–15)
Physicians and dentists (26)	4 (0.8)	1 (0.6)	1.4 (0.1–13)
Registered nurses (29)	13 (2.7)	7 (3.9)	2.4 (0.9–6.8)
Writers, artists, performers, and related workers (32)	18 (3.7)	5 (2.8)	1.0 (0.3–2.8)
Editors, reporters, public relations specialists (33)	5 (1.0)	2 (1.1)	1.8 (0.3–10)
Health technologists and technicians (36)	13 (2.7)	4 (2.2)	0.7 (0.2–2.3)
Engineering and related technologists and technicians (37)	10 (2.1)	3 (1.7)	0.7 (0.2–2.8)
Technicians, except health, engineering, or science (39)	9 (1.9)	2 (1.1)	0.7 (0.2–3.6)
Supervisors, marketing, and sales occupations (40)	18 (3.7)	8 (4.4)	1.6 (0.7–3.8)
Insurance, securities, real estate, and business service sales occupations (41)	9 (1.9)	9 (5.0)	4.2 (1.5–11)
Insurance, real estate, and securities sales occupations (412)	7 (1.5)	6 (3.3)	3.4 (1.0–11)
Sales occupations, commodities except retail (42)	15 (3.1)	6 (3.3)	1.3 (0.5–3.5)
Sales occupations, retail (43)	64 (13)	26 (14)	1.4 (0.8–2.4)
Sales-related occupations (44)	4 (0.8)	2 (1.1)	1.8 (0.3–11)
Supervisors: administrative support occupations (45)	8 (1.7)	4 (2.2)	1.3 (0.4–4.6)
Administrative support occupations (46)	178 (37)	54 (30)	1.2 (0.8–1.9)
Information clerks (464)	2 (0.4)	6 (3.3)	8.2 (1.5–46)
Administrative support occupations (47)	56 (12)	24 (13)	1.2 (0.7–2.0)
Private household occupations (50)	11 (2.3)	7 (3.9)	1.9 (0.7–5.4)
Protective service occupations (51)	10 (2.1)	2 (1.1)	0.6 (0.1–2.7)

TABLE II. (Continued)

Occupation (SOC code)	Controls (n = 481), n (% of controls)	Cases (n = 180), n (% of cases)	OR (95% CI) ^{a,b}
Service occupations, except private household or protective (52)	77 (16)	45 (25)	1.9 (1.2–3.0)
Food and beverage preparation and service occupations (521)	41 (8.5)	20 (11)	2.0 (1.1–3.8)
Personal service occupations (525) ^c	9 (1.9)	9 (5.0)	2.5 (0.9–7.0)
Farm operators and managers (55) ^c	3 (0.6)	1 (0.6)	
Other agricultural and related occupations (56) ^c	15 (3.1)	6 (3.3)	0.9 (0.3–2.6)
Mechanics and repairers (61)	44 (9.2)	16 (8.9)	1.0 (0.5–1.9)
Construction trades (64) ^c	39 (8.1)	13 (7.2)	0.8 (0.4–1.7)
Painters, paperhangers, and plasterers (644) ^c	3 (0.6)	3 (1.7)	3.6 (0.7–19)
Precision production occupations (68)	17 (3.5)	10 (5.6)	1.5 (0.6–3.6)
Plant and system operators (69)	1 (0.2)	5 (2.8)	8.0 (0.9–72)
Supervisors: production operators (71)	0	5 (2.8)	NA
Machine operators and tenders: metal and plastic processing (75)	23 (4.8)	16 (8.9)	1.6 (0.8–3.4)
Metalworking and plastic working machine operators and tenders (751) ^c	18 (3.7)	9 (5.0)	1.1 (0.5–2.6)
Machine operators and tenders: not elsewhere classified (76)	29 (6.0)	22 (12)	1.8 (1.0–3.3)
Woodworking machine operators and tenders (763) ^c	6 (1.3)	0	NA
Textile, apparel, and furnishing machine operators and tenders (765)	4 (0.8)	9 (5.0)	6.0 (1.7–21)
Fabricators, assemblers, and hand working occupations (77)	43 (8.9)	22 (12)	0.9 (0.5–1.7)
Production inspectors, testers, samplers, and weighers (78)	15 (3.1)	11 (6.1)	1.7 (0.7–3.9)
Supervisors: transportation and material moving occupations (81)	3 (0.6)	3 (1.7)	2.6 (0.4–15)
Transportation occupations (82)	45 (9.4)	22 (12)	1.3 (0.7–2.3)
Material moving occupations, except transportation (83)	16 (3.3)	11 (6.1)	1.6 (0.7–3.7)
Handlers, equipment cleaners, and laborers (87)	50 (10)	21 (12)	1.1 (0.6–2.0)
Military occupations (91)	19 (4.0)	7 (3.9)	0.7 (0.3–1.8)
No jobs outside home	67 (14)	10 (5.6)	0.2 (0.1–0.4)

