Risk of Multiple Myeloma following Medication Use and Medical Conditions: A Case-Control Study in Connecticut Women

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Abstract

Background: **Certain commonly used drugs and medical conditions characterized by chronic immune dysfunction and/or antigen stimulation have been suggested to affect important pathways in multiple myeloma tumor cell growth and survival. We conducted a population-based case-control study to investigate the role of medical history in the etiology of multiple myeloma among Connecticut women.**
Methods: **A total of 179 incident multiple myeloma cases (21-84 years, diagnosed 1996-2002) and 691 population-based controls was included in this study. Information on medical conditions, medications, and medical radiation was obtained by in-person interviews. We calculated odds ratios (OR) as measures of relative risks using logistic regression models.**
Results: **A reduced multiple myeloma risk was found among women who had used antilipid statin therapy [OR, 0.4; 95% confidence interval (95% CI), 0.2-0.8] or estrogen replacement therapy (OR, 0.6; 95% CI, 0.4-0.99) or who had a medical history of allergy (OR, 0.4; 95% CI, 0.3-0.7), scarlet fever (OR, 0.5; 95% CI, 0.2-0.9), or bursitis (OR, 0.4; 95% CI, 0.2-0.7). An increased risk of multiple myeloma was found among women who used prednisone (OR, 5.1; 95% CI, 1.8-14.4), insulin (OR, 3.1; 95% CI, 1.1-9.0), or gout medication (OR, 6.7; 95% CI, 1.2-38.0).**
Conclusions: **If our results are confirmed, mechanistic studies examining how prior use of insulin, prednisone, and, perhaps, gout medication might promote increased occurrence of multiple myeloma and how antilipid statins, estrogen replacement therapy, and certain medical conditions might protect against multiple myeloma may provide insights to the as yet unknown etiology of multiple myeloma.** (Cancer Epidemiol Biomarkers Prev 2006;15(12):2342–7)

Introduction

Multiple myeloma is a malignant clonal neoplasm of plasma cells of B lymphocyte origin characterized by an overproduction of large amounts of monoclonal immunoglobulins. Clinical symptoms may include bone pain, infections, neurologic deficits, cytopenias, hypercalcemia, renal failure, or other abnormalities (1). Data from the United States Surveillance, Epidemiology, and End Results program estimate the recent age-adjusted incidence to be 5.6/100,000 overall and 30.4/100,000 for individuals >65 years (2). Incidence rates among men are 1.5 times higher than among women and two times higher among African Americans than among whites. The median age at diagnosis of multiple myeloma is 71.0 years among whites and 67.0 years among African Americans (2).

Although etiologic factors for multiple myeloma are not well established, case-control and cohort studies have shown elevated risks associated with occupational exposure to ionizing radiation following long latency periods in radiologists (3, 4) and unidentified occupational exposures among some, but not all, studies of farmers (5, 6), petrochemical, and rubber workers (7-9). Elevated risk of multiple myeloma has been associated with lower levels of education, income, and socioeconomic status in case-control (10) and cohort studies (11), although the results are not consistent (4, 12). Familial studies (13-16) have found 2- to 5-fold increased risk of multiple myeloma among first-degree relatives of multiple myeloma cases. Associations between multiple myeloma and past history of disorders characterized by chronic immune dysfunction and/or antigen stimulation have been suggested in epidemiologic studies; however, there are inconsistencies in the literature on this topic (13, 17-19).

Use of various medications, such as antibiotics (20-22), nonsteroidal anti-inflammatory drugs and other analgesics (20, 23-25), corticosteroids and other immunosuppressants (20, 23, 26-29), histamine2 receptor antagonists (30, 31), psychotropic drugs (20, 28, 32), anticonvulsants (33-35), estrogen replacement therapy (20, 36), antidepressants or antianxiety drugs (37, 38), amphetamines (38), and digitalis or digitoxin (20, 39), has been associated with risk of non–Hodgkin's lymphoma (NHL). However, to our knowledge, there is very little information on medication use and subsequent risks of multiple myeloma or other lymphoproliferative malignancies. Given the fact that certain drugs among those suggested to be associated with risk for NHL and other cancers have been found to affect pathways of importance in multiple myeloma tumor cell growth and survival (40-42) as well as mechanisms observed to be involved in resistance to cytotoxic multiple myeloma therapy (43), we were intrigued to quantify risks of multiple myeloma in relation to previous medication use.

