Medical History, Lifestyle, Family History, and Occupational Risk Factors for Mycosis Fungoides and Sézary Syndrome: The InterLymph Non-Hodgkin Lymphoma Subtypes Project

Briseis Aschebrook-Kilfoy, Pierluigi Cocco, Carlo La Vecchia, Ellen T. Chang, Claire M. Vajdic, Marshall E. Kadin, John J. Spinelli, Lindsay M. Morton, Eleanor V. Kane, Joshua N. Sampson, Carol Kasten, Andrew L. Feldman, Sophia S. Wang, Yawei Zhang

Correspondence to: Yawei Zhang, PhD, Department of Environmental Health Sciences, Yale School of Public Health, 60 College Street, New Haven, CT 06520 (e-mail: yawei.zhang@yale.edu)

Background	Mycosis fungoides and Sézary syndrome (MF/SS) are rare cutaneousT-cell lymphomas. Their etiology is poorly understood.
Methods	A pooled analysis of 324 MF/SS cases and 17217 controls from 14 case–control studies from Europe, North America, and Australia, as part of the International Lymphoma Epidemiology Consortium (InterLymph) Non-Hodgkin Lymphoma (NHL) Subtypes Project, was carried out to investigate associations with lifestyle, medical history, family history, and occupational risk factors. Multivariate logistic regression models were used to calculate odds ratios (OR) and 95% confidence intervals (CI).
Results	We found an increased risk of MF/SS associated with body mass index equal to or larger than 30 kg/m^2 (OR = 1.57, 95% CI = 1.03 to 2.40), cigarette smoking for 40 years or more (OR = 1.55, 95% CI = 1.04 to 2.31), eczema (OR = 2.38, 95% CI = 1.73 to 3.29), family history of multiple myeloma (OR = 8.49, 95% CI = 3.31 to 21.80), and occupation as crop and vegetable farmers (OR = 2.37, 95% CI = 1.14 to 4.92), painters (OR = 3.71, 95% CI = 1.94 to 7.07), woodworkers (OR = 2.20, 95% CI = 1.18 to 4.08), and general carpenters (OR = 4.07, 95% CI = 1.54 to 10.75). We also found a reduced risk of MF/SS associated with moderate leisure time physical activity (OR = 0.46, 95% CI = 0.22 to 0.97).
Conclusions	Our study provided the first detailed analysis of risk factors for MF/SS and further investigation is needed to confirm these findings in prospective data and in other populations.

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Mycosis fungoides and Sézary syndrome (MF/SS) are mature T-cell lymphomas that originate in the skin. The age-adjusted incidence rate per 100 000 person-years in the United States in 2005–2008 was 0.01 for SS and 0.55 for MF (1), with the latter showing a slight increase compared with the rate of 0.41 per 100 000 person-years in 2001–05 (1,2). While the age-adjusted incidence rates vary between countries, a slightly increased incidence of MF has also been reported in Norway (3) and Japan (4) over the past decades. The incidence of MF/SS is around 1.5 times higher in males than females (2,3). In the United States, the highest incidence rate of MF is observed among African Americans, with a black-to-white incidence rate ratio of 1.55 (2).

MF presents in the skin with patches/plaques and is characterized by epidermal and dermal infiltration of small to medium-sized T cells with cerebriform nuclei (5). MF generally has a long natural history and is likely to be diagnosed at an early stage, resulting in a generally good prognosis with a median survival of more than 25 years (6,7). SS is characterized by the presence of erythroderma, lymphadenopathy, and neoplastic T lymphocytes in the blood and its behavior is much more aggressive with a median survival of about 5 years (6,7).

Because of the rarity of these diseases, very few epidemiologic studies on MF/SS risk factors have been conducted thus far, and the only identified risk factors are male gender, advanced age, and African American descent (8). Smoking and alcohol consumption (9), several occupations and the related exposures (9–12), atopic diseases (9,13), sun exposure (14,15), and several infectious agents such as human herpesvirus 8, hepatitis C virus (HCV), *Borrelia burgdorferi*, and cytomegalovirus (16–20) have been studied, but their roles in the etiology of MF/SS remain unestablished.

To advance our understanding of MF/SS etiology, we investigated associations with lifestyle, medical history, family history, and occupational risk factors in a pooled analysis of 324 cases and 17 217 controls from 14 case-control studies from Europe, North America, and Australia as part of the International Lymphoma Epidemiology Consortium (InterLymph) Non-Hodgkin Lymphoma (NHL) Subtypes Project.

Methods

Study Population

Detailed methodology for the InterLymph NHL Subtypes Project is provided elsewhere in this issue. Studies eligible for inclusion in this pooled analysis fulfilled the following criteria: 1) case–control design, with incident, histologically confirmed cases of MF/SS, and 2) availability of individual-level data for at least several risk factors of interest by December 31, 2011. Most studies excluded individuals with a known history of solid organ transplantation or HIV/ AIDS.

Contributing studies were approved by local ethics review committees, and all participants provided written, informed consent before interview.

NHL Subtype Ascertainment and Harmonization

Cases were classified according to the World Health Organization classification (5,21) using guidelines from the InterLymph Pathology Working Group (22,23). Most studies had some form of centralized pathology review by at least one expert hematopathologist to confirm the diagnoses. Each participating study's pathology review procedures, rules for NHL subtype classification, and NHL subtype distribution were reviewed by an interdisciplinary team of pathologists and epidemiologists.

Risk Factor Ascertainment and Harmonization

Each study collected data on putative NHL risk factors in a standardized, structured format by in-person or telephone interviews and/or self-reported questionnaires. Risk factors selected for inclusion in this analysis were lifestyle, medical history, family history, and occupational risk factors with data from at least four studies. Centralized harmonization of de-identified individual-level data from each study was a key element of the project. Each exposure variable was harmonized separately, before being reviewed for consistency among related exposure variables. Details of the data harmonization rules are provided elsewhere in this issue.

Statistical Analysis

Risk of MF/SS associated with each exposure variable was examined using logistic regression models adjusted for age, race/ethnicity, and gender. Statistical significance of each relationship was evaluated by a likelihood ratio test, comparing models with and without the exposure variable of interest, with P values less than .05 identifying putatively influential factors. To evaluate effect heterogeneity among the 14 studies, we performed a separate logistic regression within each study and then quantified the variability of the coefficients by the H statistic, adapting the definition by Higgins and Thompson to categorical variables (24).

We then examined the relationship between case/control status and each putative risk factor considering possible effect modification and accounting for other potential confounders. To consider possible effect modification, we stratified the above logistic regression analyses by age, gender, race/ethnicity, region (ie, Northern Europe, Southern Europe, North America, and Australia) study, study design (ie population-based vs. hospital-based), or other putative risk factors identified in the analysis. Also, we set multivariate regression models adjusting each risk estimate for the other putative risk factor included one at the time, and a forward step-wise single regression model including all putative risk factors. Because the results did not change substantially with use of the multivariate models, ORs are presented from the minimally adjusted models only.

Because controls for most original studies were frequencymatched to the age and gender distribution of all NHL cases, rather than just MF/SS, we conducted sensitivity analyses using a subset of controls that were frequency-matched by age and gender to cases of MF/SS. The results from these sensitivity analyses were very similar to the results obtained using the full set of controls; thus, we retained the full set of controls for our main analyses to increase statistical power.

Results

This pooled analysis included the largest number of subjects from North America (61% cases and 43% controls), followed by Northern Europe (20% cases and 34% controls), Southern Europe (17% cases and 19% controls), and Australia (1% cases and 4% controls). Most of the study population came from population-based studies (86% cases and 80% controls), with the remainder coming from hospital-based studies (14% cases and 20% controls). Of the 324 cases, 271 (84%) were MF, 13 (4%) were SS, and 40 (12%) were unclassified MF/ SS; the majority (78%) of MF/SS cases were histologically classified based on the WHO Classification. Cases and controls showed similar distributions of age, gender, and socioeconomic status (Table 1). MF/SS cases had higher percentages of African Americans and Asians compared with controls (due to the distribution in US studies).

The associations between lifestyle factors and risk of MF/SS based on basic adjusted models are presented in Table 2. An increased risk was observed for people who had smoked for 40 years or longer (OR = 1.60, 95% CI = 1.08 to 2.38), and for obesity [body mass index (BMI) \geq 30 kg/m²: OR = 1.58, 95% CI = 1.04 to 2.41] with reference to BMI between 18.5 and 22.4 kg/m². However, no evidence of an increasing trend was observed with increasing years of smoking or BMI. On the other hand, compared with people who were not engaged in leisure-time physical activity, those who reported moderate (OR = 0.44, 95% CI = 0.21 to 0.91) or vigorous (OR = 0.50, 95% CI = 0.28 to 0.90) physical activity was inversely associated with a reduced risk of MF/SS. Again, no trend was detected with level of physical activity. We did not observe an association with alcohol consumption, hair dye use or sun exposure.

Among previous medical conditions, eczema was significantly associated with an increased risk of MF/SS (Table 3). Although the association was stronger for those who were diagnosed within 10 years of MF/SS diagnosis (OR = 4.12, 95% CI = 1.54 to 11.04 for 2–<5 years before diagnosis; OR = 4.87, 95% CI = 2.15 to 11.02 for 5–<10 years before diagnosis), suggesting possible misdiagnosis of eczema as MF/SS, risk was statisticalltly elevated also for history of eczema beyond 10 years (OR = 1.90, 95% CI = 1.27 to 2.85). An evaluation of individual autoimmune diseases was not permissible due to small numbers. We observed two cases of autoimmune diseases that activate both B and T cells, resulting in a significant increase in MF/SS risk. Other medical conditions, including atopic disorders other than eczema, psoriasis, inflammatory bowel disorders, blood transfusion, HCV infection, oral contraceptive use, and hormone replacement therapy showed weak associations (Table 3).

