

Medical History, Lifestyle, Family History, and Occupational Risk Factors for Diffuse Large B-Cell Lymphoma: The InterLymph Non-Hodgkin Lymphoma Subtypes Project

James R. Cerhan, Anne Kricker, Ora Paltiel, Christopher R. Flowers, Sophia S. Wang, Alain Monnereau, Aaron Blair, Luigino Dal Maso, Eleanor V. Kane, Alexandra Nieters, James M. Foran, Lucia Miligi, Jacqueline Clavel, Leslie Bernstein, Nathaniel Rothman, Susan L. Slager, Joshua N. Sampson, Lindsay M. Morton, Christine F. Skibola

Correspondence to: James R. Cerhan, MD, PhD, Department of Health Sciences Research, 200 1st St SW, Rochester, MN 55905 (e-mail: cerhan.james@mayo.edu).

Background	Although risk factors for diffuse large B-cell lymphoma (DLBCL) have been suggested, their independent effects, modification by sex, and association with anatomical sites are largely unknown.
Methods	In a pooled analysis of 4667 cases and 22 639 controls from 19 studies, we used stepwise logistic regression to identify the most parsimonious multivariate models for DLBCL overall, by sex, and for selected anatomical sites.
Results	DLBCL was associated with B-cell activating autoimmune diseases (odds ratio [OR] = 2.36, 95% confidence interval [CI] = 1.80 to 3.09), hepatitis C virus seropositivity (OR = 2.02, 95% CI = 1.47 to 2.76), family history of non-Hodgkin lymphoma (OR = 1.95, 95% CI = 1.54 to 2.47), higher young adult body mass index (OR = 1.58, 95% CI = 1.12 to 2.23, for 35+ vs 18.5 to 22.4 kg/m ²), higher recreational sun exposure (OR = 0.78, 95% CI = 0.69 to 0.89), any atopic disorder (OR = 0.82, 95% CI = 0.76 to 0.89), and higher socioeconomic status (OR = 0.86, 95% CI = 0.79 to 0.94). Additional risk factors for women were occupation as field crop/vegetable farm worker (OR = 1.78, 95% CI = 1.22 to 2.60), hairdresser (OR = 1.65, 95% CI = 1.12 to 2.41), and seamstress/embroider (OR = 1.49, 95% CI = 1.13 to 1.97), low adult body mass index (OR = 0.46, 95% CI = 0.29 to 0.74, for <18.5 vs 18.5 to 22.4 kg/m ²), hormone replacement therapy started age at least 50 years (OR = 0.68, 95% CI = 0.52 to 0.88), and oral contraceptive use before 1970 (OR = 0.78, 95% CI = 0.62 to 1.00); and for men were occupation as material handling equipment operator (OR = 1.58, 95% CI = 1.02 to 2.44), lifetime alcohol consumption (OR = 0.57, 95% CI = 0.44 to 0.75, for >400g vs nondrinker), and previous blood transfusion (OR = 0.69, 95% CI = 0.57 to 0.83). Autoimmune disease, atopy, and family history of non-Hodgkin lymphoma showed similar associations across selected anatomical sites, whereas smoking was associated with central nervous system, testicular and cutaneous DLBCLs; inflammatory bowel disease was associated with gastrointestinal DLBCL; and farming and hair dye use were associated with mediastinal DLBCL.
Conclusion	Our results support a complex and multifactorial etiology for DLBCL with some variation in risk observed by sex and anatomical site.

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Diffuse large B-cell lymphoma (DLBCL) is the most common non-Hodgkin lymphoma (NHL) subtype in Western countries (1,2). In Europe and the United States, the age-adjusted incidence rates range from 3.1 to 5.7 per 100 000, with a median age at diagnosis in the sixth decade (1,2). DLBCLs are heterogeneous in histology, immunophenotype, and site of presentation (3,4), mostly presenting in the lymph node although extranodal presentations are increasingly recognized (5). Several anatomical sites appear to have distinct epidemiological or clinical characteristics (6–10), but they have generally been too rare to evaluate in individual studies. DLBCLs have also been categorized based on cell of origin (activated B cell, germinal center, and other), which have distinct biological and clinical characteristics (11), although the epidemiological implications of this classification is unknown.

Although medical history, lifestyle, and other risk factors for DLBCL have been published in previous pooled International Lymphoma

Epidemiology Consortium (InterLymph) analyses (12–21), there has been no multivariate assessment of factors simultaneously, and limited assessment of risk factors stratified by sex and age or for specific anatomical sites. To advance our understanding of the etiology of DLBCL, we investigated these issues in the most complete and comprehensive pooled analysis to date, which combined 4667 cases and 22 639 controls from 19 case-control studies conducted in Europe, North America, and Australia as part of the InterLymph NHL Subtypes Project.

Methods

Detailed methodology, including inclusion and exclusion criteria and pathology review, is provided elsewhere in this issue (22). Contributing studies were approved by local ethics committees, and all participants provided informed consent before interview.

NHL Subtype Ascertainment and Harmonization

Cases were classified according to the World Health Organization classification (23,24) using guidelines from the InterLymph Pathology Working Group (25,26). For Working Formulation cases with no immunophenotyping data, only those from category G (diffuse large cell lymphoma) were assigned to DLBCL (overall reliability of 88.2%), and for those Working Formulation cases with B/T immunophenotyping data, both category G (overall reliability 92.3%) and H (large cell, immunoblastic, B cell; overall reliability 98.9%) were assigned to DLBCL (25). In most studies, primary site of lymphoma was recorded where known, irrespective of disease stage, following Surveillance, Epidemiology, and End Results coding rules (27); primary site of lymphoma was coded as missing when primary site could not be distinguished from biopsy site. We conducted exploratory analyses of risk factors for central nervous system (CNS), gastrointestinal (GI), testis, cutaneous and mediastinal DLBCL; these sites were selected a priori based on known distinct epidemiological or clinical characteristics (6–10).

Risk Factor Ascertainment and Harmonization

Risk factors selected for inclusion in this analysis were medical history, lifestyle, family history, and occupations where data were available from at least four studies. Centralized harmonization of de-identified individual-level data from each study center was a key element of the project. Each exposure variable was harmonized individually, and data were reviewed for consistency among related exposure variables. Details of the data harmonization rules are provided elsewhere in this issue (22).