We used data from a population-based case-control study among Connecticut women to explore the role of prior medication use in relation to risk of multiple myeloma. In addition, we assessed the association between multiple

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Note: Certain data used in this study were obtained from the Connecticut Tumor Registry located in the Connecticut Department of Public Health. The authors assume full responsibility for analyses and interpretation of these data.

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myeloma risk and a past history of selected conditions involving stimulation of the immune system (autoimmune, allergic, infectious, and inflammatory disorders) or prior exposure to diagnostic or therapeutic medical radiation.

Materials and Methods

Cases and Controls. Cases consisted of female residents of Connecticut, ages 21 to 84, diagnosed with multiple myeloma between January 1, 1996 and December 31, 2002, with no previous diagnosis of cancer other than nonmelanoma skin cancer, who were alive at the time of the interview and identified through the Connecticut Tumor Registry. Of a potential total of 409 histologically confirmed multiple myeloma cases identified during the study period, 86 (21%) cases died before they were contacted for interview and 140 cases refused to participate in the study (69 due to physician refusal and 71 due to case refusal). A total of 183 cases completed in-person interviews. This corresponds to a response rate of 57% among survivors.

The population-based controls for the multiple myeloma cases were the same controls who were selected for a parallel study of NHL (28). They consisted of female residents of Connecticut, ages 21 to 84 years, and were selected using two sources. Random digit dialing was used to contact women ages <65 years, and the Centers for Medicare and Medicaid Services was used to identify controls ages ≥65 years. Controls were frequency matched to the NHL case series by age within 5-year age groups. This matching procedure provided abundant controls across all ages for the multiple myeloma cases. Including the initial telephone screening, the response rate for the random digit dialing participants was 69% (calculated as the initial screening response rate of 87% to locating potential controls times the interview rate of 79%; 398 completed interviews, 176 refusals, and 1 deceased before interview). For those identified through the Centers for Medicare and Medicaid Services, the response rate was 47% (320 completed interviews, 354 refusals, and 53 deceased before interview). A total of 717 controls completed interviews.

Interviews. All procedures were done in accordance with a protocol approved by Human Investigation Committees at Yale University, the Connecticut Department of Public Health, and the National Cancer Institute. After approval by the hospitals and by each subject's physician (for cases) or following selection through random sampling or Centers for Medicare and Medicaid Services (for controls), potential participants were approached by letter and/or by phone. Subjects who agreed to participate were interviewed by trained study interviewers either at the subject's home or at a convenient location. A standardized, structured questionnaire was used to obtain information on medical history and other major known or suspected risk factors, including family history of cancer, diet, occupation, tobacco use, alcohol consumption, blood transfusion history, menopausal status, and demographic factors, which might confound the association between prior medical conditions and medication use and risk of multiple myeloma. Because current medical condition and/or medication use may reflect the preclinical manifestation of multiple myeloma or part of the treatment of the symptoms caused by multiple myeloma, past medical conditions and medicine use data were restricted to those that occurred 1 year before diagnosis for cases or 1 year before interview for controls. Using a list of 36 medical conditions, subjects were asked whether they had been diagnosed with each condition by a physician before 1 year ago; if so, subjects were asked the year and age at which the condition was first diagnosed. An open-ended question was used to ask whether the subject had taken any medicine at least once a day for a period of 6 months or longer before 1 year ago. If yes, the age at first and last use and the total months of use of the medicine were also ascertained. After exclusions for missing data and subjects who reported ''other race'' or refused to report race, our analyses was based on 179 cases (23 blacks and 156 whites) and 691 controls (25 blacks and 666 whites).

Data on prior medical conditions, medication use, and medical radiation are reported only when based on three or more exposed cases and seven or more exposed cases and controls combined.

Statistical Analyses. We calculated odds ratios (OR) as measures of association using unconditional logistic regression, adjusting for age, race, education, and body mass index (BMI). When the number of exposed cases or controls was zero, we instead present unadjusted P values derived using Fisher's exact test. Prior medication use was categorized into groups based on the published literature (28). Duration of use for each medication group was divided into tertiles based on the distribution among controls. Models were fitted using Statistical Analysis System software version 8 (SAS Institute, Inc., Cary, NC).