^aOdds ratios and 95% confidence intervals are shown only for two-digit SOC codes with at least five exposed participants and the three-digit codes that were statistically significant with at least five exposed participants or were significantly associated with incident MM in at least two prior studies.

^bOR (95% CI) = odds ratios and 95% confidence intervals, adjusted for age, gender, race, education, and study site.

^cReference group consists of participants who were never employed in each SOC.

^dSOC code was significantly associated with incident MM in at least two prior studies.

religious workers (SOC 20) was also significantly associated with MM (OR = 5.9, CI = 1.5–22) and showed increasing risk by duration ($P = 0.02$).

Several typically “office” occupations were significantly associated with increased risk of MM, including insurance, securities, real estate, and business service sales occupations (SOC 41) (OR = 4.2, CI = 1.5–11), insurance, real estate, and securities sales occupations (SOC 412) (OR = 3.4, CI = 1.0–11), and information clerks (SOC 464) (OR = 8.2, CI = 1.5–46). All showed trends of increasing risk by duration of employment ($P = 0.01$, 0.08, and 0.08, respectively).

Persons employed in service occupations, except private household or protective (SOC 52), were at increased risk of MM (OR = 1.9, CI = 1.2–3.0), with a trend of increasing risk by duration of employment ($P = 0.001$). Within this SOC, food and beverage preparation occupations (SOC 521) were at increased risk of MM (OR = 2.0, CI = 1.1–3.8; P -trend by

duration = 0.05). Most people in SOC 521 were waiters and waitresses, bartenders, or cooks. This association was only seen among Detroit participants and was only observed in women.

Machine operators and tenders, not elsewhere classified (SOC 76), particularly textile, apparel, and furnishing machine operators and tenders (SOC 765), were at increased risk of MM (OR for SOC 76 = 1.8, CI = 1.0–3.3; for SOC 765 OR = 6.0, CI = 1.7–21, P -trend by duration = 0.07 and 0.01, respectively). Most of the participants in SOC 765 were textile sewing machine operators, pressing machine operators, or laundering and dry cleaning machine operators and tenders. Other job titles within machine operators and tenders included woodworking, printing press, and boiler machine operators and tenders.

Two occupations that we hypothesized to be associated with increased risk of MM, based on previous studies, showed elevated, but not statistically significant, associa-

TABLE III. Associations Between Selected Occupations (SOC) and Risk of MM by Duration of Job*