Table 1	. Characteristics of studies in	ncluded in the	InterLymph N	١HL
Subtyp	es Project*			

Table 2.	Associations	between	lifestyle	factors	and	risk	of My	cosis
fungoide	es and Sézary	syndrom	ne*					

	Controls	Cases	Total	
	No. (%)	No. (%)	No. (%)	
Total	17217 (98.2)	324 (1.8)	17 541	
Study				
North America				
British Columbia	845 (4.9)	42 (13.0)	887	
Mayo Clinic	1314 (7.6)	9 (2.8)	1323	
NCI-SEER	1055 (6.1)	26 (8.0)	1081	
Nebraska (newer)	533 (3.1)	7 (2.2)	540	
UCSF1	2402 (14.0)	47 (14.5)	2449	
UCSF2	457 (2.7)	54 (16.7)	511	
University of Rochester	139 (0.8)	2 (0.6)	141	
Yale	717 (4.2)	12 (3.7)	729	
Furope	, ., ()	12 (017)	, 20	
Enilymph	2460 (14.3)	38 (117)	2498	
Italy multi-center	1771 (10 3)	25 (77)	1796	
Italy (Aviano-Nanles)	504 (2.9)	2 (0.6)	506	
SCALE	3187 (18 5)	/1 (12 7)	3228	
United Kingdom	1139 (6.6)	15 (4.6)	115/	
Australia	1155 (0.0)	13 (4.0)	1134	
Now South Wales	604 (4 0)	4 (1 2)	600	
Region	034 (4.0)	4 (1.2)	038	
North Amorica	7162 (12 2)	100 (61 4)	7661	
Northern Europe	7402 (43.3) E020 (22.0)	65 (20.1)	700 T	
Southern Europe	0020 (00.0) 0041 (10.0)	00 (20.1) EC (170)	2000	
	3241 (18.8)	50 (17.3)	3297	
Australia	694 (4.0)	4 (1.2)	698	
Design	10.040 (00.4)	200 (00 4)	14100	
Population-based	13846 (80.4)	280 (86.4)	14 126	
Hospital-based	3371 (19.6)	44 (13.6)	3415	
Age, y				
<30	993 (5.8)	8 (2.5)	1001	
30–39	1686 (9.8)	33 (10.2)	1/19	
40-49	2543 (14.8)	57 (17.6)	2600	
50–59	3940 (22.9)	90 (27.8)	4030	
60–69	4848 (28.2)	83 (25.6)	4931	
70–79	2949 (17.1)	47 (14.5)	2996	
≥80	258 (1.5)	6 (1.9)	264	
Sex				
Male	9240 (53.7)	184 (56.8)	9424	
Female	7977 (46.3)	140 (43.2)	8117	
Race				
White, non-Hispanic	15849 (92.1)	271 (83.6)	16 120	
Black	329 (1.9)	19 (5.9)	348	
Asian	308 (1.8)	22 (6.8)	330	
Hispanic	289 (1.7)	7 (2.2)	296	
Other/unknown/missing	442 (2.6)	5 (1.5)	447	
Socioeconomic status	6170 (35.8)	117 (36.1)	6287	
Medium	5292 (30.7)	94 (29.0)	5386	
High	5507 (32.0)	109 (33.6)	5616	
Other/missing	248 (1.4)	4 (1.2)	252	
NHL classification				
World Health Organization	13044 (75.8)	252 (77.8)	13296	
Working Formulation	4173 (24.2)	72 (22.2)	4245	

NHL = non-Hodgkin Lymphoma; NCI-SEER = National Cancer Institute Surveillance, Epidemiology, and End Results; SCALE = Scandinavian Lymphoma Etiology Study; UCSF = University of California San Francisco.

A family history of multiple myeloma, but not family history of hematologic malignancies overall, or history of other specific lymphohemopoietic cancer, showed an excess risk (OR = 6.17, 95% CI = 2.39 to 15.91, based on six cases).

An elevated risk of MF/SS was associated with several occupations (Table 4), including crop and vegetable farm workers (OR = 2.76, 95%

	Controls	Cases	
	No. (%)	No. (%)	OR (95% CI)†
History of alcohol			
consumption			
Non-drinker	3003 (19.2)	73 (26.3)	1.00 (referent)
Drinker (at least one	8289 (52.9)	146 (52.5)	0.80 (0.58 to 1.09)
drink per month)			
History of cigarette			
smoking‡			
No	6997 (42.7)	121 (42.9)	1.00 (referent)
Yes	8451 (51.6)	139 (49.3)	0.97 (0.75 to 1.25)
0–20, y	3090 (18.9)	47 (16.7)	0.86 (0.61 to 1.23)
21–<30, y	1783 (10.9)	27 (9.6)	0.83 (0.54 to 1.28)
30–<40, y	1737 (10.6)	24 (8.5)	0.79 (0.50 to 1.24)
40≥, y	1742 (10.6)	40 (14.2)	1.60 (1.08 to 2.38)
Missing	1023 (6.2)	23 (8.2)	
Physical activity			
None	716 (10.1)	20 (14.7)	1.00 (referent)
Mild	474 (6.7)	14 (10.3)	0.64 (0.29 to 1.40)
Moderate	934 (13.2)	20 (14.7)	0.44 (0.21 to 0.91)
Vigorous	3037 (43.0)	45 (33.1)	0.50 (0.28 to 0.90)
Usual adult BMI, kg/m ²			
15-<18.5	209 (1.4)	5 (1.7)	1.30 (0.50 to 3.39)
18.5-<22.5	2943 (19.9)	47 (15.9)	1.00 (referent)
22.5-<25	3601 (24.4)	59 (20.0)	1.03 (0.69 to 1.52)
25-<30	5220 (35.4)	107 (36.3)	1.25 (0.87 to 1.80)
35–50	2175 (14.7)	55 (18.6)	1.58 (1.04 to 2.41)
Used hair dyes before 1980			
Never hair dye	1406 (14.4)	27 (13.7)	1.00 (referent)
Ever hair dye use <1980	1101 (11.3)	21 (10.7)	1.08 (0.55 to 2.10)
Hair dye use only 1980≥	966 (9.9)	12 (6.1)	0.78 (0.36 to 1.71)
Hair dye use, time period	986 (10.1)	25 (12.7)	0.99 (0.48 to 2.05)
unknown			
Male	5071 (51.8)	108 (54.8)	
Total sun exposure (h/wk)			
Q1	1508 (18.7)	24 (21.2)	1.00 (referent)
Q2	1594 (19.8)	21 (18.6)	0.83 (0.46 to 1.50)
Q3	1633 (20.3)	21 (18.6)	0.83 (0.45 to 1.51)
Q4	1714 (21.3)	21 (18.6)	0.75 (0.41 to 1.40)

* CI = confidence interval; OR = odds ratio.

† OR (95% CI) adjusted for age, sex, and race.

‡ Smoked longer than 6 months or more than 100 cigarettes in lifetime.

CI = 1.35 to 5.61), painters (OR = 3.42, 95% CI = 1.81 to 6.47), woodworkers (OR = 2.19, 95% CI = 1.19 to 4.03), and general carpenters (OR = 4.50, 95% CI = 1.74 to 11.62). A significant linear trend was observed with years of employment for woodworkers (P for trend = .025) but not others (data not shown). None of the other occupations evaluated showed a significant association with MF/SS risk.

Results from multivariate analysis are presented in Table 5. All statistically significant associations remained except for vigorous leisure time physical activity.

Limiting our analysis to MF cases (n = 271) did not change the results (data not shown). No meaningful inter-study heterogeneity was detected.

Discussion

The results of our pooled analysis of 324 cases and 17217 controls from 14 case-control studies from Europe, North America,