Results

Table 1 shows the demographic characteristics of the study subjects. A lower proportion of cases than controls were <50 years of age (7.3% of cases versus 21.3% of controls) because controls were frequency matched by age to the NHL cases. The majority of subjects were white, with a higher proportion of cases than controls being black (12.9% versus 3.6%, respectively) and having elevated BMI.

The associations of prior medical conditions with risk of multiple myeloma are presented in Table 2. A significantly reduced risk was found for women who had a history of allergy [OR, 0.4; 95% confidence interval (95% CI), 0.3-0.7], bursitis (OR, 0.4; 95% CI, 0.2-0.7), or scarlet fever (OR, 0.5; 95% CI, 0.2-0.9). None of the other prior medical conditions under study were significantly associated with the risk of multiple myeloma.

We found a significantly increased risk of multiple myeloma among women who had used insulin (OR, 3.1; 95% CI, 1.1-9.0), prednisone treatment (OR, 4.4; 95% CI, 1.4-13.3), or gout medication (four cases and two controls; OR, 6.7; 95% CI, 1.2-38.0; Table 3). When stratified by duration of treatment, long prednisone use (OR, 9.9; 95% CI, 1.6-60.1; $P_{trend} = 0.015$) was associated with further elevated multiple myeloma risk; however, the analyses were based on small numbers. For gout

Table 1. Selected distributions of multiple myeloma cases and controls by age, race, and BMI

	Cases, *n* (%)	Controls, *n* (%)
Total	179 (100.0)	691 (100.0)
Age (y)		
<50	13 (7.3)	147 (21.3)
50-59	39 (21.8)	129 (18.7)
60-69	54 (30.2)	155 (22.4)
70+	73 (40.8)	260 (37.6)
Race		
White	156 (87.2)	666 (96.4)
Black	23 (12.9)	25 (3.6)
BMI based on adult usual weight		
<25	78 (43.6)	383 (55.4)
25-29.99	63 (35.2)	188 (27.2)
30+	38 (21.2)	120 (17.4)
Education		
Graduate degree/professional	16 (8.9)	101 (14.6)
College degree	21 (11.7)	124 (18.0)
Vocational/some college	48 (26.8)	211 (30.5)
High school graduate	64 (35.8)	181 (26.2)
<12 years	30 (16.8)	74 (10.7)

Table 2. ORs for multiple myeloma in relation to prior medical conditions

Medical conditions	Cases (*n*)	Controls (*n*)	OR* (95% CI)
Allergy	**18**	**142**	**0.4 (0.3-0.7)**
Anemia	40	118	1.4 (0.9-2.1)
Asthma	15	58	1.1 (0.6-2.0)
Bronchitis	38	214	0.7 (0.5-1.1)
Bursitis	**13**	**111**	**0.4 (0.2-0.7)**
Degenerative joint disease	6	27	0.7 (0.3-1.8)
Eczema	10	58	0.8 (0.4-1.7)
EBV	4	8	2.6 (0.7-9.3)
Gout	6	25	0.8 (0.3-2.0)
Hay fever	25	102	1.1 (0.7-1.8)
Herpes simplex virus	12	46	1.5 (0.8-3.1)
Infectious mononucleosis	3	35	0.6 (0.2-2.0)
Psoriasis	4	23	0.7 (0.2-2.0)
Rheumatoid arthritis	7	9	2.3 (0.8-6.5)
Scarlet fever	**10**	**82**	**0.5 (0.2-0.9)**
Shingles	8	52	0.6 (0.3-1.3)
Sinusitis	35	192	0.7 (0.4-1.0)
Urinary tract infection	54	281	0.7 (0.5-1.0)
Various disc diseases	6	12	1.2 (0.5-3.1)

NOTE: The first year before multiple myeloma diagnosis was censored. Entries in bold font have P values of <0.05.

*Adjusted for age, race, education, and BMI; the estimates were virtually unchanged when we fit the models unadjusted.

medication, numbers were too small to be meaningful for analyses stratified by duration. A significantly reduced risk of multiple myeloma was found for women who had used antilipid statins (OR, 0.4; 95% CI, 0.2-0.8), and a borderline significantly decreased risk of multiple myeloma was observed among those who had been on estrogen replacement therapy (OR, 0.6; 95% CI, 0.4-0.99). Again hampered by limited numbers, there was no significant trend with duration of estrogen replacement therapy ($P_{trend} = 0.108$) or antilipid statin therapy ($P_{trend} = 0.077$).

