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Risk of multiple myeloma in a case–spouse study

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Abstract

This study examined lifestyle, occupation, medical history and medication use with multiple myeloma risk in a case–spouse study (481 patients, 351 spouses). Odds ratios (ORs) and 95% confidence intervals (CI) were calculated using logistic regression. Compared to spouse controls, cases were more likely to have a family history of multiple myeloma (OR = 2.8, 95% CI = 1.2–6.4) and smoked cigarettes (OR = 1.7, 95% CI = 1.2–2.5), but less likely to have consumed alcohol (OR = 0.6, 95% CI = 0.4–0.9). Nurse/health practitioners (OR = 2.8, 95% CI = 1.3–6.2) and production workers (OR = 3.7, 95% CI = 1.0–13.7) had significantly increased risks; and some occupations linked to diesel exhaust had elevated, but non-significant, risks. History of herpes simplex (OR = 1.7, 95% CI = 1.2–2.4), shingles (OR = 1.7, 95% CI = 1.1–2.7), sexually transmitted diseases (OR = 2.0, 95% CI = 1.0–3.7) and medication allergies (OR = 1.7, 95% CI = 1.2–2.4) were associated with higher risks. Use of angiotensin-converting enzyme inhibitors, anti-convulsants, antidepressants, statins and diuretics were associated with reduced risks. The results are consistent with previous population-based studies and support the utility of patient databanks and spouse controls as a resource in epidemiologic research.

Keywords

Myeloma; epidemiology; case–spouse

[†]Mike Katz, a myeloma patient advocate and educator, passed away on April 26, 2015. He is sorely missed by his family, friends and all who knew him in the myeloma community. This study would not have been possible without Mike's expertise and commitment. A special tribute to Mike can be accessed at *Myeloma Today*, Vol 15 # 3 Summer 2015 (<http://myeloma.org/pdfs/MT153%20Summer%202015.pdf>).

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Introduction

Multiple myeloma is a cancer of the plasma cells, characterized by over-production of monoclonal immunoglobulins. In the US it accounts for 1.3% of all diagnosed cancers and is the second most common hematological malignancy [1]. In regard to mortality, multiple myeloma accounts for 1.9% of all cancer deaths, with an age-adjusted death rate of 3.4 per 100 000 per year between 2006–2010 [1]. Both incidence and mortality rates in the US rose between the 1950s and 1990s, but have been decreasing since then [1]. Decreasing mortality rates are consistent with the increasing survival rates, likely due to improved medical treatments [2], but reasons for the decreasing incidence are unclear.

The etiology of this malignancy remains elusive, yet several risk factors have been identified. Incidence in the US is ~ 1.5-times higher in men than women and ~2-times higher in blacks than whites [3]. Obesity is one of the most consistently reported modifiable risk factors [4] and there is evidence suggesting that alcohol consumption may be linked with a reduced risk [4]. Suspected risk factors include immune-stimulating conditions and infections; and studies of occupational exposures have reported positive associations with ionizing radiation, pesticides and engine exhaust [4].

To further explore the etiology of this malignancy, we examined demographic and lifestyle factors, occupation, medical history and prior medication use in a case–spouse study. We utilized a unique multiple myeloma databank to identify cases and spouse controls as a practical alternative to a population-based study [5–7].

Materials and methods

Study design and population

Data for this study were obtained from the *Bank On A Cure*® initiative, which was funded by the International Myeloma Foundation and started in 2003 to establish a databank with the purpose of studying environmental and genetic risk factors for multiple myeloma [8]. As part of this initiative, a case–spouse study was designed; cases were collected in collaboration with clinical institutions and a broad awareness campaign within the myeloma community using resources such as Myeloma ListServ (on-line messaging and chat service), myeloma support groups, International Myeloma Foundation's 1-800 hotline, patient and family seminars and newsletter announcements. Patients were invited to participate without any commentary about risks factors to be assessed. Controls were spouses of the identified cases. All participants were US residents, representing 47 states, with the largest number coming from California (17.1% cases), Florida (7.3% cases) and Texas (6.9% cases).