Table 3.	Associations	between	medical	history	and r	isk of N	Aycosis	fungoides	and Sézary	syndrome*
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mass 300 (12.2.1) 0 (0.1.2) No 6746 (66.8) 128 (73.6) 1.00 (referent) Ness 152 (1.5) 1 (0.6) 0.47 (0.07 to 3.47) Masing 3194 (31.6) 45 (25.9) 100 (referent) No 11 639 (62.8) 240 (86.3) 1.00 (referent) Yes 120 (73) 17 (6.1) 0.93 (0.56 to 154) Psoriasis 76 (2.1) 7 (4.2) 1.94 (0.85 to 154) Infarmatory bowel disorder 7 7 (4.2) 1.94 (0.85 to 154) No 10756 (67.4) 158 (65.5) 1.00 (referent) Yes 7.79 (1.2) 7 (2.4) 1.82 (0.85 to 3.9) Ulcerative colitis 7 7.0 (95.2) 1.00 (referent) No 11 826 (67.2) 2.6 (95.2) 1.00 (referent) Yes 17.97 (1.2) 7 (2.4) 1.82 (0.85 to 4.70) No 1.826 (65.8) 3.05 (94.1) 1.00 (referent) Yes 1.650 (97.7) 2.0 (0.5) 1.02 (referent) Ves 1.650 (97.7 (2.4) 1.68 (67.7 o 4.2)	Yes Mala	1072 (10.7)	22 (17.6)	1.17 (0.65 to 2.13)
Internation Transmission 6746 (66.5) 128 (73.6) 1.00 (referent) Yes 152 (1.5) 1 (0.6) 0.47 (0.07 to 3.47) Missing 1914 (3.16) 45 (25.9) 100 (referent) Vice 240 (86.3) 1.00 (referent) 0.93 (0.5 to 1.54) Yes 1020 (73) 17 (8.1) 0.93 (0.5 to 1.54) Porialis 1000 (referent) 0.93 (0.5 to 1.54) 1.84 (0.5 to 1.54) No 1076 (97.4) 158 (95.8) 1.00 (referent) Yes 250 (2.3) 7 (4.2) 1.84 (0.85 to 4.23) Inflammatory lowel disorder 1 1.82 (0.83 to 3.99) 1.00 (referent) Yes 276 (95.2) 1.00 (referent) 1.82 (0.83 to 3.99) No 144 454 (97.5) 276 (95.2) 1.00 (referent) Yes 179 (1.2) 5 (2.0) 1.88 (0.16) (16.10 (15.10 (2.10 (15.10 (17.10 (15.10 (17.10 (15.10 (17.10 (15.10 (17.10 (1	Infaction of HCV	3331 (32.2)	04 (31.2)	
Yes 10 (15) 10 (16) 0.47 (0.07 to 3.47) Missing 3194 (31.6) 45 (25.9) Ulcer	No	6746 (66.8)	128 (73.6)	100 (referent)
Missing 3194 (31.6) 45 (25.9) Ulcar 1 1639 (82.8) 240 (86.3) 1.00 (referent) Yes 1202 (7.3) 17 (6.1) 0.33 (0.56 to 15.4) Paridasis 1 120 (7.3) 17 (6.1) 0.33 (0.56 to 15.4) Paridasis 1 120 (7.3) 17 (4.2) 1.94 (0.89 to 4.23) Inflammatory bowel disorder 7 (4.2) 1.94 (0.89 to 4.23) 1.93 (0.85 to 15.4) No 14454 (975) 2.76 (95.2) 1.00 (referent) Yes 179 (1.2) 7 (2.4) 1.82 (0.83 to 3.99) Uccerative colits 1 186 (972) 2.80 (95.2) 1.00 (referent) No 11886 (972) 2.93 (95.4) 1.00 (referent) 1.93 (0.73 to 15.4) 1.00 (referent) See 145 (1.2) 5 (2.0) 1.66 (0.67 to 4.2) 1.00 (referent) 1.93 (0.23 to 4.70) No autoimmune disease 16500 (95.8) 305 (94.1) 1.00 (referent) 1.93 (0.21 to 4.70) 2.00 (91 (0.21 to 4.70) As atopic disorder # 1 130 (.1) 2.00 (91 (0.21 to 4.70) <t< td=""><td>Yes</td><td>152 (15)</td><td>1 (0.6)</td><td>0.47 (0.07 to 3.47)</td></t<>	Yes	152 (15)	1 (0.6)	0.47 (0.07 to 3.47)
Ulcar 16.0 (b) 10.0 (referent) No 16.0 (b) 240 (B, B, 3) 0.00 (referent) Portasis - - - No 10.756 (B7.4) 158 (B5.8) 1.00 (referent) Yes 256 (2.3) 7 (4.2) 1.24 (0.89 (a.4.2)) Infarmatory bowel disorder - - - No 14.454 (975) 276 (B5.2) 1.00 (referent) Yes 179 (1.2) 7 (2.4) 182 (0.83 to 3.99) Ulcerative coltis - - - No 14.454 (975) 238 (95.2) 1.00 (referent) Sets 179 (1.2) 7 (2.4) 182 (0.87 to 4.2) 1 Ilterry of autoimmune disease - - - No 19 (36.0) (95.8) 305 (94.1) 1.00 (referent) Secolic disorder # - - - - No 12 (26.7) 2.0.6) 1.02 (0.87 to 1.2) - No 13 (0.1) 2.0 (0.6) 1.02 (0.69 to 1.6) - No	Missing	3194 (31.6)	45 (25.9)	0.47 (0.07 to 0.47)
Two 11 689 (62.8) 240 (86.3) 1.00 (referent) Psoriasis 1020 (7.3) 17 (6.1) 0.93 (0.56 to 1.54) Psoriasis 1020 (7.3) 17 (4.2) 1.94 (0.89 to 4.23) Infarmatory bowel disorder 1020 (7.3) 7 (4.2) 1.94 (0.89 to 4.23) Infarmatory bowel disorder 1020 (7.2) 7 (2.4) 1.82 (0.83 to 3.99) Uccentry 11 686 (67.2) 2.38 (95.2) 1.00 (referent) Yes 179 (1.2) 7 (2.4) 1.88 (0.67 to 4.21) No 11 886 (67.2) 2.38 (95.2) 1.00 (referent) Yes 14 51 (1.2) 5 (2.0) 1.86 (0.67 to 4.21) No autoimmune disease 16500 (95.8) 305 (94.1) 1.00 (referent) No autoimmune disease 16500 (95.8) 305 (94.1) 1.00 (referent) No autoimmune disease 1270 (7) 2 (0.6) 1.92 (0.25 to 4.7) No disorder # 13 (0.1) 2 (0.6) 9.82 (2.05 to 4.703) Ary atopic disorder # 13 (0.1) 2 (0.6) 9.82 (2.05 to 4.703) No 9.254 (68.6) 16	Ulcer	0101 (01.0)	10 (20.0)	
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Psoriasis 10756 (97.4) 158 (95.8) 1.00 (referent) Na 256 (2.3) 7 (4.2) 1.94 (0.89 to 4.23) Inflarmatory bowel disorder 7 1.22 7 (2.4) 1.82 (0.83 to 3.99) Uccrative collisis 7 7 (2.4) 1.82 (0.83 to 3.99) 1.00 (referent) Yes 17 (12) 7 (2.4) 1.82 (0.83 to 3.99) 1.00 (referent) Ves 17 (16,1) 5 (2.0) 1.68 (0.67 to 4.21) 1.00 (referent) Yes 14 56 (1.2) 5 (2.0) 1.68 (0.67 to 4.21) 1.02 (0.25 to 4.17) No autoimmune disease 16 500 (95.8) 305 (94.1) 1.00 (referent) Soution 127 (0.7) 2 (0.6) 1.49 (0.87 to 2.50) Both 13 (0.1) 2 (0.6) 9.82 (2.05 to 4.70) No 11 285 (65.5) 185 (57.1) 1.00 (referent) Yes 5690 (3.30) 128 (38.2) 1.00 (referent) No 11 285 (65.5) 185 (67.1) 1.00 (referent) Yes 3238 (2.4) 73 (88.2) 1.00 (referent)	Yes	1020 (7.3)	17 (6.1)	0.93 (0.56 to 1.54)
No 10 756 (97.4) 158 (95.8) 1.00 (referent) Yes 256 (2.3) 7 (4.2) 194 (0.89 to 4.23) Inflammatory bowel disorder 7 (4.2) 7 (4.2) 1.00 (referent) No 14454 (97.5) 276 (95.2) 1.00 (referent) Yes 179 (12.2) 7 (2.4) 1.82 (0.83 to 3.99) Ucerative colitis	Psoriasis			
Yes 256 (2.3) 7 (4.2) 1.94 (0.89 to 4.23) Infammatory bowel disorder 1 1.00 (referent) 1.00 (referent) No 119 86 (97.2) 276 (95.2) 1.00 (referent) Yes 179 (1.2) 7 (2.4) 1.82 (0.83 to 3.99) Ves 119 86 (97.2) 236 (95.2) 1.00 (referent) Yes 145 (1.2) 5 (2.0) 1.68 (10.67 to 4.21) No autoimmune disease 16500 (95.8) 305 (94.1) 1.00 (referent) No autoimmune disease 13 (0.1) 2 (0.6) 1.02 (0.25 to 4.70) No autoimmune disease 13 (0.1) 2 (0.6) 1.02 (0.25 to 4.70) Ary atopic disorder1 12 (0.5) 185 (67.1) 1.00 (referent) No 12 25 (65.5) 185 (67.1) 1.00 (referent) Yes 36 (92.0) 1.20 (8.0) 0.91 (0.67 to 1.24) No 12 25 (65.5) 185 (67.1) 1.00 (referent) Yes 36 (2.8) 161 (61.7) 1.00 (referent) Yes 36 (2.8) 161 (61.67) 1.00 (referent)	No	10756 (97.4)	158 (95.8)	1.00 (referent)
Inflammatory bowel disorder No 14454 (975) 276 (95.2) 100 (referent) Yes 179 (1.2) 7 (2.4) 182 (0.83 to 3.99) Ulcerative colitis No 11886 (97.2) 238 (95.2) 100 (referent) Yes 20.00 (referent) Yes 20.00 (referent) Seal activation 1888 (97.2) 238 (95.2) 100 (referent) History of autoimmune disease Na disea	Yes	256 (2.3)	7 (4.2)	1.94 (0.89 to 4.23)