Occupation (SOC code)	Jobs held 1–5 years			Jobs held more than 5 years			P-value of trend
	n (% of controls) (n = 481)	n (% of cases) (n = 180)	OR (95% CI) ^{a,b}	n (% of controls) (n = 481)	n (% of cases) (n = 180)	OR (95% CI) ^{a,b}	
Engineers, surveyors, and architects (16)	7 (1.5)	1 (0.6)	0.5 (0.1–4.3)	18 (3.7)	11 (6.1)	2.5 (1.1–5.8)	0.03
Engineers (163)	5 (1.0)	3 (1.7)	2.6 (0.6–12)	7 (1.5)	7 (3.9)	3.7 (1.2–12)	0.02
Social, recreation, and religious workers (20)	2 (0.4)	2 (1.1)	4.6 (0.6–37)	2 (0.4)	5 (2.8)	7.0 (1.2–40)	0.02
Librarians, archivists, and curators (25)	1 (0.2)	1 (0.6)	5.8 (0.3–99)	4 (0.8)	2 (1.1)	2.7 (0.5–16)	0.22
Registered nurses (29)	2 (0.4)	0		11 (2.3)	7 (3.9)	3.0 (1.0–8.6)	NA
Insurance, securities, real estate, and business service sales occupations (41)	3 (0.6)	3 (1.7)	3.4 (0.6–20)	6 (1.3)	6 (3.3)	4.5 (1.4–15)	0.01
Insurance, real estate, and securities sales occupations (412)	1 (0.2)	2 (1.1)	6.2 (0.5–76)	6 (1.3)	4 (2.2)	3.0 (0.8–12)	0.08
Sales occupations, retail (43)	39 (8.1)	19 (11)	1.8 (0.9–3.2)	25 (5.2)	7 (3.9)	0.9 (0.4–2.3)	0.73
Information clerks (464)	1 (0.2)	4 (2.2)	12 (1.0–140)	1 (0.2)	2 (1.1)	7.6 (0.6–98)	0.08
Service occupations, except private household or protective (52)	45 (9.4)	18 (10)	1.3 (0.7–2.5)	32 (6.7)	27 (15)	2.7 (1.5–4.9)	0.001
Food and beverage preparation and service occupations (521)	25 (5.2)	11 (6.1)	1.9 (0.9–4.3)	16 (3.3)	9 (5.0)	2.2 (0.9–5.5)	0.05
Personal service occupations (525)	7 (1.5)	2 (1.1)	0.6 (0.1–3.2)	2 (0.4)	7 (3.9)	9.2 (1.8–48)	0.01
Painters, paperhangers, and plasterers (644)	1 (0.2)	3 (1.7)		2 (0.4)	0		NA
Plant and system operators (69)	0	0		1 (0.2)	5 (2.8)	8.0 (0.9–72)	NA
Machine operators and tenders: not elsewhere classified (76)	14 (2.9)	9 (5.0)	1.5 (0.6–3.7)	15 (3.1)	13 (7.2)	2.0 (0.9–4.5)	0.07
Textile, apparel, and furnishing machine operators and tenders (765)	3 (0.6)	4 (2.2)	3.6 (0.7–17)	1 (0.2)	5 (2.8)	12 (1.3–110)	0.01
Supervisors: transportation and material moving occupations (81)	2 (0.4)	0		1 (0.2)	3 (1.7)	7.6 (0.6–90)	NA

*Odds ratios and 95% confidence intervals are shown only for SOC codes that were statistically significant or had ORs ≥ 2.0 or ≤ 0.5 in the initial analyses.

^aOR (95% CI) = odds ratios and 95% confidence intervals, adjusted for age, gender, race, education, and study site.

^bReference group consists of participants who were never employed in each SOC.

tions: painters, paperhangers, and plasterers (SOC 644) (OR = 3.6, CI = 0.7–19; n = 3 exposed cases and 3 exposed controls; all were men) and personal service occupations (SOC 525) (OR = 2.5, CI = 0.9–7.0; n = 9 exposed cases and 9 exposed controls, driven by an association among Detroit participants only). Included in SOC 525 were barbers, hairdressers, and cosmetologists; amusement and recreational facilities attendants; ushers; and public transportation attendants. All of the barbers and hairdressers or cosmetologists (n = 4) were cases. We did not observe an increased risk between MM and agricultural occupations (SOCs 551 and 561), based on four cases and seven controls who reported working in agricultural occupations.

We detected an inverse association for the development of MM with never having been employed outside of the home (OR = 0.2, CI = 0.1–0.4). Most of these subjects were female (69%), residents of the Detroit metropolitan area (96%), and white (77%). People who did not report employment outside the home tended to be in the higher categories of education: 38% reported more than 16 years education.

Industries

Analyses of associations between employment in specific industries and risk of MM are shown in Table IV and analyses by duration are shown in Table V. Participants who reported employment in the food and kindred products industry (SIC 20) were at increased risk of MM (OR = 4.5, CI = 1.6–13) with a trend by duration ($P = 0.03$). Most of these were involved in food packaging, processing, or distribution.

Increased risk of MM was seen for several manufacturing industries, including stone, clay, and glass products (SIC 32) (OR = 12, CI = 1.2–126 (not shown), n = 3 exposed cases and 1 exposed control; unable to assess trend because of empty cells), machinery manufacturing, except electrical (SIC 35) (OR = 3.3, CI = 1.7–6.7; P -trend by duration = 0.0004), metalworking machinery manufacturing (SIC 354) (OR = 5.5, CI = 1.3–23; P -trend = 0.05), and guided missiles, space vehicles, and parts (SIC 376) (OR = 4.9, CI = 1.6–15; P -trend = 0.004).