A total of 952 multiple myeloma patients were identified and were asked to complete a self-administered questionnaire eliciting information on demographic characteristics, lifestyle behaviors, medical history, medication use and occupation. Cases and spouses were given essentially the same questionnaire, with a few wording modifications. For example, cases were asked to report information occurring 1 year prior to their multiple myeloma diagnosis, while spouses were asked to report the same information occurring 1 year prior to their

interview date. For all participants, cigarette smoking status was based on ever smoking at least 100 cigarettes and alcohol consumption was based on drinking at least 12 drinks per year of beer, wine or liquor. Family medical history was limited to first-degree blood relatives. Participants were asked to report their usual occupation and if they had worked for 12 months or longer in selected jobs having diesel exhaust exposure (truck/bus/taxi driver, operator of heavy equipment, vehicle/machinery mechanic, construction/dock/warehouse/railroad worker or gas station attendant). Usual occupation was coded according to the standard occupational classification (SOC) systems at the two-digit level [9], but jobs linked to diesel exhaust were not classified into SOC groups. For personal medical history, participants were asked if they had been diagnosed as an adult (at least 21 years) with various viral and bacterial infections, chronic conditions, allergies or had received certain vaccinations. Participants were also asked to report medications they had taken at least once per day for 6 months or longer.

Of the 952 multiple myeloma patients, 481 returned the questionnaire (51% case response rate). Among the 466 patients who did not return the questionnaire, 75 were deceased and 77 were returned-to-sender, leaving 314 (33%) non-responders. A separate questionnaire was also mailed to all identified cases to be completed by their spouses. A total of 351 spouses completed a questionnaire. Three spouses of deceased cases completed a questionnaire, leaving 348 couples who completed their respective questionnaires. We estimate that 72% ($n = 685$) of patients were married based on the ratio: 348 couples/481 responding patients = 0.72; this corresponds to an approximate spouse response rate of 51% (348 responding spouses/685 eligible spouses).

Statistical analysis

The risk of multiple myeloma was assessed by calculating odds ratios (ORs) and 95% confidence intervals (CI) using unconditional logistic regression. We examined the risk of multiple myeloma in relation to selected characteristics including, gender, age at interview (<50, 50–59, 60–69, 70 years), race (white, black, other), education (high school or less, vocational, college, more than college), cigarette smoking (never, ever, former, current) and alcohol drinking (never, ever, former, current), body mass index (BMI; calculated from self-reported height and usual weight (< 18.5, 18.5–24.9, 25–29.9, 30 kg/m²) and family history of any cancer and multiple myeloma, adjusting for gender and age group (using age at diagnosis for cases and age at interview for controls). We also examined the associations for 27 occupations and jobs linked with diesel exhaust exposure. In relation to medical conditions we examined the risks associated with seven viral and 11 bacterial diseases, four chronic conditions, six allergies and 10 vaccinations. We also examined the risks associated with use of 30 medications. Risk estimates for occupation, medical condition and medication use were initially adjusted for gender, age (diagnosis age for cases and interview age for controls), race, education, cigarette smoking, alcohol drinking, BMI and family history of multiple myeloma; but final models only included gender, age, race, education and BMI, as these factors resulted in a 10% or more change in risk estimates using likelihood regression.

To evaluate potential survival and/or recall bias we conducted a stratified analysis among cases who completed the questionnaire within 4 years of diagnosis and 5 or more years after diagnosis. Among the cases, the median time between multiple myeloma diagnosis and interview was 5.6 years, with a range between 1–29 years. We also evaluated potential survival bias by conducting a stratified analysis by multiple myeloma relapse status (yes/no) since those that suffered a relapse may be more ill or could have survived longer. We also examined multiple myeloma risks restricted to the 348 case–spouse pairs with complete questionnaires to see if the patterns of association were different from the entire study population. The case–spouse analysis was conducted using conditional logistic regression matched by couple status. Both of these sensitivity analyses were adjusted for the same factors as the main analyses. In all analyses, missing data were excluded from the models.