Diagnostic radiation procedures were not significantly associated with subsequent multiple myeloma risk (Table 4). An increased risk of multiple myeloma was observed among women who reported they had a history of prior radiation treatment (OR, 4.4; 95% CI, 1.2-4.6).

Estimates were virtually the same when analyses were restricted to individuals with high education status (data not shown).

Discussion

In this population-based case-control study among Connecticut women, we found significantly reduced risks of multiple myeloma among women who had used antilipid statin drugs or estrogen replacement therapy as well as among women with previous medical history of allergy, scarlet fever, or bursitis. Elevated risks of multiple myeloma were found among women who had used insulin, steroidal anti-inflammatory drugs, or gout medication.

Antilipid statins belong to a class of agents designed to inhibit 3-hydroxy-3-methylglutaryl CoA reductase and are effective in the management of hypercholesterolemia. Owing to the involvement of 3-hydroxy-3-methylglutaryl CoA reductase in cholesterol synthesis and growth control, statins have also been proposed to have chemopreventive activity against cancer (44). Epidemiologic studies have found protective effects of statins with regard to risk of breast, colorectal, lung, and prostate cancer (45-48). Furthermore, experimental studies have shown that statins induce apoptosis in cancer cell lines *in vitro* (49, 50). However, a very recent cohort study did not support the hypothesis that statin use strongly reduces risk of colorectal cancer (51) and another very recent meta-analyses reported no reductions for cancers of the breast, colon, gastrointestinal tract, prostate, respiratory tract, or skin (melanoma) when statins were used (52). In our study, we found a significantly 60% decreased risk of multiple myeloma among women with prior use of antilipid statin drugs. Interestingly, a previous study by Durie and Mundy (53) on 409 multiple myeloma patients found a trend toward less severe bone disease (such as lytic lesions and/or osteoporosis) among those who had received antilipid statins. This clinical observation is supported by the finding that antilipid statins stimulate bone formation in cultured osteoblasts in mouse neonatal calvaria and cortical bone by increasing the synthesis of bone morphogenic protein-2 (54). Furthermore, preliminary results from a study of 81 refractory and relapsed multiple myeloma patients showed that 43 (53%) of the patients who were given statins in addition to conventional multiple myeloma therapy had a better response rate and longer survival (55). The underlying mechanisms for a possible association between antilipid statin use and subsequent multiple myeloma development require further examination.

Elevated levels of the proinflammatory cytokine interleukin-6 has been found to be an important pathogenetic mediator involved in growth and survival of plasma cells (40). Estrogen has been reported to be a negative regulator of lymphopoiesis (56), and recently, it has also been found to have blocking effect on interleukin-6-mediated cell proliferation in human multiple myeloma cells (57). We found a borderline 40% reduced risk of multiple myeloma among women who reported use of estrogen replacement therapy. Our observation might provide important clues in the pathogenesis of multiple myeloma and needs confirmation.

We found increased risk of multiple myeloma after use of steroids. Previous studies have shown increased risk of NHL after use of steroids (20, 23, 28, 31), although not consistently (58). Immune modulation has been postulated to be the potential underlying mechanism for the increased NHL risk following steroid use. To our knowledge, there is very little information on multiple myeloma risk among individuals who used steroids. Recently, we observed an increased risk of multiple myeloma in patients with a prior history of polymyalgia rheumatica (13), an autoimmune condition that is treated with high doses of steroids (59). In this previous study, we had no information on treatment; however, we speculated whether the observed positive association between polymyalgia rheumatica and multiple myeloma was not a true biological finding but rather reflected misclassification caused by early multiple myeloma manifestations mimicking polymyalgia rheumatica (60). However, taking all these findings together increases the plausibility of the association between steroid use and risk of multiple myeloma.

Our finding of a >3-fold increased risk of multiple myeloma among women with prior insulin use is interesting in that it might reflect an effect mediated by insulin itself or it could be a surrogate marker for an unknown risk factor or a combination of the two. Recent studies have suggested that insulin-like growth factor-I receptors are important mediators of tumor cell survival and resistance to cytotoxic therapy in multiple myeloma (41, 43).