TABLE IV. Associations Between the Industry (SIC) and Risk of MM*

Industry (SIC code)	Controls (n = 481), n (% of controls)	Cases (n = 180), n (% of cases)	OR (95% CI) ^{a,b}
Agricultural production—crops (01) ^c	7 (1.5)	3 (1.7)	0.8 (0.2–3.8)
Agricultural production—livestock (02) ^c	2 (0.4)	2 (1.1)	
Agricultural services (07)	9 (1.9)	3 (1.7)	1.1 (0.3–4.3)
General building contractors (15)	26 (5.4)	11 (6.1)	1.2 (0.6–2.7)
Heavy construction contractors (16)	12 (2.5)	5 (2.8)	0.8 (0.3–2.6)
Special trade contractors (17)	24 (5.0)	9 (5.0)	1.1 (0.5–2.5)
Food and kindred products (20)	8 (1.7)	9 (5.0)	4.5 (1.6–13)
Apparel and other textile products (23)	4 (0.8)	3 (1.7)	2.1 (0.4–9.9)
Lumber and wood products (24) ^c	14 (2.9)	1 (0.6)	0.3 (0.03–2.0)
Paper and allied products (26)	7 (1.5)	4 (2.2)	1.9 (0.5–6.7)
Printing and publishing (27)	20 (4.2)	4 (2.2)	0.7 (0.2–2.0)
Chemicals and allied products (28)	12 (2.5)	5 (2.8)	1.1 (0.4–3.4)
Primary metal industries (33) ^c	12 (2.5)	9 (5.0)	1.6 (0.6–4.1)
Fabricated metal products manufacturing (34) ^c	13 (2.7)	6 (3.3)	1.3 (0.5–3.6)
Machinery manufacturing, except electrical (35)	18 (3.7)	21 (12)	3.3 (1.7–6.7)
Metalworking machinery manufacturing (354)	3 (0.6)	7 (3.9)	5.5 (1.3–23)
Electric and electronic equipment manufacturing (36)	26 (5.4)	12 (6.7)	1.3 (0.6–2.8)
Transportation equipment manufacturing (37)	107 (22)	51 (28)	1.1 (0.7–1.6)
Guided missiles, space vehicles, and parts manufacturing (376)	7 (1.5)	7 (3.9)	4.9 (1.6–15)
Instruments and related products manufacturing (38)	13 (2.7)	2 (1.1)	0.5 (0.1–2.2)
Local and interurban passenger transportation (41)	4 (0.8)	2 (1.1)	0.8 (0.1–5.0)
Trucking and warehousing (42)	13 (2.7)	7 (3.9)	1.5 (0.6–4.0)
US Postal Service (43)	5 (1.0)	4 (2.2)	3.3 (0.8–14)
Water transportation (44)	6 (1.3)	2 (1.1)	1.0 (0.2–5.2)
Transportation by air (45)	5 (1.0)	3 (1.7)	1.7 (0.4–7.9)
Transportation services (47)	1 (0.2)	4 (2.2)	17 (1.8–160)
Communication (48)	12 (2.5)	4 (2.2)	1.0 (0.3–3.2)
Electric, gas, and sanitary services (49)	8 (1.7)	8 (4.4)	1.6 (0.6–4.6)
Wholesale trade-durable goods (50)	13 (2.7)	6 (3.3)	1.5 (0.5–4.1)
Wholesale trade-non-durable goods (51)	9 (1.9)	4 (2.2)	1.2 (0.3–4.4)
Building materials and garden supplies (52)	8 (1.7)	1 (0.6)	0.4 (0.1–3.6)
General merchandise stores (53)	39 (8.1)	15 (8.3)	1.4 (0.7–2.7)
Food stores (54)	33 (6.9)	10 (5.6)	0.8 (0.4–1.8)
Automotive dealers and services (55)	22 (4.6)	12 (6.7)	1.7 (0.8–3.6)
Apparel and accessories stores (56)	9 (1.9)	2 (1.1)	0.7 (0.1–3.6)
Furniture and home furnishings (57)	6 (1.3)	2 (1.1)	1.0 (0.2–5.6)
Eating and drinking places (58)	38 (7.9)	18 (10)	2.0 (1.0–3.7)
Miscellaneous retail (59)	24 (5.0)	12 (6.7)	2.0 (0.9–4.3)
Banking (60)	17 (3.5)	8 (4.4)	1.6 (0.7–4.0)
Credit agencies other than banks (61)	5 (1.0)	1 (0.6)	0.6 (0.1–5.2)
Security and commodity brokers and dealers (62)	3 (0.6)	2 (1.1)	2.3 (0.3–15)
Insurance carriers (63)	23 (4.8)	10 (5.6)	1.2 (0.5–2.7)
Real estate (65)	14 (2.9)	8 (4.4)	2.1 (0.8–5.2)
Hotels and other lodging places (70)	6 (1.3)	4 (2.2)	2.6 (0.7–10)
Personal services (72)	19 (4.0)	11 (6.1)	1.6 (0.7–3.6)
Business services (73)	31 (6.4)	10 (5.6)	1.1 (0.5–2.3)
Auto repair, services, and garages (75)	4 (0.8)	6 (3.3)	3.8 (1.0–15)
Miscellaneous repair services (76)	5 (1.0)	1 (0.6)	0.4 (0.04–3.7)
Amusement and recreation services (79)	15 (3.1)	6 (3.3)	1.0 (0.3–2.6)