Results

Fifty-one per cent of the cases, vs 44% of the spouse controls were men. Men had a 50% (95% CI = 1.12–2.04) higher risk of multiple myeloma than women [Table I]. Age of multiple myeloma diagnosis ranged between 24–81 years, with a mean of 59 years. The mean age at interview was 65 years among cases and 64 years among controls. Although not statistically significant, black participants had a slightly higher risk compared to whites (OR = 1.25, 95% CI = 0.38–4.07) and those with more than a college degree had a higher risk than those with a high school degree or less (OR = 1.23, 95% CI = 0.82–1.84). Cigarette smoking was associated with an increased risk for those who ever smoked (OR = 1.74, 95% CI = 1.22–2.47) and those who formerly smoked (OR = 1.95, 95% CI = 1.34–2.84), but not for those who were current smokers at interview (OR = 0.81, 95% CI = 0.35–1.89). Alcohol drinking was associated with a reduced risk for those who ever drank (OR = 0.62, 95% CI = 0.43–0.89) and those who were current drinkers (OR = 0.58, 95% CI = 0.40–0.84), but not for former drinkers (OR = 1.45, 95% CI = 0.69–2.05). We also saw a non-significant, but monotonic increase in risk with higher BMI (p -trend = 0.17), with obese participants (BMI 30 kg/m²) having a 30% higher risk than those with a normal BMI (18.5–24.9 kg/m²). Participants reporting any cancer diagnosis in a first-degree family member had a 1.35-fold (95% CI = 0.99–1.85) risk and those with multiple myeloma in a first-degree family member had a 2.76-fold (95% CI = 1.19–6.40) risk.

Table II shows the associations between usual occupation and multiple myeloma adjusted for gender, age, race, education and BMI. Two occupation groups showed statistically significant increased risks: Nurse, Health Practitioner (SOC 28–29) (OR = 2.80, 95% CI = 1.25–6.23) and Production Workers (e.g. inspector, precision worker, machine/plant/system operator, assembler, fabricator) (SOC 68–71) (OR = 3.71, 95% CI = 1.01–13.70). We observed a 50% higher, although non-significant (95% CI = 0.92–2.42), risk for persons working in occupations linked with diesel exhaust. Within this occupational group we saw non-significant elevated risks for railroad workers, vehicle mechanics, gas station attendants, dock/warehouse workers and machinery mechanics, but null associations for taxi/bus/truck drivers, equipment operators and construction workers. We also saw a non-significant higher risk for Computer, Mathematical, Operations Researchers (SOC = 17) (OR = 2.92, 95% CI = 0.76–11.19) and lower risks for Writers/Editors (SOC = 32–33) (OR = 0.46, 95% CI = 0.20–1.06) and Housewives (SOC = 99) (OR = 0.50, 95% CI = 0.24–1.06).

Associations between selected medical conditions and the risk of multiple myeloma adjusted for sex, age, race, education and BMI are shown in Table III. Of the 28 medical conditions examined, we found statistically significant excess risks of multiple myeloma among subjects with a history of two viral conditions: herpes simplex (OR = 1.67, 95% CI = 1.15–2.41) and shingles (OR = 1.67, 95% CI = 1.05–2.66). One infectious condition, sexually transmitted disease (gonorrhea, syphilis, chlamydia, genital warts) (OR = 1.95, 95% CI = 1.02–3.73) was significantly associated with multiple myeloma and two bacterial conditions were borderline significant, bronchitis (OR = 1.37, 95% CI = 0.99–1.89) and pneumonia (OR = 1.44, 95% CI = 0.99–2.09). One chronic disease, diabetes, showed a borderline significant reduced risk (OR = 0.49, 95% CI = 0.24–1.01). Allergies to medications were significantly associated with excess risk (OR = 1.73, 95% CI = 1.22–2.44), while allergies to animals were associated with a significant reduced risk (OR = 0.60, 95% CI = 0.38–0.94). Vaccination to Hepatitis B was associated with a significant reduced risk (OR = 0.63, 95% CI = 0.41–0.96), while vaccinations to polio, tetanus and tuberculosis were associated with non-significant increased risks.

Of the 30 medications examined, five were significantly associated with a reduced risk of multiple myeloma adjusting for sex, age, race, education and BMI [Table IV]: angiotensin-converting enzyme (ACE) inhibitor (OR = 0.40, 95% CI = 0.23–0.70), diuretic (OR = 0.37, 95% CI = 0.20–0.68), antidepressant (OR = 0.47, 95% CI = 0.29–0.77), anti-lipemic (OR = 0.43, 95% CI = 0.25–0.76) and anti-convulsant (OR = 0.32, 95% CI = 0.11–0.94). Borderline significant associations were seen for anti-asthma (OR = 0.40, 95% CI = 0.23–0.70) and for antibiotic medications (OR = 2.68, 95% CI = 0.85–8.43).

In the sensitivity analyses we found the same patterns of association for lifestyle factors, occupation, medical history and medication use in men and women separately (data not shown). We also found no measureable differences in the patterns of associations between cases who completed the questionnaire within 4 years or 5 or more years after their multiple myeloma diagnosis [Supplemental Table 1; see <http://dx.doi.org/10.3109/10428194.2015.1094693>]. Furthermore, there were no differences between patients who suffered a relapse of multiple myeloma (37%) and those who did not (data not shown). Finally, when the analysis was restricted to the 348 patient-spouse pairs, the associations were not measurably changed [Supplemental Table 2].