Finally, based on very small numbers, we observed increased risk of multiple myeloma following gout medication as has been reported in previous case reports (61). Although increased urate excretion is often seen at diagnosis in patients with hematologic malignancies with rapid cell turnover, it may, much less commonly, also be seen in patients with newly diagnosed multiple myeloma. Thus, reverse causality could also contribute to the findings. Further studies are warranted to confirm the results above and to explore underlying pathogenetic mechanisms.

We observed an ~50% reduced risk of multiple myeloma among women who reported a personal history of allergy, scarlet fever, or bursitis. Allergy has previously been associated

Table 3. ORs for multiple myeloma in relation to prior medical use

Medication groups	Cases (*n*)	Controls (*n*)	OR* (95% CI)
Acetyl salicylic acid	9	35	0.9 (0.4-2.0)
Analgesics	3	9	1.4 (0.4-5.5)
Angiotensin converting enzyme inhibitors	11	50	0.7 (0.3-1.3)
Angiotensin II receptor blocking agents	3	8	1.1 (0.3-4.4)
Antidepressants	9	43	0.8 (0.4-1.8)
Antidiabetics (insulin)	**8**	**8**	**3.1 (1.1-9.0)**
Short duration †	2	4	1.6 (0.3-9.6)
Moderate duration †	**4**	**2**	5.5 (0.98-31.2)
Long duration †	2	2	3.6 (0.5-26.8)
Antidiabetics (noninsulin medications)	4	30	0.4 (0.1-1.1)
Antihistamines	3	19	0.5 (0.1-1.8)
Anti-inflammatory drugs (nonsteroid, excluding acetyl salicylic acid)	4	27	0.6 (0.2-1.8)
Antineoplastic	3	6	1.6 (0.4-7.2)
Benzodiazepine drugs	5	21	0.9 (0.3-2.6)
β-Adrenergic blocking agents	15	56	0.9 (0.5-1.7)
Bronchodilators	5	9	2.0 (0.6-6.1)
Calcium channel blockers	18	41	1.5 (0.8-2.8)
Clot inhibiting medication (warfarin)	6	12	2.2 (0.8-6.2)
Diuretics	19	69	0.9 (0.5-1.5)
Estrogen replacement therapy	**28**	**148**	**0.6 (0.4-0.99)**
Short duration †	7	52	0.5 (0.2-1.1)
Moderate duration †	12	48	0.8 (0.4-1.6)
Long duration †	9	48	0.6 (0.3-1.2)
Glycoside	4	14	1.0 (0.3-3.1)
Gout medication	**4**	**2**	**6.7 (1.2-38.0)**
Antilipid statin therapy	**7**	**59**	**0.4 (0.2-0.8)**
Short duration †	0	22	0 (***P* = 0.013**)
Moderate duration †	4	21	0.5 (0.2-1.7)
Long duration †	3	16	0.5 (0.2-2.0)
Oral contraceptives	27	149	1.1 (0.6-1.8)
Prednisone	**7**	**7**	**4.4 (1.4-13.3)**
Short duration †	2	3	3.1 (0.5-20.0)
Moderate duration †	1	2	1.7 (0.1-19.8)
Long duration †	**4**	**2**	**9.9 (1.6-60.1)**
Thyroid medication	16	74	0.8 (0.4-1.4)
Vitamins	3	9	1.7 (0.4-6.6)

NOTE: The first year before multiple myeloma diagnosis was censored. *P* values (two sided) based on the Fisher's exact test are given when cases or controls have zero individuals. Entries in bold font have *P* values of <0.05.

*Adjusted for age, race, education, and BMI; the estimates were virtually unchanged when we fit the models unadjusted.

†Categorizing duration into tertile based on the distribution of the duration of use of the controls. Duration (mean number of months) categories for short, moderate, and long use were as follows: insulin, 64, 156, and 339; estrogen replacement therapy, 27, 99, and 263; antilipid statin therapy, 22, 45, and 134; and prednisone, 25, 60, and 186.

with a decreased risk of some cancers (62) but associated with increased risk of other cancers (63). Our study also shows conflicting results because certain conditions (such as allergy, bronchitis, psoriasis, and eczema) were associated with reduced risk of multiple myeloma, whereas others (such as asthma and hay fever) were not associated with multiple myeloma risk. Clearly, there is need for additional studies to better understand the role of chronic immune stimulation in relation to host-related immune response to uncover causal pathways in the etiology of multiple myeloma.