No 14454 (975) 276 (95.2) 1.00 (referent) Yes 179 (1.2) 7 (2.4) 182 (0.83 to 3.99) Ulcerative colitis 7 238 (95.2) 1.00 (referent) Yes 145 (1.2) 5 (2.0) 1.88 (0.67 to 4.21) No autoimmune disease 7 7 2.06 1.00 (referent) Beell activation 127 (0.7) 2.06 1.02 (0.25 to 4.17) Tecell activation 577 (3.4) 15 (4.6) 1.49 (0.87 to 2.55) Both 13 (0.1) 2 (0.6) 9.82 (2.05 to 4203) Any atopic disorder‡ 7 3.30 (0.1) 2.06) 9.82 (2.05 to 4203) No 1285 (65.5) 185 (57.1) 1.00 (referent) Yes No 1285 (65.5) 185 (57.1) 1.00 (referent) Yes No 1285 (65.5) 185 (57.1) 1.00 (referent) Yes No 9.254 (68.8) 16 16 (1.7) 1.00 (referent) Yes No 9.254 (68.8) 73 (28.0) 0.91 (0.67 to 1.24) 1.00 (referent) Yes <td>Inflammatory bowel disorder</td> <td></td> <td></td> <td></td>	Inflammatory bowel disorder			
Yes 179 (1,2) 7 (2,4) 1.82 (0.83 to 3.99) Ulcarative colitis 1.00 (referent) No 11.866 (97.2) 2.38 (95.2) 1.00 (referent) History of autoimmune disease 152 (0.63 to 4.21) Boal autoimmune disease 11600 (95.8) 305 (94.1) 1.00 (referent) B-cell activation 127 (0.7) 2 (0.6) 1.02 (0.25 to 4.7) Toell activation 137 (0.7) 2 (0.6) 1.02 (0.25 to 4.7) Ary atopic disorder‡ 2 (0.6) 9.82 (2.05 to 47.03) Ary atopic disorder‡ 1.00 (referent) Yes 5690 (30.0) 129 (39.8) 1.25 (0.98 to 1.61) Ary atopic disorder‡ No 11.285 (65.5) 185 (67.1) 1.00 (referent) Yes 3338 (24.8) 73 (28.0) 0.91 (0.67 to 1.24) Rod 11.065 (82.2) 178 (68.2) 1.00 (referent) Yes 373 (28.0) 0.91 (0.67 to 1.42) 1.00 (referent) Yes 9272 (72) 218 (0.8) </td <td>No</td> <td>14454 (97.5)</td> <td>276 (95.2)</td> <td>1.00 (referent)</td>	No	14454 (97.5)	276 (95.2)	1.00 (referent)
Ulcerative colitis No 11 886 (97.2) 238 (95.2) 1.00 (referent) Yes 145 (1.2) 5 (2.0) 1.68 (0.67 to 4.21) History of autoimmune disease No autoimmune disease 15500 (95.8) 305 (94.1) 1.00 (referent) B-cell activation 127 (0.7) 2 (0.6) 1.02 (0.25 to 4.7) Toell activation 577 (3.4) 15 (4.6) 1.49 (0.87 to 2.5 to 470.3) Ary atopic disorder‡ 30.1) 2 (0.6) 9.82 (2.05 to 470.3) No 11285 (65.5) 185 (57.1) 1.00 (referent) No 12825 (66.8) 161 (61.7) 1.00 (referent) Yes 3238 (24.8) 73 (28.0) 0.91 (0.67 to 1.24) Pool 9254 (66.8) 161 (61.7) 1.00 (referent) Yes 3238 (24.8) 73 (28.0) 0.91 (0.67 to 1.49) Pool 11065 (82.2) 178 (66.2) 1.00 (referent) Yes 144 (82.8) 28 (8.7) 0.99 (0.67 to 1.49) Asthma 21 (46	Yes	179 (1.2)	7 (2.4)	1.82 (0.83 to 3.99)
No 11 886 (97.2) 238 (95.2) 1.00 (referent) Yes 145 (1.2) 5 (2.0) 1.68 (0.67 to 4.21) History of autoimmune disease 15 (2.0) 1.00 (referent) B-cell activation 127 (0.7) 2 (0.6) 1.02 (0.25 to 4.17) Teell activation 577 (3.4) 15 (4.6) 1.49 (0.87 to 2.55) Both 13 (0.1) 2 (0.6) 0.82 (2.05 to 4.70) Any atopic disorder‡ 7 2 1.00 (referent) No 11 285 (65.5) 185 (57.1) 1.00 (referent) Yes 5690 (33.0) 129 (39.8) 1.25 (0.98 to 1.61) Allergy \$ 7 7 1.00 (referent) Yes 3338 (2.4.8) 73 (28.0) 0.91 (0.67 to 1.24) Food allergy 7 7 1.80 1.00 (referent) Yes 972 (7.2) 21 (8.0) 1.00 (referent) Yes 972 (7.2) 21 (8.0) 1.00 (referent) Yes 972 (7.2) 21 (8.0) 0.90 (0.63 to 1.30) Hay fever 7 7	Ulcerative colitis			
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History of autoimmune disease No autoimmune disease 16500 (95.8) 305 (94.1) 1.00 (referent) B-cell activation 127 (0.7) 2 (0.6) 1.02 (0.25 to 4.17) T-cell activation 377 (3.4) 15 (4.6) 1.49 (0.87 to 2.55) Both 13 (0.1) 2 (0.6) 9.82 (2.05 to 47.03) Any atopic disorder4 No 11285 (65.5) 185 (57.1) 1.00 (referent) Yes 5600 (33.0) 129 (39.8) 125 (0.9 to 1.61) Allergy 5 No 9 254 (68.8) 161 (61.7) 1.00 (referent) Yes 3338 (24.8) 73 (28.0) 0.91 (0.67 to 1.24) Food allergy No 11065 (82.2) 178 (68.2) 0.91 (0.67 to 1.24) Food allergy No 11065 (82.2) 178 (68.2) 1.00 (referent) Yes 9 72 (7.2) 21 (8.0) 1.04 (0.64 to 1.69) Asthma No 0 11065 (82.2) 178 (68.2) 0.91 (0.67 to 1.24) Food allergy No 0 11065 (82.2) 178 (68.2) 0.00 (referent) Yes 0 14140 (82.8) 260 (80.7) 1.00 (referent) Yes 0 144 (0.64 to 1.69) Asthma No 0 19188 (64.9) 132 (48.4) 1.00 (referent) Yes 0 2740 (19.3) 55 (20.1) 0.90 (0.67 to 1.48) Hay fever No or <2 y before diagnosis 12 157 (84.9) 205 (74.5) 1.00 (referent) Yes 0.92 (0.67 to 1.48) Yes 0.92 (0.61 to 1.63) 4.12 (1.54 to 1.04) Yes 5-c10 y before diagnosis 92 (0.61 to 7.2,5) 4.87 (2.15 to 11.02) Yes, Unovma age 333 (2.4) 10 (3.6) 2.05 (74.5) The output of eczema No or <2 y before diagnosis 92 (0.61 to 7.2,5) 4.87 (2.15 to 11.02) Yes, Johorow age 333 (2.4) 10 (3.6) 2.05 (74.5) The output of eczema No or <2 y before diagnosis 92 (0.61 to 7.2,5) 4.87 (2.15 to 11.02) Yes, Johorow age 33 (2.4) 10 (3.6) 2.04 (1.03 to 4.04) Missing 751 (5.2) 18 (6.5) First degree family history Any hematologic malignancy No 10152 (76.1) 202 (72.4) 1.00 (referent) Yes (Johorow age 36 (0.3) 1.6 (2.71.1) 1.00 (referent) Yes (Johorom age 36 (0.3) 6.0 (2.0 1.10) 1.00 (referent) Yes (Johorom age 36 (0.3) 6.0 (2.0 1.10) 1.00 (referent) Yes (Johorom age 36 (0.3) 6.0 (2.0 1.10) 1.00 (referent) Yes (Johorom age 36 (0.3) 6.0 (2.0 1.10) 1.00 (referent) Yes (Johorom age 36 (0.3) 6.0 (2.0 1.00 (referent) 1.00 (referent) Yes (Johorom age 36 (0.3) 6.0 (2.0 1.00 (referent) 1.00 (referent) Yes (Johorom age 36 (0.3) 6.0 (2.0 1.00 (referent) 1.00 (re	Yes	145 (1.2)	5 (2.0)	1.68 (0.67 to 4.21)
No autoimmune disease 16500 (95.8) 305 (94.1) 1.00 (referent) B-cell activation 127 (0.7) 2 (0.6) 1.02 (0.25 to 4.7.03) Any atopic disorder4 13 (0.1) 2 (0.6) 9.82 (2.05 to 47.03) Any atopic disorder4 13 (0.1) 2 (0.6) 9.82 (2.05 to 47.03) No 11 285 (65.5) 185 (57.1) 1.00 (referent) Yes 5690 (33.0) 129 (39.8) 1.25 (0.98 to 1.61) Allergy No 9254 (68.8) 161 (61.7) 0.00 (referent) Yes 3338 (24.8) 73 (28.0) 0.91 (0.67 to 1.24) Food allergy No 11065 (82.2) 178 (68.2) 1.00 (referent) Yes 972 (7.2) 21 (8.0) 1.04 (0.64 to 1.69) Asthma 374 (28.1) 1.00 (referent) 1.44 (0.64 to 1.69) Yes 240 (19.3) 55 (20.1) 0.99 (0.67 to 1.48) Hay fever No 9198 (64.9) 132 (48.4) 1.00 (referent) Yes 249 before diagnosis 740 (19.3) 55 (20.1) 0.30 (0.63 to 1.30) History of eczema No 72 (94 before diagnosis 92 (0.6)	History of autoimmune disease			
B-cell activation 127 (0.7) 2 (0.6) 1.02 (0.22 to 4.17) T-cell activation 577 (3.4) 15 (4.6) 1.49 (0.87 to 2.55) Both 13 (0.1) 2 (0.6) 9.82 (2.05 to 47.03) Ary atopic disorder‡	No autoimmune disease	16500 (95.8)	305 (94.1)	1.00 (referent)
1-cell activation 577 (3.4) 15 (4.6) 1.49 (0.87 to 2.55) Both 13 (0.1) 2 (0.6) 9.82 (2.05 to 4703) Any atopic disorder‡	B-cell activation	127 (0.7)	2 (0.6)	1.02 (0.25 to 4.17)