Discussion

In this case–spouse study we found significantly higher risks of multiple myeloma for men, cigarette smokers and those with a family history of multiple myeloma, while significantly lower risks were seen for those who consumed alcohol. Excess risks were observed for nurse/health practitioner, production worker and some jobs linked with diesel exhaust exposure. Participants who reported a history of herpes simplex, shingles and medication allergies had higher risks, while those with animal allergies and hepatitis B vaccine had lower risks. We also found lower risks associated with regular use of angiotensin-converting enzyme inhibitors, diuretics, antidepressants, anti-lipemic and anti-convulsant medications.

Our findings for demographic and lifestyle factors generally agreed with results from previous studies. Higher risks of multiple myeloma among men have been consistently reported across studies [4]. Also, one of the highest risks we observed was for family history of multiple myeloma, which has been reported in several studies [4]. The familial aggregation of multiple myeloma has been attributed to both genetic susceptibility and shared environmental exposures [4]. To date some of the strongest and consistent genetic associations have been in genes regulating immune response and inflammation [4]. Our finding for an increased risk among smokers is consistent with a cohort study of Seventh Day Adventists that found excess risks among former smokers [10] and in two case-control studies [11,12]. However, several cohort studies [13–16], two meta-analyses [17,18], and a pooled analysis [19] reported null associations. While smoking is not considered a strong risk factor for hematologic malignancies, some suggestions have been made that smoking may be linked to an up-regulation of anti-inflammatory cytokines and impairment of cellular immunity [20]. Smoking may also suppress apoptosis in cancer cells and lead to chromosomal aberrations [21]. In contrast to smoking, we found a decreased risk associated with ever and current alcohol drinking. This is consistent with a pooled analysis of six case-control studies [22] and two cohort studies [23,24]. It has been suggested that light-to-moderate alcohol intake may attenuate pro-inflammatory cytokines and chemokines that may promote lymphomagenesis [25,26], improve cellular and humoral immune responses and improve DNA repair capacity [27].

Although not statistically significant, we found higher risks among blacks, higher education level and higher BMI; these patterns of association are generally consistent with previous studies [4]. For example, increased risks associated with overweight and obesity have been reported in two meta-analyses [28,29] and cohort studies [30–32]. It is thought that obesity promotes the growth, survival and migration of malignant plasma cells, potentially via reduced adiponectin and pro-inflammatory cytokines and increased insulin-like growth factors [33–35].

For occupation, we found increased risks for nurse/health practitioners and production workers who work in a variety of environments processing products or services and perform such tasks as shipping, assembling, sorting, testing and inspecting. A population-based case-control study using the Surveillance Epidemiology and End Results (SEER) cancer registries in Seattle-Puget sound and Detroit reported a borderline significant 2-fold risk for registered nurses (SOC = 29) and increased, although non-significant, risks for precision production (SOC = 68) and plant and system operators (SOC = 69) [36]. A previous study of cancer mortality among female healthcare workers found a significant 1.3-fold mortality for multiple myeloma among black nurses, but a null association among white nurses [37]. It has been suggested that service-related occupations and industries related to healthcare may have a higher risk due to exposure to viral and bacterial infections [36]. We also found a non-significant excess risk related to diesel exhaust. Some studies have reported a link between diesel exhaust and multiple myeloma [38], yet others are null [39]. While it is established that diesel exhaust contains nitro-PAHs, which are mutagenic and carcinogenic in *in vitro* tests [40–42], the mechanisms that underlie the associations between occupational exposures and multiple myeloma are unclear.