(Continued)

TABLE IV. (Continued)

Industry (SIC code)	Controls (n = 481), n (% of controls)	Cases (n = 180), n (% of cases)	OR (95% CI) ^{a,b}
Health services (80)	46 (9.6)	31 (17)	2.3 (1.4–4.1)
Nursing and personal care, NEC (805)	3 (0.6)	6 (3.3)	5.3 (1.2–24)
Hospitals (806)	25 (5.2)	21 (12)	2.7 (1.4–5.3)
Educational services (82)	92 (19)	39 (22)	1.6 (1.0–2.6)
Schools and educational services, NEC (829)	4 (0.8)	4 (2.2)	4.2 (1.0–19)
Social services (83)	13 (2.7)	7 (3.9)	1.6 (0.6–4.5)
Membership organizations (86)	11 (2.3)	7 (3.9)	2.0 (0.7–5.5)
Religious organizations (866)	4 (0.8)	6 (3.3)	5.2 (1.3–20)
Research and testing services (87)	6 (1.3)	1 (0.6)	0.7 (0.1–6.4)
Private households (88)	11 (2.3)	6 (3.3)	1.7 (0.6–5.1)
Miscellaneous services (89)	13 (2.7)	8 (4.4)	1.8 (0.7–4.6)
Executive, legislative, and general government offices (91)	13 (2.7)	4 (2.2)	0.7 (0.2–2.4)
Justice, public order, and safety (92)	15 (3.1)	2 (1.1)	0.4 (0.1–2.0)
Administration of human resources (94)	3 (0.6)	4 (2.2)	4.2 (0.8–22)
Environmental quality and housing (95)	4 (0.8)	1 (0.6)	0.7 (0.1–7.0)
Administration of economic programs (96)	4 (0.8)	3 (1.7)	1.8 (0.4–8.5)
National security and international affairs (97)	88 (18)	31 (17)	0.9 (0.5–1.5)
Unknown (99)	45 (9.4)	6 (3.3)	0.5 (0.2–1.2)

^aOdds ratios and 95% confidence intervals are shown only for two-digit SOC codes with at least five exposed participants and the three-digit codes that were statistically significant with at least five exposed participants or were significantly associated with incident MM in at least two prior studies.

^bOR (95% CI) = odds ratios and 95% confidence intervals, adjusted for age, gender, race, education, and study site.

^cReference group consists of participants who were never employed in each SIC.

^dSIC code was significantly associated with incident MM in at least two prior studies.