Both 13 (0.1) 2 (0.6) 9.82 (2.0s to 4/.03) Any atopic disorder‡	I-cell activation	577 (3.4)	15 (4.6)	1.49 (0.87 to 2.55)
Any action closer definition No 11285 (65.5) 185 (57.1) 1.00 (referent) Yes 5690 (33.0) 129 (39.8) 1.25 (0.98 to 1.61) Allergy	Both	13 (0.1)	2 (0.6)	9.82 (2.05 to 47.03)
No 11285 (65.5) 165 (57.1) 1.00 (referent) Yes 5690 (33.0) 129 (39.8) 125 (0.98 to 1.61) Allergyš	Any atopic disorder#			100 (referent)
Tes 569 (35.0) 129 (35.0) 129 (35.0) 129 (35.0) 129 (35.0) 120 (0.58 (0.1.61)) No 9254 (68.8) 161 (61.7) 1.00 (referent) Yes 3338 (24.8) 73 (28.0) 0.91 (0.67 to 1.24) Food allergy	INO Yes	11285 (05.5) ECOD (22.0)	185 (57.1)	1.00 (referent)
Name Participys Participys No 9254 (68.8) 161 (61.7) 1.00 (referent) Yes 3338 (24.8) 73 (28.0) 0.91 (0.67 to 1.24) Food allergy	105 Allerav&	5690 (33.0)	129 (39.6)	1.25 (0.98 (0 1.61)
No 10 (0.61 (n)) 10 (0.61 (n)) Yes 333 (24.8) 73 (28.0) 0.91 (0.67 to 1.24) Food allergy 11 (065 (82.2) 178 (68.2) 1.00 (referent) Yes 972 (7.2) 21 (8.0) 1.04 (0.64 to 1.69) Asthma 1.00 (referent) Yes 14140 (82.8) 260 (80.7) 1.00 (referent) Yes 1441 (8.4) 28 (8.7) 0.99 (0.67 to 1.48) Hay fever 100 (referent) Yes 246 (4.9) 132 (48.4) 1.00 (referent) Yes 2740 (19.3) 55 (20.1) 0.90 (0.63 to 1.30) History of eczema No r <2 y before diagnosis	No	9254 (68.8)	161 (617)	100 (referent)
Top of allergy Top of allergy Top of allergy Top of allergy No 11 065 (82.2) 178 (68.2) 1.00 (referent) Yes 972 (7.2) 21 (8.0) 1.04 (0.64 to 1.69) Asthma	Yes	3338 (24.8)	73 (28 0)	0.91 (0.67 to 1.24)
No 11 065 (82.2) 178 (68.2) 1.00 (referent) Yes 972 (72) 21 (8.0) 1.04 (0.64 to 1.69) Astma	Food allergy	3330 (24.0)	73 (20.0)	0.01 (0.07 to 1.24)
Yes 972 (7.2) 21 (8.0) 1.04 (0.64 to 1.69) Asthma No 14 140 (82.8) 260 (80.7) 1.00 (referent) Yes 1441 (8.4) 28 (8.7) 0.99 (0.67 to 1.48) Hay fever No 9198 (64.9) 132 (48.4) 1.00 (referent) Yes 2740 (19.3) 55 (20.1) 0.90 (0.63 to 1.30) History of eczema Vor <2 y before diagnosis	No	11 065 (82.2)	178 (68.2)	1.00 (referent)
Asthma No 14 140 (82.8) 260 (80.7) 1.00 (referent) Yes 1441 (8.4) 28 (8.7) 0.99 (0.67 to 1.48) Hay fever 7 7 1.00 (referent) No 9198 (64.9) 132 (48.4) 1.00 (referent) Yes 2740 (19.3) 55 (20.1) 0.99 (0.63 to 1.30) History of eczema 7 7 1.00 (referent) Yes 2740 (19.3) 55 (20.1) 0.90 (0.63 to 1.30) History of eczema 7 1.00 (referent) 0.90 (0.63 to 1.30) Yes, 5- 10 before diagnosis 12 157 (84.9) 205 (74.5) 1.00 (referent) Yes, 5- 10 before diagnosis 92 (0.6) 7 (2.5) 4.87 (2.15 to 11.02) Yes, 10 y or more before diagnosis 894 (6.2) 30 (10.9) 1.90 (1.27 to 2.85) Yes, unknown age 343 (2.4) 10 (3.6) 2.04 (1.03 to 4.04) Missing 751 (5.2) 18 (6.5) 18 First degree family history 751 (5.2) 18 (6.5) 1.00 (referent) Yes 581 (4.4)	Yes	972 (7.2)	21 (8.0)	1.04 (0.64 to 1.69)
No 14 140 (82.8) 260 (80.7) 1.00 (referent) Yes 1441 (8.4) 28 (8.7) 0.99 (0.67 to 1.48) Hay fever No 9198 (64.9) 132 (48.4) 1.00 (referent) Yes 2740 (19.3) 55 (20.1) 0.90 (0.63 to 1.30) History of eczema No or <2 y before diagnosis	Asthma			
Yes 1441 (8.4) 28 (8.7) 0.99 (0.67 to 1.48) Hay fever	No	14 140 (82.8)	260 (80.7)	1.00 (referent)
Hay fever No 9198 (64.9) 132 (48.4) 1.00 (referent) Yes 2740 (19.3) 55 (20.1) 0.90 (0.63 to 1.30) History of eczema No or <2 y before diagnosis	Yes	1441 (8.4)	28 (8.7)	0.99 (0.67 to 1.48)
No 9198 (64.9) 132 (48.4) 1.00 (referent) Yes 2740 (19.3) 55 (20.1) 0.90 (0.63 to 1.30) History of eczema No or <2 y before diagnosis	Hay fever			
Yes 2740 (19.3) 55 (20.1) 0.90 (0.63 to 1.30) History of eczema	No	9198 (64.9)	132 (48.4)	1.00 (referent)
History of eczema No or <2 y before diagnosis	Yes	2740 (19.3)	55 (20.1)	0.90 (0.63 to 1.30)
No or <2 y before diagnosis 12 157 (84.9) 205 (74.5) 1.00 (referent) Yes, 2-<5 y before diagnosis	History of eczema			
Yes, 2-<5 y before diagnosis	No or <2 y before diagnosis	12 157 (84.9)	205 (74.5)	1.00 (referent)
Yes, 5-<10 y before diagnosis	Yes, 2–<5 y before diagnosis	74 (0.5)	5 (1.8)	4.12 (1.54 to 11.04)
Yes, 10 y or more before diagnosis 894 (6.2) 30 (10.9) 1.90 (1.27 to 2.85) Yes, unknown age 343 (2.4) 10 (3.6) 2.04 (1.03 to 4.04) Missing 751 (5.2) 18 (6.5) First degree family history Any hematologic malignancy 10 152 (76.1) 202 (72.4) 1.00 (referent) Yes 581 (4.4) 16 (5.7) 1.16 (0.68 to 1.98) Multiple myeloma 7671 (74.5) 162 (71.1) 1.00 (referent) Yes 36 (0.3) 6 (2.6) 6 17 (2.39 to 15.91)	Yes, 5–<10 y before diagnosis	92 (0.6)	7 (2.5)	4.87 (2.15 to 11.02)
Yes, unknown age 343 (2.4) 10 (3.6) 2.04 (1.03 to 4.04) Missing 751 (5.2) 18 (6.5) First degree family history 751 (5.2) 18 (6.5) Any hematologic malignancy 751 (5.2) 18 (6.5) No 10 152 (76.1) 202 (72.4) 1.00 (referent) Yes 581 (4.4) 16 (5.7) 1.16 (0.68 to 1.98) Multiple myeloma 7671 (74.5) 162 (71.1) 1.00 (referent) Yes 36 (0.3) 6 (2.6) 6 17 (2.39 to 15.91)	Yes, 10 y or more before diagnosis	894 (6.2)	30 (10.9)	1.90 (1.27 to 2.85)
Missing 751 (5.2) 18 (6.5) First degree family history Any hematologic malignancy 10152 (76.1) 202 (72.4) 1.00 (referent) No 10 152 (76.1) 202 (72.4) 1.00 (referent) Yes 581 (4.4) 16 (5.7) 1.16 (0.68 to 1.98) Multiple myeloma 7671 (74.5) 162 (71.1) 1.00 (referent) Yes 36 (0.3) 6 (2.6) 6 17 (2.39 to 15.91)	Yes, unknown age	343 (2.4)	10 (3.6)	2.04 (1.03 to 4.04)
First degree family history Any hematologic malignancy No 10 152 (76.1) 202 (72.4) 1.00 (referent) Yes 581 (4.4) 16 (5.7) 1.16 (0.68 to 1.98) Multiple myeloma 7671 (74.5) 162 (71.1) 1.00 (referent) Yes 36 (0.3) 6 (2.6) 6 17 (2.39 to 15.91)	Missing	751 (5.2)	18 (6.5)	
Any nematologic malignancy 10 152 (76.1) 202 (72.4) 1.00 (referent) Yes 581 (4.4) 16 (5.7) 1.16 (0.68 to 1.98) Multiple myeloma 7671 (74.5) 162 (71.1) 1.00 (referent) Yes 36 (0.3) 6 (2.6) 6 17 (2.39 to 15.91)	First degree family history			
No 10 152 (70.1) 202 (72.4) 1.00 (referent) Yes 581 (4.4) 16 (5.7) 1.16 (0.68 to 1.98) Multiple myeloma 7671 (74.5) 162 (71.1) 1.00 (referent) Yes 36 (0.3) 6 (2.6) 6 17 (2.39 to 15.91)	Any nematologic malignancy		202 (72 4)	100 (referent)
No 7671 (74.5) 162 (71.1) 1.00 (referent) Yes 36 (0.3) 6 (2.6) 6 17 (2.39 to 15.91)	Voe		202 (72.4) 16 /5 7)	
No 7671 (74.5) 162 (71.1) 1.00 (referent) Yes 36 (0.3) 6 (2.6) 6 17 (2.39 to 15.91)	Nultinle myelome	001 (4.4)	10 (5.7)	1. 10 (0.00 (0 1.36)
Yes 36 (0.3) 6 (2.6) 6 17 (2.39 to 15.91)	Νο	7671 (74 5)	162 (71 1)	100 (referent)
	Yes	36 (0.3)	6 (2 6)	6.17 (2.39 to 15.91)