In relation to medical history, we found significant increased risks for two viral infections: herpes zoster (shingles) and herpes simplex (oral or genital herpes). Previous studies of herpes zoster have reported significant [43–46] and non-significant [47,48] increased risks, while others are null [49]. Non-significant increased risks [45,49] and null associations [46] were reported in previous studies of herpes simplex. We also found an increased risk with bacterial sexually transmitted diseases. Lindqvist *et al.* [46] reported a non-significant increased risk with a history of syphilis, but a null association for gonorrhea. We observed borderline significant associations with two other bacterial conditions, bronchitis and pneumonia. Previous studies of pneumonia have shown significant increased risks [45,46,50], whereas the associations for bronchitis were null [49,50]. In our analysis, we only had information on medical conditions occurring 1 year prior to diagnoses and, therefore, could not conduct latency analyses to account for potential disease effect. Previous studies of medical history and multiple myeloma have analyzed latency differently, which may be contributing to some of the variability in results. Furthermore, little is known about the association between prior medical conditions and monoclonal gammopathy of undetermined significance (MGUS), the known precursor to multiple myeloma. Regarding a history of viral and/or bacterial infections, it has been postulated that they could trigger multiple myeloma MGUS by interacting with plasma cell growth, differentiation and survival [45,50,51]. A 2-fold increased risk of MGUS has been linked with bacterial and viral infections, specifically including bacterial pneumonia and herpes zoster in a large population-based study in Sweden [52]. These findings could suggest that such infections are either risk factors for early changes related to MGUS or sequelae of both MGUS and multiple myeloma [52,53].

We also observed a significant increased risk with allergy to medications, but a decreased risk with allergy to animals. Previous studies of allergies and multiple myeloma are inconsistent. Allergies in general were significantly associated with a reduced risk of multiple myeloma in a study of US women [49], but null in a study of US veterans [45]. Few studies of specific allergies and multiple myeloma risk have been reported; however, several studies have examined animal or agricultural exposures and multiple myeloma risks. Results of these studies have also varied [39], with some reporting increased risks [54–56] and others reporting null or decreased risks [43,44,57].

Of the vaccinations we examined, only hepatitis B vaccine was significantly associated with a reduced risk of multiple myeloma. Previous studies of vaccinations and multiple myeloma risk are limited. Prevention of hepatitis B has been linked to decreased incidence of hepatocellular carcinoma worldwide [58], but has not been linked to the prevention of hematological malignancies. In our study we did not see an association between hepatitis and multiple myeloma risk, but a significant association was observed in US male veterans [45] and a non-significant association between hepatitis C and multiple myeloma in a Swedish population [46].

We also found a borderline significant reduced risk of multiple myeloma with a history of diabetes. Previous studies of diabetes and multiple myeloma are limited and contradictory. Khan *et al.* [59] reported no association between self-reported diabetes and multiple

myeloma, while high post-load glucose was associated with increased mortality from multiple myeloma [60].

Of the 30 medications we examined, five were significantly associated with a reduced risk of multiple myeloma. Our finding of a reduced risk associated with anti-lipemic medication is consistent with the results among US women [49]. It has been previously reported that anti-lipemic statin use could stimulate apoptosis of cancer cells [61] and have chemopreventive effects [62]. In addition, anti-lipemic statins have also been linked to less severe bone disease [63], as well as increased bone formation [64]. The mechanism underlying these findings for anti-lipemic medications and multiple myeloma require further investigation. The inverse associations for angiotensin-converting enzyme (ACE) inhibitors, diuretics and antidepressants were null in the Landgren *et al.* [49] study.

Overall, the associations observed in this case–spouse study are generally consistent with previous population-based studies. This provides additional evidence that case–spouse studies are a valid study design producing statistically stable associations [5–7]. Also, it has been reported that case–spouse studies are a time and cost-effective approach compared to population-based studies [65–67]. As epidemiologists are facing increasing challenges (i.e. tighter budgets and lower study participation), utilizing convenience samples, such as spouse controls or existing healthcare administration and patient databases, may be a valuable resource for epidemiologic research. Nevertheless, several potential limitations must be acknowledged.

Selection bias is a possibility due to assortative mating, i.e. selecting a partner with similar phenotypes, such as race, age, weight, education and occupation level [68,69]. Consistent with assortative mating, we saw similar distributions of age, race and education between cases and controls. However, we believe that this created a natural matching effect that reduced potential confounding and could have resulted in an underestimation of multiple myeloma risks. Similarly, a few small clinical studies have reported multiple myeloma in couples [70]. While none of the studies indicate that the incidence is higher among spouses than the general population, they do suggest that a shared non-genetic factor may play a role [70]. Selection bias due to nonresponse among the databank population is also a possibility. However, the non-response rate of 33% in this study is in line with the previous US population-based case-control studies of multiple myeloma [71,72].