Statistical Analysis

We first used unconditional logistic regression models to estimate odds ratios (ORs) and 95% confidence intervals (CIs) for risk of DLBCL with each exposure variable, adjusted for age, sex, race/ethnicity, and study (“basic adjusted models”). The 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. Individuals with missing data for the exposure variable of interest were excluded. To evaluate effect heterogeneity among the 19 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 (28).

To consider possible effect modification, we repeated the above logistic regression analyses stratified by sex and age (<60 and 60+ years). We tested for effect heterogeneity by calculating the Wald statistic for the interaction term between each exposure and stratification variable. We also evaluated heterogeneity using forest plots by study design characteristics. Finally, we conducted an exploratory analysis of selected anatomical sites, modeling risk of DLBCL at a specific anatomical site (excluding all other DLBCL cases), adjusted for age, sex, race/ethnicity, and study.

To build a multivariate model for DLBCL, we reviewed the basic adjusted models and then selected the best variable within a given class of related variables to move forward to stepwise regression. A variable was selected after considering the effect size (i.e., stronger OR), exposure prevalence (e.g., choosing either a

summary variable or a more common exposure over a rarer one to maximize power), and *P* value. From this set of selected factors, we evaluated the correlations of these variables as well as the risk estimate for each factor in a series of models that adjusted for other risk factors individually as well as age, race/ethnicity, sex, and study. We then conducted a single logistic regression model including all the selected risk factors, this time including a separate missing category for each variable to ensure that the entire study population was included in the analysis (i.e., not dropped due to missing data). Finally, we conducted a forward stepwise logistic regression with all the selected risk factors, adjusting for age, sex, race/ethnicity, and study; the risk factors remaining in this model were considered to be independent of each other (“final stepwise model”). We conducted these analyses for the entire study population, then separately for men and women. Because of small sample sizes, we did not conduct stepwise logistic regression for DLBCL site-specific analyses. All analyses were conducted using SAS software, version 9.2 (SAS Institute, Inc, Cary, NC).

Results

The pooled study population included 4667 DLBCL cases and 22 639 controls from 19 InterLymph studies; full characteristics are provided in Table 1. As has been previously noted for DLBCL (1,2), the percentage of men (55.2%) was higher than that for women (44.8%). Controls for most studies were chosen to approximate the age and sex distribution of all lymphoma cases, leading to some imbalance of the age and sex distribution for the controls used in this analysis. In a sensitivity analysis, we used a subset of controls that were frequency matched by age and sex to the DLBCL cases, which produced similar results to those obtained using the full set of controls (data not shown). Therefore, we retained the full set of controls for our main analyses to increase statistical power.

Overall and Sex- and Age-Specific Associations From the Basic Adjusted Models

The basic adjusted model results are shown in Supplementary Table 1. The variables selected for incorporation into the final stepwise models (bolded in Supplementary Table 1) included socioeconomic status (SES); B/T-cell activating autoimmune diseases (selected from a group of 18 autoimmune variables, which also included positive associations for Sjögren syndrome, systemic lupus erythematosus, hemolytic anemia, celiac disease, and rheumatoid arthritis); history of any atopic disorder (selected from six atopy variables, which also included inverse associations with allergy, food allergy, asthma, and hay fever); hepatitis C virus (HCV) seropositivity; history of blood transfusion (selected from five transfusion variables); family history of NHL (selected from 15 family history variables, which also included positive associations with family history of any hematologic malignancy and Hodgkin lymphoma); usual and young adult body mass index (BMI) (selected from three anthropometric variables, which also included a positive association with weight); lifetime alcohol use (selected from 16 variables, the majority of which showed inverse associations by current status, type, intensity and duration of use); recreational sun exposure; and occupation as a cleaner/related worker, driver/material handling equipment operator, field crop and vegetable farmer,

Table 1. Characteristics of studies included in the diffuse large B-cell lymphoma analysis, InterLymph NHL Subtypes Project*

	Controls	Cases	Total
	No. (%)	No. (%)	
Total	22 639 (82.9)	4667 (17.1)	27 306
Study			
North America			
British Columbia	845 (3.7)	218 (4.7)	1063
Iowa/Minnesota	1245 (5.5)	112 (2.4)	1357
Kansas	948 (4.2)	27 (0.6)	975
Los Angeles	375 (1.7)	151 (3.2)	526
Mayo Clinic	1314 (5.8)	210 (4.5)	1524
NCI-SEER	1055 (4.7)	413 (8.8)	1468
Nebraska (newer)	533 (2.4)	103 (2.2)	636
Nebraska (older)	1432 (6.3)	94 (2.0)	1526
UCSF1	2402 (10.6)	509 (10.9)	2911
UCSF2	0 (0.0)	0 (0.0)	0
University of Rochester	139 (0.6)	32 (0.7)	171
Yale	717 (3.2)	189 (4.0)	906
Europe			
Engela	722 (3.2)	174 (3.7)	896
EpiLymph	2460 (10.9)	516 (11.1)	2976
Italy multicenter	1771 (7.8)	407 (8.7)	2178
Italy (Aviano-Milan)	1157 (5.1)	47 (1.0)	1204
Italy (Aviano-Naples)	504 (2.2)	112 (2.4)	616
SCALE	3187 (14.1)	796 (17.1)	3983
United Kingdom	1139 (5.0)	326 (7.0)	1465
Australia			
New South Wales	694 (3.1)	231 (4.9)	925
Region			
North America	11 005 (48.6)	2058 (44.1)	13 063
Northern Europe	6542 (28.9)	1624 (34.8)	8166
Southern Europe	4398 (19.4)	754 (16.2)	5152
Australia	694 (3.1)	231 (4.9)	925
Design			
Population-based	17 389 (76.8)	3799 (81.4)	21 188
Hospital-based	5250 (23.2)	868 (18.6)	6118
Age			
<30	1356 (6.0)	210 (4.5)	1566
30–39	2143 (9.5)	452 (9.7)	2595
40–49	3090 (13.6)	609 (13.0)	3699
50–59	4870 (21.5)	1128 (24.2)	5998
60–69	6277 (27.7)	1351 (28.9)	7628
70–79	4048 (17.9)	816 (17.5)	4864
≥80	839 (3.7)	84 (1.8)	923
Missing	16 (0.1)	17 (0.4)	33
Sex			
Men	13 228 (58.4)	2578 (55.2)	15 806
Women	9411 (41.6)	2089 (44.8)	11 500
Race			
White, non-Hispanic	21 145 (93.4)	4217 (90.4)	25 362
Black	351 (1.6)	74 (1.6)	425
Asian	321 (1.4)	111 (2.4)	432
Hispanic	334 (1.5)	101 (2.2)	435
Other/unknown/missing	488 (2.2)	164 (3.5)	652
Socioeconomic status			
Low	9266 (40.9)	1948 (41.7)	11 214
Medium	6577 (29.1)	1355 (29.0)	7932
High	6386 (28.2)	1296 (27.8)	7682
Other/missing	410 (1.8)	68 (1.5)	478
NHL subtype classification			
World Health Organization		3320 (71.1)	3320
Working Formulation		1347 (28.9)	1347