* CI = confidence interval; HCV = hepatitis C virus; HRT = hormone replacement therapy; OC = oral contraceptives; OR = odds ratio.

† OR (95% CI) adjusted for age, sex, and race.

‡ Atopic disorders include asthma, eczema, hay fever, or other allergies, excluding drug allergies.

§ History of allergy excludes drug allergies, asthma, eczema, and hay fever.

Table 4.	Associations	between	occupation	and	risk of	Mycosis
fungoid	es and Sézary	syndrom	ne*			

No. (%) No. (%) OR (95% CI)t Baker and miller No 11 152 (96.0) 209 (96.8) 1.00 (referent) Yes 141 (1.2) 4 (1.9) 1.80 (0.65 to 4.95) Cleaner No 10775 (92.8) 207 (95.8) 1.00 (referent) Yes 518 (4.5) 6 (2.8) 0.64 (0.28 to 1.46) Driver No 10467 (90.1) 200 (92.6) 1.00 (referent) Yes 826 (71) 13 (6.0) 0.83 (0.46 to 1.48) Electrical and electronics worker electronics worker No 10589 (91.2) 202 (93.5) 1.00 (referent) Yes 345 (3.2) 5 (2.5) 0.74 (0.30 to 1.83) Ever worked in farming Ma farm workers any type No 9980 (85.9) 185 (85.6) 1.00 (referent) Yes 1313 (11.3) 28 13.0) 1.45 (0.34 to 2.22) Crop and vegetable farm workers Mo 9677 (94.5) 156 (93.4) 1.00 (referent) Yes 1144 (95.9) 210 (97.2) 1.00 (referent) Yes 124 (1.3) 3 (1.4) 1.24 (0.39		Controls	Cases	
Transmission Transmission Transmission Baker and miller No 11 152 (96.0) 209 (96.8) 1.00 (referent) Yes 141 (1.2) 4 (1.9) 1.80 (0.65 to 4.95) Cleaner No 10 775 (92.8) 207 (95.8) 1.00 (referent) Yes 518 (4.5) 6 (2.8) 0.64 (0.28 to 1.46) Driver No 10 467 (90.1) 200 (92.6) 1.00 (referent) Yes 826 (71) 13 (6.0) 0.83 (0.46 to 1.48) Electrical and electronics worker electronics worker No 10 589 (91.2) 202 (93.5) 1.00 (referent) Yes 704 (6.1) 11 (5.1) 0.83 (0.46 to 1.48) Electrical and electronics worker No 10231 (93.9) 196 (96.1) 1.00 (referent) Yes 345 (3.2) 5 (2.5) 0.74 (0.30 to 1.83) Electrical and Ever worked in farming 1133 (11.3) 28 13.0) 1.45 (0.94 to 2.22) Crop and vegetable farm worker No 9677 (94.5) 156 (93.4) 1.00 (referent) Yes		No. (%)	No. (%)	OB (95% CI)†
No 11 152 (96.0) 209 (96.8) 1.00 (referent) Yes 141 (1.2) 4 (1.9) 1.80 (0.65 to 4.95) Cleaner No 10775 (92.8) 207 (95.8) 1.00 (referent) Yes 518 (4.5) 6 (2.8) 0.64 (0.28 to 1.46) Driver No 10467 (90.1) 200 (92.6) 1.00 (referent) Yes 826 (7.1) 13 (6.0) 0.83 (0.46 to 1.48) Electronics worker No 10589 (91.2) 202 (93.5) 1.00 (referent) Yes 704 (6.1) 11 (5.1) 0.83 (0.44 to 1.54) Engine mechanic No 10231 (93.9) 196 (96.1) 1.00 (referent) Yes 345 (3.2) 5 (2.5) 0.74 (0.30 to 1.83) Ever worked in farming and farm workers any type No 9980 (85.9) 185 (85.6) 1.00 (referent) Yes 1313 (11.3) 28 13.0) 1.45 (0.94 to 2.22) Crop and vegetable farm worker No 9677 (94.5) 156 (93.4) 1.00 (referent) Yes 226 (2.2) 9 (5.4)	Baker and miller	110. (70)	100. (70)	
No 11 (1.2) 20 (10.0) 1.80 (1.65 to 4.95) Cleaner No 10 775 (92.8) 207 (95.8) 1.00 (referent) Yes 518 (4.5) 6 (2.8) 0.64 (0.28 to 1.46) Driver No 10 467 (90.1) 200 (92.6) 1.00 (referent) Yes 826 (7.1) 13 (6.0) 0.83 (0.46 to 1.48) Electrical and electronics worker No 10 529 (91.2) 202 (93.5) 1.00 (referent) Yes 704 (6.1) 11 (5.1) 0.83 (0.44 to 1.54) Engine mechanic No 10 231 (93.9) 196 (96.1) 1.00 (referent) Yes 704 (6.1) 11 (5.1) 0.83 (0.44 to 1.83) Ever worked in farming and farm workers 345 (3.2) 5 (2.5) 0.74 (0.30 to 1.83) Sever worker No 9677 (94.5) 156 (93.4) 1.00 (referent) Yes 131 (11.3) 28 13.0) 1.45 (0.94 to 2.22) Crop and vegetable farm worker No 9677 (94.5) 156 (93.4) 1.00 (referent) Yes 120 (677 (94.5) <t< td=""><td>No</td><td>11 152 (96 0)</td><td>209 (96 8)</td><td>100 (referent)</td></t<>	No	11 152 (96 0)	209 (96 8)	100 (referent)
Cleaner No 10775 (92.8) 207 (95.8) 1.00 (referent) Yes 518 (4.5) 6 (2.8) 0.64 (0.28 to 1.46) Driver No 10467 (90.1) 200 (92.6) 1.00 (referent) Yes 826 (7.1) 13 (6.0) 0.83 (0.46 to 1.48) Electrical and electronics worker No 10589 (91.2) 202 (93.5) 1.00 (referent) Yes 704 (6.1) 11 (5.1) 0.83 (0.44 to 1.54) Engine mechanic No 10231 (93.9) 196 (96.1) 1.00 (referent) Yes Sever worked in farming and farm workers any type No 9980 (85.9) 185 (85.6) 1.00 (referent) Yes 1313 (11.3) 28 13.0) 1.45 (0.94 to 2.22) Crop and vegetable farm worker No 9677 (94.5) 156 (93.4) 1.00 (referent) Yes 226 (2.2) 9 (5.4) 2.76 (1.35 to 5.61) Hair dresser No 1144 (95.9) 210 (97.2) 1.00 (referent) Yes 126 (5.4) 7 (3.2) 0.60 (0.28 to 1.29) Leather worker	Yes	141 (12)	203 (30.8) 4 (1 9)	1.00 (referenc) 1.80 (0.65 to 4.95)
No 10775 (92.8) 207 (95.8) 1.00 (referent) Yes 518 (4.5) 6 (2.8) 0.64 (0.28 to 1.46) Driver No 10467 (90.1) 200 (92.6) 1.00 (referent) Yes 826 (7.1) 13 (6.0) 0.83 (0.46 to 1.48) Electronics worker No 10589 (91.2) 202 (93.5) 1.00 (referent) Yes 704 (6.1) 11 (5.1) 0.83 (0.44 to 1.54) Engine mechanic No 10231 (93.9) 196 (96.1) 1.00 (referent) Yes 345 (3.2) 5 (2.5) 0.74 (0.30 to 1.83) Ever worked in farming and farm workers 313 (11.3) 28 13.0) 1.45 (0.94 to 2.22) Crop and vegetable farm worker 704 (5.2) 156 (93.4) 1.00 (referent) Yes 1313 (11.3) 28 13.0) 1.45 (0.94 to 2.22) Crop and vegetable farm worker 149 (1.3) 3 (1.4) 1.24 (0.39 to 3.95) General unspecified laborer 149 (1.3) 3 (1.4) 1.24 (0.39 to 3.95) General unspecified laborer 149 (1.3) 3 (1.4) 1.24 (0.39 to 5.37) <td>Cleaner</td> <td>141 (1.2)</td> <td>4 (1.0)</td> <td>1.00 (0.00 to 4.00)</td>	Cleaner	141 (1.2)	4 (1.0)	1.00 (0.00 to 4.00)
Yes 10 (0.28,0) 20 (0.28,0) 0.64 (0.28 to 1.46) Driver No 10 467 (90.1) 200 (92.6) 1.00 (referent) Yes 826 (7.1) 13 (6.0) 0.83 (0.46 to 1.48) Electrical and electronics worker No 10589 (91.2) 202 (93.5) 1.00 (referent) Yes 704 (6.1) 11 (5.1) 0.83 (0.44 to 1.54) Engine mechanic No 10231 (93.9) 196 (96.1) 1.00 (referent) Yes 345 (3.2) 5 (2.5) 0.74 (0.30 to 1.83) Ever worked in farming and farm workers any type No 9980 (85.9) 185 (85.6) 1.00 (referent) Yes 1313 (11.3) 28 13.0) 1.45 (0.94 to 2.22) Crop and vegetable farm worker No 9677 (94.5) 156 (93.4) 1.00 (referent) Yes 129 (1.3) 3 (1.4) 1.24 (0.39 to 3.95) General unspecified laborer No 10667 (91.8) 206 (95.4) 1.00 (referent) Yes 626 (5.4) 7 (3.2) 1.00 (referent) Yes 626 (5.4) 7 (3.2)	No	10775 (92.8)	207 (95.8)	100 (referent)
Diver Diver <th< td=""><td>Yes</td><td>518 (4 5)</td><td>6 (2.8)</td><td>0.64 (0.28 to 1.46)</td></th<>	Yes	518 (4 5)	6 (2.8)	0.64 (0.28 to 1.46)
No 10467 (90.1) 200 (92.6) 1.00 (referent) Yes 826 (7.1) 13 (6.0) 0.83 (0.46 to 1.48) Electronics worker No 10589 (91.2) 202 (93.5) 1.00 (referent) Yes 704 (6.1) 11 (5.1) 0.83 (0.44 to 1.54) Engine mechanic No 10231 (93.9) 196 (96.1) 1.00 (referent) Yes 345 (3.2) 5 (2.5) 0.74 (0.30 to 1.83) Ever worked in farming and farm workers 345 (3.2) 5 (2.5) 0.74 (0.30 to 1.83) Ever worked in farming and farm worker 1.00 (referent) Yes 1.45 (0.94 to 2.22) Crop and vegetable farm worker 980 (85.9) 185 (85.6) 1.00 (referent) Yes 2.26 (2.2) 9 (5.4) 2.76 (1.35 to 5.61) Hair dresser No 1144 (95.9) 210 (97.2) 1.00 (referent) Yes 2.66 (5.4) 7 (3.2) 0.60 (0.28 to 1.29) Leather worker No 10667 (91.8) 206 (95.4) 1.00 (referent) Yes 626 (5.4) 7 (3.2) 0.60 (0.28 to 5.37)	Driver	010 (4.0)	0 (2.0)	0.04 (0.20 to 1.40)