As with most retrospective studies, we have to acknowledge the potential for recall bias in using a self-administered questionnaire that was not validated against medical records. Despite this, previous studies have reported that case–spouse studies have less recall bias than population-based studies [65–67]. Survival bias is another possibility if patients who survive longer have different risk factors. The mean age at diagnosis was 59 and 65 at interview, thus our population is relatively young and may survive longer. Also, since 58% of the study population completed the interview 5 or more years after their diagnosis, our cases are largely comprised of patients who have survived longer than an average myeloma patient. Nevertheless, we did not see considerable differences in risks between cases who completed the questionnaire within 4 year of diagnosis or 5 or more years after diagnosis,

nor did we see differences in risk between cases reporting a relapse of multiple myeloma vs those who did not.

While we were able to control for confounding and assess potential interactions, we lacked quantitative information of cigarette smoking and alcohol consumption, as well as duration of occupation, diagnosis dates of medical conditions and duration and quantity of medication use. This limited our ability to assess exposure-response associations and to fully interpret the temporality and strength of the associations. We also did not have information on the types of cancer, except for multiple myeloma, among first-degree family members. Finally, we cannot rule out the potential for chance findings, especially given the large number of factors examined, the small number of participants in certain sub-groups and missing values.

In this study we were able to examine several potential risk factors for multiple myeloma in a unique and relatively large case–spouse population, while adjusting for potential confounding factors. We observed an increased risk of multiple myeloma with family history of multiple myeloma, cigarette smoking and obesity, but a reduced risk with consumption of alcohol. Also, our observations related to medical history support the role of infections in multiple myeloma etiology. Our findings are consistent with those from population based studies and support the utility of existing patient databanks as well as the use of spouse controls as an additional resource in epidemiologic research.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgments

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Table I.

Risk of multiple myeloma in relation to selected characteristics.

Characteristics	Cases ^a	%	Controls ^a	%	OR ^b	95% CI ^b	p-trend ^b
Total	481	100.0	351	100.0	—	—	—
Gender							
Female	229	48.7	194	56.1	1.00	Referent	
Male	241	51.3	152	43.9	1.51	1.12–2.04	—
Age at diagnosis (years)							
<50	76	17.8	—	—	—	—	
50–59	130	30.4	—	—	—	—	
60–69	171	40.0	—	—	—	—	
70	50	11.7	—	—	—	—	—
Age at interview (years)							
< 50	25	6.0	22	6.5	1.00	Referent	
50–59	90	21.6	84	24.7	0.93	0.49–1.77	
60–69	166	39.9	128	37.6	1.11	0.60–2.06	
70	135	32.5	106	31.2	1.04	0.55–1.95	0.65
Race							
White	459	95.6	337	96.0	1.00	Referent	
Black	9	1.9	6	1.7	1.25	0.38–4.07	
Other	12	2.5	8	2.3	0.63	0.22–1.76	—
Highest Education							
High school	105	22.1	90	26.0	1.00	Referent	
Vocational	42	8.8	37	10.7	0.79	0.45–1.40	
College	147	30.9	109	31.5	0.94	0.63–1.41	
>College	182	38.2	110	31.8	1.23	0.82–1.84	0.27
Cigarette smoking ^c							
Never	305	65.2	226	76.1	1.00	Referent	
Ever	163	34.8	71	23.9	1.74	1.22–2.47	
Former	146	31.2	59	19.9	1.95	1.34–2.84	
Current	17	3.6	12	4.0	0.81	0.35–1.89	—

Characteristics	Cases ^a	%	Controls ^a	%	OR ^b	95% CI ^b	p-trend ^b
Alcohol consumption ^d							
No	119	24.8	78	22.4	1.00	Referent	
Yes	360	75.2	270	77.6	0.62	0.43–0.89	
Former	39	8.1	16	4.6	1.45	0.69–2.05	
Current	321	67.0	254	73.0	0.58	0.40–0.84	—
Body Mass Index (BMI) ^e (kg/m ²)							
<18.5	8	1.7	7	2.1	0.69	0.21–2.30	
18.5–24.9	183	40.0	148	44.7	1.00	Referent	
25–29.9	190	41.5	133	40.2	1.16	0.82–1.63	
30	77	16.8	43	13.0	1.30	0.81–2.07	0.17
Family history of cancer ^f							
No	150	32.2	125	37.3	1.00	Referent	
Yes	319	68.5	219	65.4	1.35	0.99–1.85	
Multiple Myeloma	27	8.8	8	3.9	2.76	1.19–6.40	—

^aSub-groups do not equal total numbers due to missing values. Missing values excluded from analyses.