In our study, there was no statistical association between prior exposure to diagnostic X-rays and subsequent multiple myeloma risk, which is in good accord with the literature (64). Our finding of a positive association between radiation treatment and multiple myeloma risk was based on small numbers and lacked information on radiation dose. Given these limitations and the generally negative findings from previous studies on subjects exposed to radiotherapy as well as among atomic bomb survivors (65, 66), the observed association should be interpreted with caution.

We used a case-control design, which reduced potential bias due to increased medication use by hospital patients seen in hospital-based studies and ensured a population-based setting and generalizability of our findings. By including incident cases of multiple myeloma, which were reviewed by experienced study pathologists, we were able to minimize disease misclassification.

Possible limitations of this study include the reliance on self-reported information on prior medical conditions, medication use, and medical radiation rather than reviewing medical records. However, differential misclassification of exposure by

Table 4. ORs for multiple myeloma in relation to prior medical radiation

Diagnostic radiation (X-ray)	Cases (*n*)	Controls (*n*)	OR* (95% CI)
Chest	130	521	1.4 (0.8-2.4)
Gallbladder	32	112	1.0 (0.7-1.6)
I.v. pyelogram (kidney)	21	85	0.9 (0.5-1.6)
Mammogram	147	579	0.8 (0.5-1.4)
Myelogram	11	38	1.0 (0.5-2.0)
Thyroid uptake	12	53	0.8 (0.4-1.5)
Upper or lower gastrointestinal	79	320	0.8 (0.6-1.2)
Venogram	9	29	1.1 (0.5-2.4)
Radiation treatment			
Any radiation treatment	**15**	**30**	**4.4 (1.2-4.6)**
Any radiation treatment or tumor and/or tumor growth	**10**	**10**	**4.4 (1.7-11.0)**

NOTE: The first year before multiple myeloma diagnosis was censored. Entries in bold font have *P* values of <0.05.

*Adjusted for age, race, education, and BMI; the estimates were virtually unchanged when we fit the models unadjusted.

case-control status is unlikely because interviewers and interviewees did not know the study hypotheses related to medical history. In addition, unlike other well-known diseases, little is known about the relationship between past medical history and risk of multiple myeloma by the study participants and interviewers. Differential reporting of past medical conditions by the cases also cannot explain the observed inverse relationships between past medical conditions and medication use and multiple myeloma risk found in our study. The differing participation rates between cases and controls and potential selection bias due to low response rates might be of importance in the interpretation of these results. Although no information was available on the characteristics of non-participants, we used vital statistics data to compare the demographic profile of participating controls with that of the Connecticut population from which they were drawn. In terms of educational attainment, controls (Table 1) were comparable with the female adult population of state of Connecticut: graduate degree/professional, 14.6% versus 12.2%; college degree, 18.0% versus 15.4%; vocational/some college, 30.5% versus 24.4%; high school graduate, 26.2% versus 30.5%; <12 years, 10.7% versus 17.7%, respectively.[3] However, because the percentages are slightly skewed toward higher education in the study controls (compared with the population), it cannot be completely ruled out that there is some bias if medication use is related to education level. Given that low socioeconomic status previously has been found to be associated with increased risk of multiple myeloma and our study independently replicated this finding, there is little to suggest a potential selection bias with regard to low socioeconomic status. In general, cases with multiple comorbid conditions might be more likely to participate because they are sicker and controls with these conditions might be more likely to participate because they would be more interested in medical studies than completely healthy control subjects. This might imply some cautious interpretation. As described above, controls were chosen for a different cancer (NHL) other than the one studied here. This could potentially have affected the results because of differences in age and race distribution in multiple myeloma cases versus controls. Because multiple myeloma is predominant in African-American males (2), the restriction to white female gender might have limiting effect on the generalizability of our results. Finally, some associations would be expected based on chance alone, given multiple statistical comparisons made by numerous medical conditions and medications used in this study.

In summary, we found certain prior medication use (antilipid statin drugs and estrogen replacement therapy) and medical conditions characterized by chronic immune dysfunction and/or antigen stimulation to be associated with an ~50% reduced risk of multiple myeloma. Prior use of prednisone, insulin, and, perhaps, gout medication was associated with increased risk of multiple myeloma. If our results are confirmed, mechanistic studies examining underlying mechanisms for the observed associations may provide insights to the as yet unknown etiology of multiple myeloma.

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