Yes B26 (7.1) 13 (6.0) 0.83 (0.46 to 1.48) Electronics worker No 10589 (91.2) 202 (93.5) 1.00 (referent) Yes 704 (6.1) 11 (5.1) 0.83 (0.44 to 1.54) Engine mechanic No 10231 (93.9) 196 (96.1) 1.00 (referent) Yes 345 (3.2) 5 (2.5) 0.74 (0.30 to 1.83) Ever worked in farming and farm workers any type No 9980 (85.9) 185 (85.6) 1.00 (referent) Yes 1313 (11.3) 28 13.0) 1.45 (0.94 to 2.22) Crop and vegetable farm worker No 9677 (94.5) 156 (93.4) 1.00 (referent) Yes 226 (2.2) 9 (5.4) 2.76 (1.35 to 5.61) Hair dresser No 11144 (95.9) 210 (97.2) 1.00 (referent) Yes 129 (1.3) 3 (1.4) 1.24 (0.39 to 3.95) General unspecified laborer No 10667 (91.8) 206 (95.4) 1.00 (referent) Yes 626 (5.4) 7 (3.2) 0.60 (0.28 to 5.37) Meat worker No 11195 (96.4)	No	10467 (90 1)	200 (92 6)	100 (referent)
Test (a)	Yes	826 (71)	13 (6 0)	0.83 (0.46 to 1.48)
electronics worker No 10589 (91.2) 202 (93.5) 1.00 (referent) Yes 704 (6.1) 11 (5.1) 0.83 (0.44 to 1.54) Engine mechanic 10231 (93.9) 196 (96.1) 1.00 (referent) Yes 345 (3.2) 5 (2.5) 0.74 (0.30 to 1.83) Ever worked in farming and farm workers any type No 9980 (85.9) 185 (85.6) 1.00 (referent) Yes 1313 (11.3) 28 13.0) 1.45 (0.94 to 2.22) Crop and vegetable farm worker No 9677 (94.5) 156 (93.4) 1.00 (referent) Yes 226 (2.2) 9 (5.4) 2.76 (1.35 to 5.61) Hair dresser No 11144 (95.9) 210 (97.2) 1.00 (referent) Yes 149 (1.3) 3 (1.4) 1.24 (0.39 to 3.95) General unspecified 1aborer No 10 667 (91.8) 206 (95.4) 1.00 (referent) Yes 626 (5.4) 7 (3.2) 0.60 (0.28 to 1.29) Leather worker No 11 195 (96.4) 210 (97.2) 1.00 (referent) Yes No 11 195	Electrical and	020 (////	10 (010)	
No 10589 (91.2) 202 (93.5) 1.00 (referent) Yes 704 (6.1) 11 (5.1) 0.83 (0.44 to 1.54) Engine mechanic No 10231 (93.9) 196 (96.1) 1.00 (referent) Yes 345 (3.2) 5 (2.5) 0.74 (0.30 to 1.83) Ever worked in farming and farm workers 345 (3.2) 5 (2.5) 0.74 (0.30 to 1.83) Ever worked in farming and farm workers 1313 (11.3) 28 13.0) 1.45 (0.94 to 2.22) No 9980 (85.9) 185 (85.6) 1.00 (referent) Yes 1313 (11.3) 28 13.0) 1.45 (0.94 to 2.22) Crop and vegetable farm worker No 9677 (94.5) 156 (93.4) 1.00 (referent) Yes 226 (2.2) 9 (5.4) 2.76 (1.35 to 5.61) Hair dresser No 11144 (95.9) 210 (97.2) 1.00 (referent) Yes 149 (1.3) 3 (1.4) 1.24 (0.39 to 3.95) General unspecified laborer No 10667 (91.8) 206 (95.4) 1.00 (referent) Yes 626 (5.4) 7 (3.2) 0.60 to 2.8 to 1.29) <td>electronics worker</td> <td></td> <td></td> <td></td>	electronics worker			
Yes 704 (6.1) 11 (5.1) 0.83 (0.44 to 1.54) Engine mechanic No 10 231 (93.9) 196 (96.1) 1.00 (referent) Yes 345 (3.2) 5 (2.5) 0.74 (0.30 to 1.83) Ever worked in farming and farm workers any type 9980 (85.9) 185 (85.6) 1.00 (referent) Yes 1313 (11.3) 28 13.0) 1.45 (0.94 to 2.22) Crop and vegetable farm worker 9677 (94.5) 156 (93.4) 1.00 (referent) Yes 226 (2.2) 9 (5.4) 2.76 (1.35 to 5.61) Hair dresser No 11144 (95.9) 210 (97.2) 1.00 (referent) Yes 149 (1.3) 3 (1.4) 1.24 (0.39 to 3.95) General unspecified laborer 10667 (91.8) 206 (95.4) 1.00 (referent) Yes 626 (5.4) 7 (3.2) 0.60 (0.28 to 1.29) Leather worker No 11195 (96.4) 210 (97.2) 1.00 (referent) Yes 98 (0.8) 3 (1.4) 1.76 (0.55 to 5.67) Medical worker No 10423 (89.7) 198 (91.7) 1.00 (referent)	No	10589 (91.2)	202 (93.5)	1.00 (referent)
Engine mechanic No 10 231 (93.9) 196 (96.1) 1.00 (referent) Yes 345 (3.2) 5 (2.5) 0.74 (0.30 to 1.83) Ever worked in farming and farm workers any type 5 (2.5) 0.74 (0.30 to 1.83) No 9980 (85.9) 185 (85.6) 1.00 (referent) Yes 1313 (11.3) 28 13.0) 1.45 (0.94 to 2.22) Crop and vegetable farm worker 226 (2.2) 9 (5.4) 2.76 (1.35 to 5.61) Hair dresser No 11144 (95.9) 210 (97.2) 1.00 (referent) Yes 149 (1.3) 3 (1.4) 1.24 (0.39 to 3.95) General unspecified laborer 149 (1.3) 3 (1.4) 1.24 (0.39 to 3.95) Mo 10 667 (91.8) 206 (95.4) 1.00 (referent) Yes 626 (5.4) 7 (3.2) 0.60 (0.28 to 1.29) Leather worker No 11 195 (96.4) 210 (97.2) 1.00 (referent) Yes 147 (1.6) 4 (2.3) 1.93 (0.69 to 5.37) Meat worker No 11 195 (96.4) 210 (97.2) 1.00 (referent) Yes	Yes	704 (6.1)	11 (5.1)	0.83 (0.44 to 1.54)
No 10 231 (93.9) 196 (96.1) 1.00 (referent) Yes 345 (3.2) 5 (2.5) 0.74 (0.30 to 1.83) Ever worked in farming and farm workers any type 9980 (85.9) 185 (85.6) 1.00 (referent) Yes 1313 (11.3) 28 13.0) 1.45 (0.94 to 2.22) Crop and vegetable farm worker 9677 (94.5) 156 (93.4) 1.00 (referent) Yes 226 (2.2) 9 (5.4) 2.76 (1.35 to 5.61) Hair dresser 11 144 (95.9) 210 (97.2) 1.00 (referent) Yes 149 (1.3) 3 (1.4) 1.24 (0.39 to 3.95) General unspecified laborer 149 (1.3) 3 (1.4) 1.24 (0.39 to 3.95) Leather worker 626 (5.4) 7 (3.2) 0.60 (0.28 to 1.29) Leather worker 147 (1.6) 4 (2.3) 1.93 (0.69 to 5.37) Meat worker 11 195 (96.4) 210 (97.2) 1.00 (referent) Yes 98 (0.8) 3 (1.4) 1.6 (0.55 to 5.67) Medical worker No 10 423 (89.7) 198 (91.7) 1.00 (referent) Yes 870 (7.5)	Engine mechanic	- (-)	,	,
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Ever worked in farming and farm workers any type Sec. Sec. <th< td=""><td>Yes</td><td>345 (3.2)</td><td>5 (2.5)</td><td>0.74 (0.30 to 1.83)</td></th<>	Yes	345 (3.2)	5 (2.5)	0.74 (0.30 to 1.83)
and farm workers any type No 9980 (85.9) 185 (85.6) 1.00 (referent) Yes 1313 (11.3) 28 13.0) 1.45 (0.94 to 2.22) Crop and vegetable farm worker 100 9677 (94.5) 156 (93.4) 1.00 (referent) Yes 226 (2.2) 9 (5.4) 2.76 (1.35 to 5.61) Hair dresser 11 144 (95.9) 210 (97.2) 1.00 (referent) Yes 149 (1.3) 3 (1.4) 1.24 (0.39 to 3.95) General unspecified laborer 149 (1.3) 206 (95.4) 1.00 (referent) Yes 626 (5.4) 7 (3.2) 0.60 (0.28 to 1.29) Leather No 8841 (95.0) 164 (95.9) 1.00 (referent) Yes 147 (1.6) 4 (2.3) 1.93 (0.69 to 5.37) Meat worker No 11 195 (96.4) 210 (97.2) 1.00 (referent) Yes 98 (0.8) 3 (1.4) 1.76 (0.55 to 5.67) Medical worker No 10 423 (89.7) 198 (91.7) 1.00 (referent) Yes 870 (7.5) 15 (6.9) 0.89 (0.52 to 1.53) Metal worker No 10 612 (91.4) 20	Ever worked in farming	. ,		
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Yes 1151 (9.9) 23 (10.6) 1.00 (referent) Textile worker No 10552 (90.8) 199 (92.1) 1.00 (referent) Yes 741 (6.4) 14 (6.5) 1.30 (0.73 to 2.32) Woodworker No 10969 (94.4) 201 (93.1) 1.00 (referent)	No	10 142 (873)	190 (RR N)	100 (referent)
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Woodworker 10 969 (94.4) 201 (93.1) 1.00 (referent)	Yes	741(6 4)	14 (6 5)	1.30 (0.73 to 2.32)
No 10969 (94.4) 201 (93.1) 1.00 (referent)	Woodworker	/+ (0.+/	1+ (0.0)	
	No	10,969 (94.4)	201 (93 1)	1.00 (referent)
Yes 324 (2.8) 12 (5.6) 2.19 (1.19 to 4.03)	Yes	324 (2.8)	12 (5.6)	2.19 (1.19 to 4.03)