^bAdjusted for gender and age group (interview for controls, diagnosis for cases).

^cEver smoked 100 cigarettes.

^dAt least 12 drinks per year of beer, wine or liquor.

^eCalculated from self-reported height and usual weight prior to diagnosis.

^fSelf-reported cancer diagnosis in first-degree family member.

Table II.

Risk of multiple myeloma in relation to usual occupation.

Occupation group (Standard Occupation Codes)	Cases	Controls	OR ^d	95% CI ^d	p ^a
Nurse, Health practitioner (28,29)	26	10	2.80	1.25–6.23	0.01
Production worker (68–71)	15	3	3.71	1.01–13.70	0.05
Writer, Editor (32,33)	13	14	0.46	0.20–1.06	0.07
Housewife (99)	13	26	0.50	0.24–1.06	0.07
Diesel exhaust ^b	89	45	1.49	0.92–2.42	0.10
Computer, Mathematical, Operations Research (17)	3	13	2.92	0.76–11.19	0.12
Pharmacist, Dietitian, Therapist, Physician Assistant (30)	5	7	0.48	0.14–1.68	0.25
Mechanic, Repairer (61)	9	9	0.56	0.20–1.56	0.26
Transportation (81,82)	7	6	0.53	0.16–1.78	0.31
Sales (40–44)	46	26	1.32	0.77–2.27	0.31
Lawyer, Judge (21)	9	8	0.61	0.22–1.70	0.34
Machine operator and tender, Fabricator (73–77)	5	2	2.30	0.41–12.97	0.35
Physician, Dentist, Veterinarian (26,27)	13	11	0.67	0.27–1.66	0.38
Construction, Handler, Equipment Cleaner, Laborer (64,87)	11	4	1.63	0.47–5.66	0.44
Teacher, Counselor, Librarian (22–25)	66	45	1.15	0.72–1.84	0.57
Technologist, Technician - Other (37–39)	8	8	0.74	0.26–2.12	0.58
Not determined (98)	6	4	1.41	0.36–5.49	0.62
Management (14)	24	18	0.86	0.43–1.69	0.65
Military (91)	4	1	1.61	0.17–15.05	0.68
Scientist - Natural (18)	12	6	1.24	0.42–3.68	0.70
Administrator (11–13)	52	35	0.92	0.57–1.48	0.73
Retired, Disabled, Welfare (95)	2	3	0.73	0.10–5.56	0.76
Private household and protective service (50–52)	19	16	0.90	0.44–1.86	0.78
Scientist - Social (19,20)	13	9	1.11	0.43–2.84	0.83
Technologist, Technician - Health (36)	5	3	1.17	0.27–4.99	0.83
Farm operators, Agriculture, Forestry (55–57)	5	3	0.93	0.21–4.23	0.93
Engineer, Surveyor, Architect (16)	19	45	0.98	0.50–1.90	0.94
Administrative support (45–47)	50	43	1.00	0.62–1.63	0.99

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^a Adjusted for gender, age group (interview for controls, diagnosis for cases), race, education, BMI. Reference groups are those not in each occupation. Missing values excluded from analyses.
^b Vehicle/machinery mechanic, construction/dock/warehouse/railroad worker, gas station attendant.

Table III.

Risk of multiple myeloma in relation to selected medical conditions.

Medical conditions	Cases	Controls	OR ^a	95% CI ^a	p ^a
Viral					
Herpes simplex	131	70	1.67	1.15–2.41	0.01
Shingles	78	40	1.67	1.05–2.66	0.03
Hepatitis	18	15	0.70	0.31–1.55	0.37
Chicken pox	126	93	0.89	0.63–1.26	0.51
Chronic fatigue	11	6	1.41	0.49–4.09	0.53
EBV	34	24	0.87	0.48–1.56	0.63
Genital herpes	26	17	1.11	0.56–2.21	0.77
Bacterial					
Sexually transmitted disease	42	15	1.95	1.02–3.73	0.04
Bronchitis	213	137	1.37	0.99–1.89	0.06
Pneumonia	120	72	1.44	0.99–2.09	0.06
Cold, flu	447	331	1.73	0.72–4.18	0.22
Candidiasis	75	50	1.33	0.83–2.12	0.24
Prostate infection	24	29	0.70	0.36–1.37	0.30
Sinus infection	262	189	1.12	0.81–1.55	0.49
Gallbladder infection	43	30	1.15	0.66–2.01	0.63
Kidney infection	143	125	1.04	0.73–1.49	0.82
Diverticulitis	61	54	1.02	0.65–1.60	0.92
Brain infection	5	4	1.04	0.26–4.23	0.96
Chronic					
Diabetes	22	29	0.49	0.24–1.01	0.05
Asthma	27	33	0.81	0.44–1.47	0.48
Eczema	34	29	0.83	0.47–1.47	0.53
Arthritis	146	132	0.91	0.65–1.28	0.58
Allergies					
Medication	164	94	1.73	1.22–2.44	0.002
Animal	52	56	0.60	0.38–0.94	0.03