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

women's hairdresser, medical worker, and seamstress/embroiderer. There were no associations with cigarette smoking (from seven variables), physical activity, personal hair dye use (from six variables), or ever having lived or worked on a farm.

We also conducted sex-stratified analyses (including a test for interaction) for all of the basic associations that were reported in [Supplementary Table 1](#) to identify variables to include in the sex-specific stepwise regression models. For women, additional variables were pack-years of smoking, oral contraceptive (OC) use by year started, and age at start of hormone therapy (HT) use. For men, the only additional variable was occupation as a metal processor. Variables selected for the stepwise models with evidence for sex-specific heterogeneity included blood transfusion ($P = .046$), young adult BMI ($P = .023$), and lifetime alcohol consumption ($P = .0029$), all of which showed stronger associations for men than for women ([Supplementary Table 1](#)). There was no strong evidence of heterogeneity by age for variables in [Supplementary Table 1](#) (data not shown).

Heterogeneity by Design Variables

In reviewing the H statistic from each of the basic adjusted models, only recreational sun exposure ($H = 2.44$, 95% CI = 1.11 to 5.34) and adult BMI ($H = 2.42$, 95% CI = 1.31 to 4.48) showed substantial heterogeneity. In further reviewing forest plots for these two variables as well as other variables selected for the final stepwise models, a majority showed no evidence for heterogeneity by study design (i.e., population-based versus hospital-/clinic-based), World Health Organization versus Working Formulation, location (North America, Northern Europe, Southern Europe, Australia), or specific study. However, there was some suggestion that the associations with adult BMI ([Supplementary Figure 1](#)), OC use before 1970 ([Supplementary Figure 2](#)), and seamstresses/embroiders ([Supplementary Figure 3](#)) were strongest in North American studies; autoimmune disease ([Supplementary Figure 4](#)) was strongest in population-based studies; and recreational sun exposure ([Supplementary Figure 5](#)) was strongest in Australia and Southern Europe.

Final Stepwise Models

The final stepwise model for all participants ([Table 2](#)) included high SES (OR = 0.86); B-cell (OR = 2.36) and both B-/T-cell (OR = 4.86) activating autoimmune diseases; any atopic disorder (OR = 0.82); HCV seropositivity (OR = 2.02); previous blood transfusion (OR = 0.81); family history of NHL (OR = 1.95); young adult BMI (OR = 1.58 for 30+ vs 18.5–22.4 kg/m²); usual adult BMI (OR = 0.58 for 15.0–18.4 vs 18.5–22.5 kg/m²); greater lifetime alcohol consumption (OR = 0.64 for >400 kg vs nondrinker); higher recreational sun exposure (OR = 0.78); and occupation as field crop and vegetable farmer (OR = 1.49), seamstress/embroiderer (OR = 1.43), and driver/material handling equipment operator (OR = 1.47). These results were consistent in pairwise adjusted models of all exposure variables, as well as the model simultaneously adjusting for all exposures, further supporting that the effects of these variables were mutually independent.

We next conducted sex-specific stepwise models ([Table 2](#)). For both sexes, SES, autoimmune disease B-/T-cell type, atopic disorder, HCV seropositivity, family history of NHL, young adult BMI,