Table 4	(Conti	nued).
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	Controls	Cases	
	No. (%)	No. (%)	OR (95% CI)†
General carpenter			
No	10493 (96.3)	196 (96.1)	1.00 (referent)
Yes	71 (0.7)	5 (2.5)	4.50 (1.74 to 11.62)

* CI = confidence interval; OR = odds ratio.

† OR(95% CI) adjusted for age, sex, and race.

Table 5.	Significant	assocatiions	from	multivariate	model*
lubic 0.	orginnount	000000000000000000000000000000000000000		manuvariato	moduli

	Controls		Cases			
	No.	(%)	No	. (%)	0	R (95% CI)†
History of cigarette smoking	‡					
No	6997	(42.7)	121	(42.9)	1.00	(reference)
1–20, y	3090	(18.9)	47	(16.7)	0.85	(0.60 to 1.21)
21–30, v	1783	(10.9)	27	(9.6)	0.77	(0.50 to 1.19)
30–39. v	1737	(10.6)	24	(8.5)	0.81	(0.51 to 1.28)
40≥. v	1742	(10.6)	40	(14.2)	1.55	(1.04 to 2.31)
Physical activity		/		. ,		, ,
None	716	(10.1)	20	(14.7)	1.00	(reference)
Mild	474	(6.7)	14	(10.3)	0.74	(0.33 to 1.64)
Moderate	934	(13.2)	20	(14.7)	0.46	(0.22 to 0.97)
Vigorous	3037	(43.0)	45	(33.1)	0.58	(0.32 to 1.08)
Usual adult BMI, kg/m ²		/		(
18.5-<22.5	2943	(19.9)	47	(15.9)	1.00	(reference)
15-<18.5	209	(14)	5	(17)	139	(0.53 to 3.70)
22 5-<25	3601	(24.4)	59	(20, 0)	1.02	(0.69 to 1.52)
25-<30	5220	(35.4)	107	(36.3)	124	(0.86 to 1.78)
30-50	2175	(147)	55	(18.6)	157	(103 to 2 40)
History of autoimmune		(,		()		(
disease						
No autoimmune	16500	(95.8)	305	(94.1)	100	(reference)
disease		(00.07	000	(0)		(1010101100)
B-cell activation	127	(07)	2	(0.6)	100	(0 24 to 4 13)
T-cell activation	577	(3.4)	15	(4.6)	148	(0.86 to 2.53)
Both	13	(0, 1)	2	(0.6)	9 4 5	(180 to 49 60)
History of eczema		(,	_	(0.0)		(
No	12 100	(84.6)	202	(73.5)	1.00	(reference)
Yes	1460	(10.2)	55	(20.0)	2 38	(173 to 3 29)
Family history of multiple		(00	(20.0)	2.00	(, 0 to 0.20)
mveloma						
No	7671	(74 5)	162	(711)	100	(reference)
Yes	.36	(0.3)	6	(2.6)	8 4 9	(3.31 to 21.80)
Crop and vegetable farm	00	(0.0)	0	(2.0)	0.10	(0.01 to 2.100)
workers						
No	9677	(94 5)	156	(93 4)	100	(reference)
Yes	226	(2 2)	.00	(5.4)	2.37	(1 14 to 4 92)
Painter	220	(2.2)	0	(0.1)	2.07	(1.11100 1.02)
No	11 099	(95 5)	202	(93 5)	100	(reference)
Yes	194	(17)	11	(5.1)	3 71	(1.94 to 707)
Woodworkers	101	(1.77		(0.1)	0.7 1	(1.0 1 to 7.07)
No	10.969	(91 1)	201	(93.1)	1 00	(reference)
Yes	324	(2 8)	12	(5.6)	2 20	(1 18 to 4 08)
General carpenter	024	12.0/	12	,0.0/	2.20	(
No	10/193	(96 3)	196	(96 1)	1 00	(reference)
Yes	71	(0 7)	-00. F	(2 5)	4 07	(1 54 to 10 75)
100	/ 1	.0.77	J	12.01	7.07	(

* CI = confidence interval; OR = odds ratio.

 $^{\dagger}~$ OR (95% CI) adjusted for age, sex, race, and all other variables listed in the table.

‡ Smoked longer than 6 months or more than 100 cigarettes in lifetime.

(Table continues)

and Australia, suggest that subjects with a positive family history of multiple myeloma and subjects working in crop and vegetable farms, or as painters, carpenters or woodworkers, might be at an increased risk of MF/SS. A history of eczema for more than 10 years before MF/SS diagnosis also increased risk. Among personal and lifestyle risk factors, only obesity and prolonged cigarette smoking seem to convey an increased risk, while a moderate/vigorous leisure time physical activity might be protective. As both MF and SS are rare, few results have previously been published and are available for comparison with our findings.

Chronic exposure to cigarette smoke has been associated with decreased immune responsiveness, particularly for T cells, in both human and animal studies (25), which would suggest a potential link to decreased immune surveillance and increased lymphoma risk. In a previous pooled InterLymph study, heavy smoking was associated with an increased risk of follicular lymphoma but not other NHL subtypes, including MF (26). In the European multicenter study of MF, a linear increase in MF risk with increasing pack-years of smoking was observed, although the trend was not statistically significant (27). In the analyses presented here, a significant association was observed among individuals who had smoked cigarettes for 40 years or more, but no dose–response was observed with increasing duration.

Obesity promotes a state of low-grade chronic inflammation and increased production of proinflammatory cytokines such as interleukin (IL)-6, tumor necrosis factor- α , IL-1b, and leptin (28). These cytokines can deregulate T- and B-cell responses and enhance B-cell proliferation and survival, factors that may provide a milieu that favors lymphomagenesis (29). In our analysis, a BMI greater than or equal to 30 kg/m^2 was associated with an increased risk of MF/SS, although we were unable to support with statistical significance the observed linear increase in risk by increasing BMI. A similar finding was reported for diffuse large B-cell lymphoma in a previous InterLymph study of NHL overall and common NHL subtypes; however, MF/SS was not analyzed as a separate outcome in that study (30).

Moderate physical activity may improve immune function and it may therefore protect against NHL and possibly MF/SS (31). In our study we found that, compared with people who were not engaged in leisure-time physical activity, those who engaged in moderate and vigorous physical activity experienced a reduced risk of MF/SS. However, the decrease in MF/SS risk by increasing level of physical activity was not linear, and the multivariate analysis partially weakened the inverse association. Previous reports suggest that moderate exercise may reduce NHL risk (32,33). More research in this area is warranted.

In agreement with a previous InterLymph study (13), we found that a previous medical history of eczema was associated with an increased risk of MF/SS, which appeared to be stronger for those who were diagnosed within 10 years of MF/SS diagnosis. Such a pattern might suggest the possibility that early MF may be mistaken for eczema in some cases. Alternatively, the association with eczema may be an indicator of eczema as an early disease rather than a risk factor as it often goes undiagnosed for years. However, the risk remained significantly elevated for those who were diagnosed more than 10 years before MF/SS diagnosis. Eczema is a form of chronic dermatitis which is known to have a pathogenetic association with early stages of MF (34). Specific autoimmune diseases were rare and no analysis of their associations with MF/SS risk was feasible; after categorizing autoimmune diseases by whether B or T cells were activated, no association was observed. However, two cases of autoimmune diseases that activate both B and T cells were observed, resulting in an elevated MF/SS risk. B cell activating diseases included Hashimoto thyroiditis, hemolytic anemia, myasthenia gravis, pernicious anemia, rheumatoid arthritis, Sjögren's syndrome, and systemic lupus erythematosus. T cell activating diseases included celiac disease, immune thrombocytopenic purpura, inflammatory bowel disorder (Crohn's disease, ulcerative colitis), multiple sclerosis, polymyositis or dermatomyositis, psoriasis, sarcoidosis, systemic sclerosis or scleroderma, and type 1 diabetes.

A role for genetic susceptibility in MF/SS is supported by the accumulating evidence of common genetic variations altering MF risk (35,36). In our study, persons with a family history of multiple myeloma had an excess risk of MF/SS, but no association was found with family history of any hematologic malignancy. In a previous pooled InterLymph analysis, risk of specific NHL subtypes, including T-cell lymphomas (MF/SS were not separately evaluated), were elevated among subjects who reported a family history of hematologic malignancies in first-degree relatives, particularly multiple myeloma in males (37). However, it is also possible that since multiple myeloma and MF are increased in blacks (37), this may confound the association.

The evaluation of occupational risk factors showed that crop and vegetable farm workers, painters, woodworkers and carpenters experienced an increased risk of MF/SS. Although we did not examine specific occupational exposures, our findings are consistent with the results of other studies that examined exposures potentially encountered in these occupations. In a European casecontrol study, occupational exposures to the broad category of aromatic and/or halogenated hydrocarbons, which are widely used as solvents, and to pesticides in general were identified as potential risk factors for MF (10). An excess risk of NHL among farmers and agricultural workers has been repeatedly reported, suggesting a potential link with farming exposures including pesticides (38,39). Among the most commonly used agrochemicals, organophosphate insecticides were associated with an increased risk in the European Epilymph study, limited to the chronic lymphocytic leukemia subtype (40). Other occupations previously associated with an increase in MF risk include different manufacturing industries, such as petrochemical, textile, and various metal industries (41-43). Painters and woodworkers may also be exposed to solvents in paint thinners and paint and grease removers, including benzene and trichloroethylene previously associated with increased risk of other NHL subtypes in prior reports from included studies (44,45). Other exposures possibly related to the excess risk we observed for these occupations include chlorophenols, wood dust, and molds (Cocco P, unpublished data). Our results suggest that these and other potentially harmful exposures should be explored in greater detail in future investigations using advanced occupational exposure assessment methods.

Although this is the largest study to date that examines numerous putative risk factors in relation to MF/SS, the small number of subjects was still a limitation. All cases were histologically confirmed, but centralized review of all cases by a team of study pathologists was not feasible, and thus some misclassification may be present. As multiple hypotheses have been tested and a number of comparisons have been made, chance findings cannot be ruled out. Since only 13 SS cases were included in this study, we were unable to examine associations specific to SS; therefore, the observed associations were predominantly driven by MF and may not apply to SS. Another limitation is related to the number of comparisons we made, which might have generated several positive findings as the sole result of chance. However, negative findings might have been missed as the study size is insufficient to detect weaker associations. In conclusion, our pooled analysis of lifestyle factors, medical history, and occupation and MF/SS suggests potential positive associations with elevated BMI, long-term cigarette smoking, eczema, and family history of multiple myeloma, and a potential negative association with moderate leisure time physical activity. Our findings for farming and other occupations point to avenues for additional research to identify specific occupational exposures that may be responsible for these associations. Future research is warranted to confirm these findings in prospectively collected data and in other populations.

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Affiliations of authors: Department of Health Studies, University of Chicago, Chicago, IL (BA-K); Department of Public Health, Clinical and Molecular Medicine, Occupational Health Section, University of Cagliari, Cagliari, Italy (PC); Dipartimento di Epidimologia, IRCCS-Istituto di Ricerche Farmacologiche Mario Negri, Milan, Italy, Community Health, University of Milan, Milan, Italy (CLV); Health Sciences Practice, Exponent, Inc., Menlo Park, CA, Department of Health Research and Policy, Stanford University, Stanford, CA (ETC); Prince of Wales Clinical School, University of New South Wales, Sydney, Australia (CMV); Department of Dermatology, Boston University, Boston, MA, Roger Williams Medical Center, Providence, RI (MEK); Cancer Control Research, BC Cancer Agency, Vancouver, BC, Canada, School of Population and Public Health, University of British Columbia, Vancouver, BC, Canada (JJS); Division of Cancer Epidemiology and Genetics, National Cancer Institute, National Institutes of Health Bethesda, MD (LMM, JNS); Epidemiology and Cancer Statistics Group, Department of Health Sciences, University of York, York, UK (EVK); Biostatistics Center, Massachusetts General Hospital, Boston, MA (CK); Department of Laboratory Medicine and Pathology, Mayo Clinic Cancer Center, Rochester, MN (ALF); Division of Cancer Etiology, Department of Population Sciences, Beckman Research Institute of the City of Hope, Duarte, CA (SSW); Department of Environmental Health Sciences, Yale School of Public Health, New Haven, CT (YZ).