Several service industries were associated with increased risk of MM, including transportation services (SIC 47) (OR = 17, CI = 1.8–160; all were women and this association was observed only in Seattle), eating and drinking places (SIC 58) (OR = 2.0, CI = 1.0–3.7; only observed in women in Detroit), auto repair, services, and garages industry (SIC 75) (OR = 3.8, CI = 1.0–15; all were men), health services (SIC 80) (OR = 2.3, CI = 1.4–4.1), nursing and personal care, not elsewhere classified (SIC 805) (OR = 5.3, CI = 1.2–24; only observed in women), hospitals (SIC 806) (OR = 2.7, CI = 1.4–5.3), educational services (SIC 82) (OR = 1.6, CI = 1.0–2.6), schools and educational services, not elsewhere classified (SIC 829) (OR = 4.2, CI = 1.0–19), and religious organizations (SIC 866) (OR = 5.2, CI = 1.3–20). We were unable to assess whether risk of MM increased by duration in the transportation services and auto repair, services, and garages industries due to empty cells. Suggestive trends by duration of employment were seen for eating and drinking places (SIC 58: $P = 0.04$), real estate (SIC 65: $P = 0.08$), health services (SIC 80: $P = 0.001$; SIC 805: $P = 0.05$; SIC 806: $P = 0.001$), educational services industries (SIC 82: $P = 0.10$; SIC 829: $P = 0.04$), membership organizations (SIC 86: $P = 0.04$), and religious organizations (SIC 866: $P = 0.02$).

DISCUSSION

We examined the risk of MM in relation to 135 occupation codes and 143 industry codes that were reported by at least five participants in our study. The resulting ORs were statistically significant at $P = 0.05$ for 9 of the occupations and 13 of the industries. The risk of MM was associated with several manufacturing occupations and industries, including machine operators and tenders, not elsewhere classified (SOC 76), particularly textile, apparel, and furnishing machine operators and tenders (SOC 765); the machinery manufacturing industry, except electrical (SIC 35), particularly metalworking machinery manufacturing (SIC 354); and manufacturing of guided missiles, space vehicles, and parts (SIC 376). Employment in the food and kindred products industry (SIC 20) was also related to MM. Additionally, we found that employment in several service-related occupations and industries was associated with increased risk of MM, including food and beverage service occupations (SOC 521), eating and drinking places (SIC 58), the auto repair, services, and garages industry (SIC 75), the health services industry (SIC 80), educational services industries (SIC 82), and religious organizations (SIC 866).

People employed as machine operators and tenders or in the machinery, missile, or auto repair industries may be

TABLE V. Associations Between Selected Industries (SIC) and Risk of MM by Duration of Job*