Table 2. Results of the final stepwise regression*

Variable	Sex-specific models							
	Controls	Cases	All participants		Men		Women	
	No. (%)	No. (%)	OR (95% CI)	P	OR (95% CI)	P	OR (95% CI)	P
SES								
Low	9266 (40.9)	1948 (41.7)	1.00 (Referent)	.002	1.00 (Referent)	.008	1.00 (Referent)	.125
Medium	6577 (29.1)	1355 (29.0)	0.88 (0.81 to 0.95)	—	0.86 (0.77 to 0.96)	—	0.92 (0.81 to 1.04)	—
High	6386 (28.2)	1296 (27.8)	0.86 (0.79 to 0.94)	—	0.84 (0.75 to 0.94)	—	0.95 (0.83 to 1.08)	—
Other/missing	410 (1.8)	68 (1.5)	0.92 (0.65 to 1.31)	—	1.13 (0.73 to 1.77)	—	0.50 (0.25 to 1.00)	—
History of autoimmune disease†								
No autoimmune disease	19423 (95.9)	4286 (94.3)	1.00 (Referent)	<.001	1.00 (Referent)	.001	1.00 (Referent)	<.001
B-cell activation	157 (0.8)	87 (1.9)	2.36 (1.80 to 3.09)	—	2.22 (1.36 to 3.61)	—	2.42 (1.73 to 3.38)	—
T-cell activation	664 (3.3)	159 (3.5)	1.03 (0.86 to 1.24)	—	1.14 (0.89 to 1.45)	—	0.90 (0.69 to 1.19)	—
Both	15 (0.1)	14 (0.3)	4.86 (2.31 to 10.25)	—	6.20 (1.35 to 28.43)	—	4.47 (1.84 to 10.84)	—
Any atopic disorder‡								
No	15601 (68.9)	3262 (69.9)	1.00 (Referent)	<.001	1.00 (Referent)	<.001	1.00 (Referent)	<.001
Yes	6442 (28.5)	1315 (28.2)	0.82 (0.76 to 0.89)	—	0.84 (0.75 to 0.93)	—	0.81 (0.72 to 0.91)	—
Missing	596 (2.6)	90 (1.9)	1.30 (0.96 to 1.75)	—	1.04 (0.69 to 1.56)	—	1.48 (0.92 to 2.38)	—
HCV positivity								
No	6746 (66.8)	1591 (66.8)	1.00 (Referent)	<.001	1.00 (Referent)	<.001	1.00 (Referent)	.004
Yes	152 (1.5)	63 (2.6)	2.02 (1.47 to 2.76)	—	2.17 (1.44 to 3.26)	—	1.98 (1.18 to 3.34)	—
Missing	3194 (31.6)	728 (30.6)	0.93 (0.83 to 1.03)	—	0.81 (0.71 to 0.94)	—	1.70 (1.40 to 2.08)	—
Blood transfusion								
No	10742 (76.7)	2654 (81.3)	1.00 (Referent)	<.001	1.00 (Referent)	<.001	(Not selected)	—
Yes	1966 (14.0)	411 (12.6)	0.81 (0.72 to 0.91)	—	0.69 (0.57 to 0.83)	—	—	—
Missing	1297 (9.3)	199 (6.1)	1.18 (0.93 to 1.49)	—	1.33 (1.00 to 1.76)	—	—	—
Year of first OC use								
No OC use	2817 (28.8)	638 (32.7)	(Not eligible)	—	(Not eligible)	—	1.00 (Referent)	.014
<1970	765 (7.8)	128 (6.6)	—	—	—	—	0.78 (0.62 to 1.00)	—
≥1970	757 (7.7)	155 (7.9)	—	—	—	—	1.06 (0.82 to 1.35)	—
OC use women, UK date	19 (0.2)	6 (0.3)	—	—	—	—	1.46 (0.55 to 3.86)	—
Unknown OC use (women)	139 (1.4)	55 (2.8)	—	—	—	—	2.29 (1.18 to 4.45)	—
Men	5277 (54.0)	970 (49.7)	—	—	—	—	—	—
Age at first HT use								
No HT use	2399 (28.4)	582 (33.0)	(Not eligible)	—	(Not eligible)	—	1.00 (Referent)	.083
<50 y	584 (6.9)	137 (7.8)	—	—	—	—	0.86 (0.68 to 1.09)	—
≥50 y	569 (6.7)	97 (5.5)	—	—	—	—	0.68 (0.52 to 0.88)	—
HT use, age unknown	38 (0.4)	10 (0.6)	—	—	—	—	1.05 (0.49 to 2.27)	—
Unknown HT use (women)	279 (3.3)	66 (3.7)	—	—	—	—	0.38 (0.22 to 0.64)	—
Men	4584 (54.2)	870 (49.4)	—	—	—	—	—	—
First-degree family history, NHL								
No	14116 (83.6)	2758 (80.7)	1.00 (Referent)	<.001	1.00 (Referent)	<.001	1.00 (Referent)	<.001
Yes	278 (1.6)	110 (3.2)	1.95 (1.54 to 2.47)	—	2.07 (1.46 to 2.92)	—	1.80 (1.30 to 2.50)	—
Missing	2485 (14.7)	551 (16.1)	0.86 (0.69 to 1.07)	—	1.12 (0.80 to 1.57)	—	0.73 (0.55 to 0.98)	—
BMI as a young adult (kg/m ²)								
15 to <18.5	384 (2.4)	64 (1.8)	0.93 (0.69 to 1.24)	.002	1.39 (0.86 to 2.26)	.025	0.75 (0.52 to 1.08)	.016
18.5 to <22.5	2804 (17.3)	517 (14.2)	1.00 (Referent)	—	1.00 (Referent)	—	1.00 (Referent)	—
22.5 to <25	1394 (8.6)	276 (7.6)	1.11 (0.93 to 1.31)	—	1.01 (0.80 to 1.27)	—	1.44 (1.10 to 1.88)	—
25 to <30	839 (5.2)	226 (6.2)	1.47 (1.22 to 1.77)	—	1.52 (1.20 to 1.93)	—	1.50 (1.05 to 2.14)	—
30 to 50	173 (1.1)	54 (1.5)	1.58 (1.12 to 2.23)	—	1.63 (1.04 to 2.55)	—	1.54 (0.88 to 2.69)	—
Missing	10580 (65.4)	2508 (68.8)	1.49 (1.24 to 1.79)	—	1.30 (1.01 to 1.68)	—	1.66 (1.23 to 2.25)	—
Usual adult BMI (kg/m ²)								
15 to <18.5	267 (1.6)	33 (0.9)	0.58 (0.39 to 0.85)	.042	(Not selected)	—	0.46 (0.29 to 0.74)	.007
18.5 to <22.5	3481 (20.3)	722 (19.7)	1.00 (Referent)	—	—	—	1.00 (Referent)	—
22.5 to <25	4276 (25.0)	850 (23.1)	0.91 (0.81 to 1.03)	—	—	—	0.89 (0.76 to 1.04)	—
25 to <30	6112 (35.7)	1310 (35.7)	0.93 (0.83 to 1.04)	—	—	—	0.92 (0.79 to 1.08)	—
30 to <35	1760 (10.3)	419 (11.4)	0.95 (0.82 to 1.10)	—	—	—	0.89 (0.73 to 1.10)	—
35 to 50	608 (3.6)	175 (4.8)	1.06 (0.86 to 1.30)	—	—	—	1.14 (0.87 to 1.49)	—
Missing	618 (3.6)	163 (4.4)	1.02 (0.81 to 1.28)	—	—	—	0.90 (0.64 to 1.25)	—
Lifetime alcohol consumption								
Nondrinker	4277 (21.7)	975 (23.6)	1.00 (Referent)	<.001	1.00 (Referent)	<.001	(Not selected)	—
1–100 kg	1444 (7.3)	305 (7.4)	0.80 (0.68 to 0.95)	—	0.69 (0.53 to 0.91)	—	—	—
101–200 kg	641 (3.3)	134 (3.2)	0.79 (0.63 to 0.98)	—	0.76 (0.56 to 1.02)	—	—	—
201–400 kg	651 (3.3)	121 (2.9)	0.66 (0.53 to 0.83)	—	0.64 (0.47 to 0.85)	—	—	—
>400 kg	759 (3.9)	137 (3.3)	0.64 (0.51 to 0.79)	—	0.57 (0.44 to 0.75)	—	—	—

(Table continues)

Table 2. (Continued).