Medical conditions	Cases	Controls	OR ^a	95% CI ^a	p ^a
Dust	107	100	0.79	0.55–1.13	0.19
Hay fever	155	123	0.90	0.65–1.26	0.55
Insect	41	36	0.91	0.53–1.55	0.73
Food	68	52	1.05	0.68–1.62	0.84
Vaccinations					
Hepatitis B	78	68	0.63	0.41–0.96	0.03
Polio	173	119	1.35	0.96–1.90	0.09
Tetanus	358	257	1.40	0.92–2.13	0.12
Tuberculosis	306	205	1.30	0.90–1.89	0.17
Measles	81	69	0.90	0.60–1.35	0.60
Mumps	57	48	0.89	0.56–1.43	0.64
Rubella	79	71	0.93	0.62–1.39	0.71
Yellow Fever	44	27	1.11	0.63–1.96	0.73
Whooping cough	68	55	0.96	0.61–1.50	0.86
Diphtheria	115	87	1.01	0.70–1.47	0.95

^a Adjusted for gender, age group (interview for controls, diagnosis for cases), race, education, BMI.
Reference groups are those without each medical condition.
Missing values excluded from analyses.

Table IV.

Risk of multiple myeloma in relation to prior medication use.

Medication	Cases	Controls	OR ^a	95% CI ^a	p ^a
Angiotensin-converting enzyme (ACE) inhibitor	23	46	0.40	0.23–0.70	0.001
Diuretic	18	43	0.37	0.20–0.68	0.001
Antidepressant	38	47	0.47	0.29–0.77	0.002
Anti-lipemic	23	43	0.43	0.25–0.76	0.004
Anti-convulsant	6	11	0.32	0.11–0.94	0.04
Anti-asthma	6	13	0.39	0.14–1.06	0.07
Antibiotic	18	4	2.68	0.85–8.43	0.09
Calcium channel blocker	17	27	0.59	0.30–1.15	0.12
B Adrenergic blocker	37	48	0.69	0.42–1.12	0.13
Antihistamine	28	29	0.65	0.36–1.16	0.14
Gastric Acid Reducer	31	35	0.67	0.39–1.15	0.14
Bone loss	16	28	0.60	0.30–1.19	0.14
Corticosteroid	9	9	0.53	0.20–1.43	0.21
Anti-BPH	9	13	0.57	0.22–1.44	0.23
Thyroid	50	40	1.34	0.83–2.17	0.24
Acetyl salicylic acid (ASA)	28	36	0.72	0.41–1.26	0.25
Anti-inflammatory (non-ASA)	35	20	1.29	0.71–2.35	0.40
Anti-inflammatory	61	57	0.88	0.58–1.34	0.56
Analgesic	6	3	1.53	0.35–6.71	0.57
Benzodiazepine, sedative	11	12	0.78	0.32–1.87	0.58
Oral contraceptive	25	19	0.83	0.43–1.61	0.58
Antineoplastic	11	7	1.33	0.47–3.77	0.59
Antidiabetic (insulin)	4	3	0.78	0.16–3.87	0.76
Clot inhibiting medication (warfarin)	7	7	0.86	0.27–2.75	0.80
Vitamin	14	14	0.91	0.40–2.06	0.82
Hormone replacement therapy	45	43	0.95	0.58–1.55	0.83
Calcium	6	8	0.91	0.29–2.91	0.88
Angiotensin II receptor blocker	19	19	1.04	0.52–2.09	0.91

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Medication	Cases	Controls	OR ^a	95% CI ^a	p ^a
Prednisone	6	5	0.98	0.27–3.57	0.97
Alpha adrenergic blocker	8	9	1.01	0.36–2.83	0.99

^a Adjusted for gender, age group (interview for controls, diagnosis for cases), race, education, BMI.
Reference groups are those not taking each medication.
Missing values excluded from analyses.