Industry (SIC code)	Jobs held 1–5 years			Jobs held more than 5 years			P-value of trend
	n (% of controls) (n = 481)	n (% of cases) (n = 180)	OR (95% CI) ^{a,b}	n (% of controls) (n = 481)	n (% of cases) (n = 180)	OR (95% CI) ^{a,b}	
Food and kindred products (20)	5 (1.0)	6 (3.3)	4.5 (1.3–16)	3 (0.6)	3 (1.7)	4.3 (0.8–24)	0.03
Apparel and other textile products (23)	3 (0.6)	1 (0.6)	1.2 (0.1–12)	1 (0.2)	2 (1.1)	4.1 (0.4–48)	0.27
Machinery manufacturing, except electrical (35)	7 (1.5)	4 (2.2)	1.7 (0.5–6.2)	11 (2.3)	19 (9.4)	4.4 (1.9–10)	0.0004
Metalworking machinery manufacturing (354)	2 (0.4)	3 (1.7)	3.7 (0.6–24)	1 (0.2)	4 (2.2)	8.6 (0.9–80)	0.05
Guided missiles, space vehicles, and parts manufacturing (376)	3 (0.6)	2 (1.1)	2.5 (0.4–16)	4 (0.8)	5 (2.8)	7.2 (1.8–28)	0.004
US Postal Service (43)	5 (1.0)	2 (1.1)	1.7 (0.3–9.8)	0	2 (1.1)		NA
Transportation services (47)	0	0		1 (0.2)	4 (2.2)	17 (1.8–160)	NA
Eating and drinking places (58)	24 (5.0)	10 (5.6)	1.7 (0.7–3.8)	14 (2.9)	8 (4.4)	2.4 (1.0–6.2)	0.04
Miscellaneous retail (59)	14 (2.9)	9 (5.0)	2.5 (1.0–6.2)	10 (2.1)	3 (1.7)	1.3 (0.3–5.0)	0.31
Security and commodity brokers and dealers (62)	2 (0.4)	1 (0.6)	2.1 (0.2–25)	1 (0.2)	1 (0.6)	2.6 (0.1–46)	0.45
Real estate (65)	6 (1.3)	2 (1.1)	1.2 (0.2–6.3)	8 (1.7)	6 (3.3)	2.7 (0.9–8.4)	0.08
Hotels and other lodging places (70)	1 (0.2)	2 (1.1)	8.4 (0.7–100)	5 (1.0)	2 (1.1)	1.5 (0.3–8.3)	0.53
Auto repair, services, and garages (75)	4 (0.8)	3 (1.7)	2.1 (0.4–11)	0	3 (1.7)		NA
Health services (80)	15 (3.1)	6 (3.3)	1.3 (0.5–3.8)	31 (6.4)	25 (14)	2.8 (1.5–5.3)	0.001
Nursing and personal care, NEC (805)	2 (0.4)	4 (2.2)	4.1 (0.7–25)	1 (0.2)	2 (1.1)	8.9 (0.7–120)	0.05
Hospitals (806)	11 (2.3)	5 (2.8)	1.5 (0.5–4.7)	14 (2.9)	16 (8.9)	3.7 (1.6–8.1)	0.001
Educational services (82)	25 (5.2)	12 (6.7)	1.6 (0.7–3.4)	67 (14)	27 (15)	1.6 (0.9–2.8)	0.10
Schools and educational services, NEC (829)	3 (0.6)	2 (1.1)	2.0 (0.3–14)	1 (0.2)	2 (1.1)	13 (1.1–140)	0.04
Membership organizations (86)	8 (1.7)	2 (1.1)	0.8 (0.2–4.3)	3 (0.6)	5 (2.8)	4.8 (1.1–21)	0.04
Religious organizations (866)	3 (0.6)	2 (1.1)	2.3 (0.3–16)	1 (0.2)	4 (2.2)	13 (1.4–130)	0.02
Administration of human resources (94)	3 (0.6)	2 (1.1)	1.4 (0.2–9.8)	0	2 (1.1)		NA

*Odds ratios and 95% confidence intervals are shown only for SIC codes that were statistically significant or had ORs ≥ 2.0 or ≤ 0.5 in the initial analyses.

^aOR (95% CI) = odds ratios and 95% confidence intervals, adjusted for age, gender, race, education, and study site.

^bReference group consists of participants who were never employed in each SIC.

exposed to a variety of chemicals that may be carcinogenic, such as solvents, cutting oils, metal dusts, and metal fumes [Demers et al., 1993; Baris et al., 2004]. Although the specific occupation “machine operators and tenders, not elsewhere classified” (SOC 76) has not been implicated as a risk factor for MM, similar occupations have been. One population-based case-control study conducted in the US in the 1980s found that heating equipment operators (SOC 7544) had an elevated risk of MM (OR = 4.7, 95% CI = 1.4–15.8) [Baris et al., 2004]; however, the similarity of exposures between this particular job and the jobs within the SOC 76 grouping in our study is unclear. Within this occupational category, we saw a particularly high risk of MM in textile, apparel, and furnishing machine operators and tenders. Participants in this occupation who were involved in dry cleaning (five cases and three controls) were likely exposed to solvents, particularly the chlorinated solvent perchloroethylene (PCE), especially since the 1970s [Gold et al., 2008]. Although few studies have examined the association between PCE and MM, an elevated risk was found in a cohort of exposed workers at an Air Force Base [Spirtas et al., 1991] and other chlorinated solvents have also been associated with MM [Spirtas et al., 1991; Anttila et al., 1995; Blair et al., 1998]. Further

investigation is warranted in order to fully evaluate the relationship between MM and exposures encountered in machine-related occupations, including chlorinated solvents, other solvents, cutting oils, and metals.