Variable	Sex-specific models							
	Controls	Cases	All participants		Men		Women	
	No. (%)	No. (%)	OR (95% CI)*	P	OR (95% CI)*	P	OR (95% CI)*	P
Drinker, lifetime consumption unknown	7499 (38.1)	1362 (33.0)	0.87 (0.77 to 0.97)	—	0.75 (0.64 to 0.88)	—	—	—
Missing	4397 (22.4)	1090 (26.4)	0.68 (0.59 to 0.80)	—	0.52 (0.42 to 0.64)	—	—	—
Recreational sun exposure (h/week) [§]								
Q1 (low)	2234 (20.6)	649 (22.7)	1.00 (Referent)	<.001	1.00 (Referent)	.033	1.00 (Referent)	.020
Q2	2332 (21.6)	619 (21.6)	0.90 (0.79 to 1.02)	—	0.83 (0.68 to 1.00)	—	0.99 (0.82 to 1.18)	—
Q3	2159 (20.0)	512 (17.9)	0.79 (0.69 to 0.90)	—	0.77 (0.63 to 0.94)	—	0.81 (0.67 to 0.99)	—
Q4 (high)	2983 (27.6)	714 (24.9)	0.78 (0.69 to 0.89)	—	0.78 (0.66 to 0.94)	—	0.79 (0.65 to 0.95)	—
Missing	1111 (10.3)	369 (12.9)	0.92 (0.74 to 1.13)	—	1.07 (0.80 to 1.42)	—	0.72 (0.49 to 1.05)	—
Field crop and vegetable farmer								
No	10392 (94.8)	2664 (96.3)	1.00 (Referent)	.004	(Not selected)	—	1.00 (Referent)	.004
Yes	233 (2.1)	79 (2.9)	1.49 (1.14 to 1.95)	—	—	—	1.78 (1.22 to 2.60)	—
Missing	335 (3.1)	22 (0.8)	0.11 (0.02 to 0.56)	—	—	—	—	—
Sewer and embroiderer								
No	11771 (95.4)	2981 (96.6)	1.00 (Referent)	.009	(Not selected)	—	1.00 (Referent)	.005
Yes	232 (1.9)	83 (2.7)	1.43 (1.10 to 1.87)	—	—	—	1.49 (1.13 to 1.97)	—
Missing	335 (2.7)	22 (0.7)	0.12 (0.02 to 0.62)	—	—	—	—	—
Women's hairdresser								
No	11357 (96.2)	2915 (97.7)	1.00 (Referent)	.011	(Not selected)	—	1.00 (Referent)	.013
Yes	113 (1.0)	46 (1.5)	1.61 (1.13 to 2.31)	—	—	—	1.65 (1.12 to 2.41)	—
Missing	335 (2.8)	22 (0.7)	0.13 (0.03 to 0.67)	—	—	—	—	—
Driver/material handling equipment operator								
No	11925 (96.7)	3031 (98.2)	1.00 (Referent)	.080	1.00 (Referent)	.047	(Not selected)	—
Yes	78 (0.6)	33 (1.1)	1.47 (0.97 to 2.25)	—	1.58 (1.02 to 2.44)	—	—	—
Missing	335 (2.7)	22 (0.7)	0.12 (0.02 to 0.62)	—	0.93 (0.15 to 5.68)	—	—	—

* Odds ratio (OR) and 95% confidence interval (CI) adjusted for age, sex, race/ethnicity, study, and other factors in the same column. BMI = body mass index; HCV = hepatitis c virus; HT = hormone therapy; NHL = non-Hodgkin lymphoma; OC = oral contraceptive; SES = socioeconomic status.

† Includes self-reported history of specific autoimmune diseases occurring ≥ 2 years before diagnosis/interview (except the New South Wales study, which did not ascertain date of onset). Autoimmune diseases were classified according to whether they are primarily mediated by B-cell or T-cell responses. 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.

‡ Includes self-reported history of atopic disorders including asthma, eczema, hay fever, or other allergies, excluding drug allergies, occurring ≥ 2 years before diagnosis/interview (except the New South Wales study, which did not ascertain date of onset).

§ Study specific quartiles among controls.

and recreational sun exposure were retained in the final models with similar ORs for men and women. For women, OC use before 1970 (OR = 0.78), HT use initiated at age at least 50 years (OR = 0.68), low usual adult BMI (OR = 0.46 for <18.5 vs 18.5–22.4 kg/m²), and occupation as field crop/vegetable farm worker (OR = 1.78), seamstress/embroiderer (OR = 1.49), and women's hairdresser (OR = 1.65) were also retained in the final model; pack-years of smoking was not retained. For men, blood transfusion (OR = 0.69), lifetime alcohol consumption (OR = 0.57 for >400 kg vs nondrinker), and occupation as a driver/material handling equipment operator (OR = 1.58) were retained in the final model; metal processor was not retained.

Site-Specific Results

We next evaluated how the variables used in the final model (Table 2), excluding the occupation and reproductive variables (due to low exposure prevalence), performed for selected anatomical sites that may have distinct epidemiological or clinical characteristics, including CNS (N = 103), GI (N = 323), testis (N = 44), cutaneous (N = 120), and primary mediastinal (N = 91) DLBCL (Table 3). In addition, we reported any additional variables from Supplementary Table 1 that were significant at P value less than

.05 for a specific site. Due to small sample sizes, we treated these as exploratory analyses and did not conduct formal heterogeneity tests. Even in this exploratory setting, we observed some notable patterns. CNS DLBCL was inversely associated with atopic disorder (OR = 0.54) and OC use before 1970 (OR = 0.19) and was positively associated with family history of NHL (OR = 4.11) and pack-years of smoking (OR = 1.52 for >35 pack-years versus non-smoker). GI tract DLBCL was positively associated with B-cell activating autoimmune diseases (OR = 2.78), young adult BMI (OR = 3.96 for 35–50 vs 18.5–22.5 kg/m²), and history of inflammatory bowel disease (OR = 2.70) and was inversely associated with atopic disorder (OR = 0.75) and greater recreational sun exposure (OR = 0.67 for highest versus lowest quartile). For testicular DLBCL, positive associations were observed for B-cell activating autoimmune diseases (OR = 5.96) and pack-years of smoking (OR = 2.72 for >35 pack-years versus nonsmoker). Cutaneous DLBCL was positively associated with B-cell activating autoimmune diseases (OR = 3.80), usual adult BMI (OR = 2.93 for 35–50 vs 18.5–22.5 kg/m²), and pack-years of smoking (OR = 2.47 for >35 pack-years vs nonsmoker). Mediastinal DLBCL was positively associated with family history of NHL (OR = 4.81), having lived on

Table 3. Results for selected sites*

Variable	CNS				Testis				GI				Cutaneous				Mediastinal			
	Controls		Cases		Controls		Cases		Controls		Cases		Controls		Cases		Controls		Cases	
	No. (%)	OR (95% CI)	P	No. (%)	OR (95% CI)	P	No. (%)	OR (95% CI)	No. (%)	OR (95% CI)	P	No. (%)	OR (95% CI)	No. (%)	OR (95% CI)	P	No. (%)	OR (95% CI)	No. (%)	P
SES																				
Low	6135 (36.1)	1.00 (Referent)	.62	3606 (37.3)	15 (34.1)	1.00 (Referent)			6190 (36.1)	142 (44.0)	1.00 (Referent)	.38	6135 (36.1)	53 (44.2)	1.00 (Referent)	.63	2690 (33.3)	24 (26.4)	1.00 (Referent)	.41
Medium	5309 (31.2)	0.96 (0.59 to 1.54)	—	2848 (29.4)	14 (31.8)	1.43 (0.68 to 3.04)	—		5344 (31.2)	88 (27.2)	0.84 (0.64 to 1.11)	—	5309 (31.2)	32 (26.7)	0.83 (0.53 to 1.32)	—	2505 (31.0)	28 (30.8)	1.03 (0.59 to 1.80)	—
High	5321 (31.3)	0.78 (0.47 to 1.32)	—	3205 (33.1)	15 (34.1)	1.30 (0.61 to 2.74)	—		5365 (31.3)	91 (28.2)	0.85 (0.64 to 1.13)	—	5321 (31.3)	32 (26.7)	0.81 (0.51 to 1.31)	—	2870 (35.5)	39 (42.9)	1.36 (0.80 to 2.32)	—
History of autoimmune disease†																				
No autoimmune disease	16250 (95.6)	1.00 (Referent)	.85	9276 (95.9)	41 (93.2)	1.00 (Referent)	.26		16370 (95.5)	299 (92.6)	1.00 (Referent)	.002	16250 (95.6)	112 (93.3)	1.00 (Referent)	.045	7754 (95.9)	86 (94.5)	1.00 (Referent)	.84
B-cell activation	152 (0.9)	0.76 (0.10 to 5.55)	—	93 (1.0)	2 (4.5)	5.96 (1.33 to 26.66)	—		153 (0.9)	7 (2.2)	2.78 (1.28 to 6.06)	—	152 (0.9)	4 (3.3)	3.80 (1.36 to 10.65)	—	85 (1.1)	2 (2.2)	1.96 (0.45 to 8.53)	—
T-cell activation	584 (3.4)	1.36 (0.55 to 3.37)	—	299 (3.1)	1 (2.3)	0.58 (0.07 to 4.52)	—		602 (3.5)	14 (4.3)	1.18 (0.68 to 2.05)	—	584 (3.4)	3 (2.5)	0.69 (0.22 to 2.20)	—	243 (3.0)	3 (3.3)	1.20 (0.37 to 3.92)	—
Both	15 (0.1)	0 (0.0)	—	7 (0.1)	0 (0.0)	—	—		15 (0.1)	3 (0.9)	14.46 (3.91 to 53.51)	—	15 (0.1)	1 (0.8)	11.99 (1.50 to 96.07)	—	6 (0.1)	0 (0.0)	—	—
Any atopic disorder‡																				
No	11181 (65.8)	1.00 (Referent)	.0080	6746 (69.7)	35 (79.5)	1.00 (Referent)	.15		11310 (66.0)	235 (72.8)	1.00 (Referent)	.029	11181 (65.8)	79 (65.8)	1.00 (Referent)	.30	5617 (69.4)	55 (60.4)	1.00 (Referent)	.60
Yes	5573 (32.8)	0.54 (0.33 to 0.87)	—	2878 (29.7)	9 (20.5)	0.58 (0.27 to 1.25)	—		5583 (32.6)	82 (25.4)	0.75 (0.57 to 0.98)	—	5573 (32.8)	39 (32.5)	1.24 (0.83 to 1.87)	—	2428 (30.0)	34 (37.4)	0.89 (0.56 to 1.40)	—
HCV positivity																				
No	6746 (66.8)	1.00 (Referent)	.65	2692 (68.3)	12 (70.6)	1.00 (Referent)	.62		6746 (66.8)	121 (73.3)	1.00 (Referent)	.11	6746 (66.8)	28 (69.6)	1.00 (Referent)	.19	1205 (78.3)	17 (68.0)	1.00 (Referent)	.76
Yes	152 (1.5)	1 (1.8)	1.67 (0.21 to 12.98)	—	64 (1.6)	0 (0.0)	—		152 (1.5)	5 (3.0)	2.38 (0.91 to 6.22)	—	152 (1.5)	2 (4.3)	3.20 (0.71 to 14.48)	—	7 (0.5)	0 (0.0)	—	—
Blood transfusion																				
No	9899 (82.2)	1.00 (Referent)	.87	6482 (83.5)	32 (91.4)	1.00 (Referent)	.28		9899 (82.2)	160 (80.0)	1.00 (Referent)	.11	9899 (82.2)	64 (86.5)	1.00 (Referent)	.19	6620 (83.3)	82 (91.1)	1.00 (Referent)	.099
Yes	1743 (14.5)	1.05 (0.57 to 1.94)	—	1108 (14.3)	3 (8.6)	0.54 (0.16 to 1.80)	—		1743 (14.5)	37 (18.5)	1.37 (0.94 to 1.98)	—	1743 (14.5)	8 (10.8)	0.63 (0.30 to 1.32)	—	1155 (14.5)	6 (6.7)	0.52 (0.22 to 1.21)	—
Year of first OC use																				
No OC use	1853 (23.5)	1.00 (Referent)	.010	—	—	—	—		1853 (23.5)	29 (26.1)	1.00 (Referent)	.56	1853 (23.5)	14 (33.3)	1.00 (Referent)	.19	1098 (31.4)	11 (44.0)	1.00 (Referent)	.096
<1970	690 (8.7)	0.19 (0.05 to 0.68)	—	—	—	—	—		690 (8.7)	9 (8.1)	0.82 (0.35 to 1.96)	—	690 (8.7)	4 (9.5)	0.58 (0.16 to 2.04)	—	402 (11.5)	0 (0.0)	—	—
≥1970	632 (8.0)	0.67 (0.20 to 2.24)	—	—	—	—	—		632 (8.0)	4 (3.6)	0.66 (0.19 to 2.24)	—	632 (8.0)	0 (0.0)	—	—	236 (6.8)	10 (40.0)	1.92 (0.63 to 5.79)	—
OC use women, UK date	19 (0.2)	1 (2.1)	6.89 (0.80 to 59.52)	—	—	—	—		19 (0.2)	1 (0.9)	4.49 (0.52 to 39.00)	—	19 (0.2)	0 (0.0)	—	—	7 (0.2)	0 (0.0)	—	—