We observed increased risks associated with several service-related occupations and industries, such as food preparation, health services, and educational services. These jobs often entail exposure to the public. A hypothesized mechanism by which exposure to the public may contribute to MM risk is through transmission of oncogenic infections. Several widespread viruses, including hepatitis C [Montella et al., 2001; Duberg et al., 2005], Epstein-Barr [Csire et al., 2007], and human herpes virus-8 [Csire et al., 2007] have been associated with MM, possibly because they allow B-cell proliferation which could lead to the cancer [Vineis, 1996; Dal Maso and Franceschi, 2006]. Some previous studies have reported associations between MM and occupations that involve exposure to the public, including service occupations (including waiters and waitresses) and teachers [Robinson and Walker, 1999; Baris et al., 2004; Svec et al., 2005]. Nevertheless, the service-related jobs and industries associated with MM in our study were diverse and many would entail exposures to agents other than to the public.

Additionally, several occupations and industries that are likely to entail exposure to the public, such as management-related occupations (SOC 12), military occupations (SOC 91), apparel and accessories stores (SIC 56), and amusement and recreation services (SIC 79), were not associated with MM in our study. Drawing conclusions about particular exposures that participants with greater than average exposure to the public had that contributed to development of MM is difficult based on occupation/industry title alone.

Although few subjects in our study reported occupation as painters, paperhangers, or plasterers (SOC 644), we did see an elevated risk of MM associated with these jobs, which is in agreement with several studies [Lundberg, 1986; Morris et al., 1986; Cuzick and De, 1988; Bethwaite et al., 1990; Demers et al., 1993; Firth et al., 1993; Lundberg and Milatou-Smith, 1998]. Painters are exposed to a variety of chemicals and chemical mixtures, including organic solvents, pigments, binders, and additives [International Agency for Research on Cancer, 1989; Lundberg and Milatou-Smith, 1998]. Also, all hairdressers were cases, supporting previous findings that this job was related to MM [Guidotti et al., 1982; Spinelli et al., 1984; Miligi et al., 1999].

Our study had several strengths. By including MM cases from two major metropolitan areas with SEER cancer registries, we conducted a relatively large study to examine occupation as a risk factor for MM. Most previous studies to examine this issue have focused on cohorts of workers in certain industries, which is inefficient for a disease as rare as MM. However, our study did have several limitations. Participation rates were relatively low among cases and controls. Although case participation was not associated with age, sex, or study site, control participation did vary by age category and we were not able to assess whether non-participants were similar to participants in terms of race or socioeconomic status indicators, which are closely tied to occupation. This might have led to selection bias and erroneous associations if, for example, controls in certain jobs (e.g., industrial sector jobs) were less likely to have participated in this study than cases in those jobs. Additionally, a substantial proportion of cases (18%) died before they could be contacted and 29% of those we did contact refused to participate, possibly because they were too ill. Our findings, therefore, might reflect relationships between occupations/industries and less aggressive forms of MM. We cannot rule out the possibility of recall bias affecting our results, in that cases may have been more likely to have reported occupations with potentially carcinogenic exposures than controls as a way of explaining their illnesses. Nevertheless, the ability of subjects to recall their work histories and starting dates has been shown to be accurate in validation studies comparing self-reports to company records [Baumgarten et al., 1983; Stewart et al., 1987; Bourbonnais et al., 1988]. The fact that we saw several associations

between MM and white collar occupations, which probably did not have exposure to carcinogenic substances, further suggests that this type of recall bias was likely to have been minimal in our study.

An inherent limitation of performing an occupation/industry analysis that does not affect the internal validity of our results is that occupation and industry titles are not necessarily indicative of specific exposures that subjects actually had. In order to assess specific occupational exposures, more detailed exposure information must be queried and analyzed. Finally, we examined many occupations and industries so some of our findings are likely to be due to chance. We did not correct our results for multiple comparisons because the purpose of this study was to provide a basis for future studies of more specific exposures. Conversely, this study also had limited power to detect statistically significant results in occupations and industries that were reported by few subjects.

This study was intended to evaluate possible associations between occupations and industries and the risk of MM. We found that several manufacturing and service-related occupations and industries were associated with increased risk of MM and these warrant further evaluation. In agreement with several prior studies, we found a non-significant increase in risk associated with occupation as a painter, paperhanger, or plasterer and an excess of cases among hairdressers. Our ongoing research of this study population includes an evaluation of the relationship between MM and chlorinated solvent exposure, which likely occurred in some of the occupations and industries linked to MM in this study. Future studies should make efforts to pool MM cases across a number of study sites in order to provide adequate power for analyzing specific jobs and exposures that may contribute to the risk of MM.

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