Unknown OC use (women)	138 (1.7)	1 (2.1)	—	—	—	—	—		138 (1.7)	0 (0.0)	—	—	138 (1.7)	2 (4.8)	—	—	2 (0.1)	0 (0.0)	—	—
Men	4568 (57.8)	19 (39.6)	—	—	—	—	—		4568 (57.8)	68 (61.3)	—	—	4568 (57.8)	22 (62.4)	—	—	1749 (50.1)	4 (16.0)	—	—
Age at first HT use																				
No HT use	1438 (21.9)	1.00 (Referent)	.16	—	—	—	—		1438 (21.9)	27 (20.8)	1.00 (Referent)	.71	1438 (21.9)	9 (19.6)	1.00 (Referent)	.66	1363 (29.4)	30 (71.4)	1.00 (Referent)	.31
<50 y	488 (7.4)	0.78 (0.28 to 2.14)	—	—	—	—	—		488 (7.4)	11 (8.5)	1.17 (0.55 to 2.49)	—	488 (7.4)	2 (4.7)	1.00 (0.29 to 3.45)	—	378 (8.2)	1 (2.4)	0.25 (0.03 to 1.90)	—
≥50 y	463 (7.0)	0.25 (0.05 to 1.14)	—	—	—	—	—		463 (7.0)	9 (6.9)	1.08 (0.48 to 2.44)	—	463 (7.0)	2 (4.3)	0.50 (0.10 to 2.47)	—	343 (7.4)	1 (2.4)	0.36 (0.04 to 2.89)	—
HT use, age unknown	37 (0.6)	0 (0.0)	—	—	—	—	—		37 (0.6)	0 (0.0)	—	—	37 (0.6)	0 (0.0)	—	—	29 (0.6)	0 (0.0)	—	—
Unknown HT use (women)	278 (4.2)	1 (2.3)	—	—	—	—	—		278 (4.2)	0 (0.0)	—	—	278 (4.2)	3 (6.5)	—	—	146 (3.2)	0 (0.0)	—	—
Men	3875 (58.9)	17 (39.5)	—	—	—	—	—		3875 (58.9)	83 (63.8)	—	—	3875 (58.9)	28 (60.9)	—	—	2374 (51.2)	10 (23.8)	—	—
First-degree family history, NHL																				
No	9907 (83.2)	53 (82.8)	1.00 (Referent)	.014	6035 (93.0)	25 (86.2)	1.00 (Referent)	.13	10053 (80.2)	168 (70.3)	1.00 (Referent)	.49	9935 (80.1)	61 (62.2)	1.00 (Referent)	.11	6314 (84.6)	45 (88.2)	1.00 (Referent)	.088
Yes	218 (2.1)	5 (7.8)	4.11 (1.58 to 10.66)	—	106 (1.6)	2 (6.9)	—	—	233 (1.9)	5 (2.1)	1.42 (0.55 to 3.63)	—	231 (1.9)	4 (4.1)	2.69 (0.92 to 7.87)	—	94 (1.4)	2 (3.9)	4.81 (1.08 to 21.46)	—
BMI as a young adult (kg/m²)																				
15<18.5	367 (3.8)	2 (3.4)	0.70 (0.16 to 3.08)	—	223 (5.6)	1 (6.3)	—	—	366 (3.1)	9 (4.3)	2.54 (1.16 to 5.55)	—	362 (3.5)	1 (1.5)	—	—	177 (4.2)	3 (7.1)	1.72 (0.45 to 6.59)	—
18.5<22.5	2610 (27.1)	16 (27.6)	1.00 (Referent)	.79	1685 (42.2)	4 (25.0)	1.00 (Referent)	.07	2652 (22.7)	27 (12.9)	1.00 (Referent)	.025	2618 (25.3)	15 (22.1)	1.00 (Referent)	.59	1478 (34.7)	11 (26.2)	1.00 (Referent)	.41
22.5<25	1247 (13.0)	8 (13.8)	1.31 (0.54 to 3.13)	—	778 (19.5)	0 (0.0)	—	—	1310 (11.2)	24 (11.4)	1.85 (1.04 to 3.28)	—	1283 (12.4)	8 (11.8)	1.17 (0.48 to 2.85)	—	755 (17.7)	2 (4.8)	0.32 (0.07 to 1.50)	—
25<30	746 (7.8)	6 (10.3)	1.74 (0.65 to 4.64)	—	486 (12.2)	4 (25.0)	2.05 (0.50 to 8.42)	—	762 (6.4)	10 (4.8)	1.33 (0.63 to 2.83)	—	744 (7.2)	6 (8.8)	1.46 (0.54 to 3.95)	—	452 (10.6)	3 (7.1)	0.89 (0.24 to 3.33)	—
30-50	147 (1.5)	1 (1.7)	—	—	92 (2.3)	1 (6.3)	—	—	149 (1.3)	5 (2.4)	3.96 (1.46 to 10.75)	—	142 (1.4)	2 (2.9)	2.94 (0.64 to 13.38)	—	70 (1.6)	1 (2.4)	1.31 (0.16 to 10.91)	—
Usual adult BMI (kg/m²)																				
15<18.5	198 (1.4)	0 (0.0)	—	—	103 (1.5)	0 (0.0)	—	—	199 (1.4)	1 (0.4)	—	—	198 (1.4)	0 (0.0)	—	—	118 (1.7)	2 (2.9)	0.60 (0.13 to 2.63)	—
18.5<22.5	2797 (19.8)	17 (19.1)	1.00 (Referent)	.56	1536 (22.5)	3 (10.0)	1.00 (Referent)	.93	2815 (19.7)	50 (22.0)	1.00 (Referent)	.26	2797 (19.8)	17 (21.3)	1.00 (Referent)	.042	1652 (23.5)	26 (38.2)	1.00 (Referent)	.49
22.5<25	3472 (24.5)	25 (28.1)	1.23 (0.65 to 2.30)	—	1779 (26.0)	6 (20.0)	0.91 (0.23 to 3.70)	—	3498 (24.5)	54 (23.8)	0.79 (0.53 to 1.18)	—	3472 (24.5)	14 (17.5)	0.67 (0.33 to 1.37)	—	1860 (26.5)	13 (19.1)	0.53 (0.27 to 1.05)	—
25<30	5061 (35.7)	30 (33.7)	0.98 (0.53 to 1.84)	—	2346 (34.3)	16 (63.3)	1.32 (0.38 to 4.64)	—	5108 (35.7)	78 (34.4)	0.78 (0.54 to 1.14)	—	5061 (35.7)	31 (38.8)	1.06 (0.58 to 2.02)	—	2326 (33.1)	20 (29.4)	0.76 (0.41 to 1.42)	—
30<35	1512 (10.7)	8 (9.0)	0.81 (0.34 to 1.94)	—	674 (9.9)	3 (10.0)	0.79 (0.15 to 4.10)	—	1539 (10.8)	32 (14.1)	1.15 (0.72 to 1.83)	—	1512 (10.7)	7 (8.8)	0.83 (0.33 to 2.08)	—	672 (9.6)	4 (5.9)	0.48 (0.16 to 1.42)	—
35-50	518 (3.7)	3 (3.4)	0.82 (0.23 to 2.86)	—	253 (3.7)	1 (3.3)	—	—	540 (3.8)	6 (2.6)	0.66 (0.28 to 1.59)	—	518 (3.7)	8 (10.0)	2.93 (1.20 to 7.13)	—	248 (3.5)	2 (2.9)	0.70 (0.16 to 3.06)	—

(Table continues)

Table 3 (Continued).

Variable	CNS				Testis				GI				Cutaneous				Mediastinal			
	Controls		Cases	P	Controls		Cases	P	Controls		Cases	P	Controls		Cases	P	Controls		Cases	
	No. (%)	No. (%)	OR (95% CI)		No. (%)	No. (%)	OR (95% CI)		No. (%)	No. (%)	OR (95% CI)		No. (%)	No. (%)	OR (95% CI)		No. (%)	No. (%)	OR (95% CI)	
Lifetime alcohol consumption																				
Nondrinker	2862 (23.3)	19 (2.71)	1.00 (Referent)	.51	1798 (22.1)	7 (20.6)	1.00 (Referent)	.081	2938 (18.8)	55 (19.8)	1.00 (Referent)	.75	2895 (18.7)	27 (23.7)	1.00 (Referent)	.33	1382 (21.1)	13 (19.7)	1.00 (Referent)	.95
1–100 kg	1099 (9.0)	3 (4.3)	0.60 (0.15 to 2.37)	—	731 (9.0)	0 (0.0)	—	—	1099 (7.0)	15 (5.4)	0.95 (0.48 to 1.88)	—	1099 (7.1)	7 (6.1)	0.79 (0.30 to 2.11)	—	1076 (16.4)	12 (18.2)	1.41 (0.47 to 4.24)	—
101–200 kg	576 (4.7)	2 (2.9)	0.80 (0.16 to 3.91)	—	358 (4.4)	3 (8.8)	1.59 (0.29 to 8.65)	—	576 (3.7)	7 (2.5)	0.78 (0.33 to 1.87)	—	576 (3.7)	5 (4.4)	1.05 (0.36 to 3.13)	—	423 (6.5)	2 (3.0)	1.50 (0.28 to 7.99)	—
201–400 kg	607 (4.9)	6 (8.6)	2.29 (0.74 to 7.11)	—	336 (4.1)	1 (2.9)	—	—	607 (3.9)	6 (2.2)	0.53 (0.21 to 1.34)	—	607 (3.9)	2 (1.8)	0.40 (0.09 to 1.87)	—	380 (5.8)	2 (3.0)	2.10 (0.39 to 11.36)	—
>400 kg	735 (6.0)	4 (5.7)	1.51 (0.41 to 5.51)	—	306 (3.8)	0 (0.0)	—	—	735 (4.7)	11 (4.0)	0.66 (0.30 to 1.45)	—	735 (4.8)	1 (0.9)	—	—	330 (5.0)	1 (1.5)	—	—
Drinker, unknown use	4715 (38.4)	29 (41.4)	0.94 (0.46 to 1.92)	—	3847 (47.3)	18 (52.9)	0.87 (0.27 to 2.76)	—	5257 (33.7)	120 (43.2)	1.02 (0.68 to 1.54)	—	5161 (33.4)	51 (44.7)	1.04 (0.58 to 1.87)	—	2268 (34.6)	34 (51.5)	0.87 (0.40 to 1.91)	—
Recreational sun exposure (h/week)																				
Q1 (low)	2059 (20.4)	16 (24.2)	1.00 (Referent)	.53	794 (17.8)	2 (8.7)	1.00 (Referent)	.32	2059 (20.4)	45 (24.3)	1.00 (Referent)	.017	2059 (20.4)	11 (20.4)	1.00 (Referent)	.88	969 (18.7)	19 (23.2)	1.00 (Referent)	.70
Q2	2160 (21.4)	12 (18.2)	0.71 (0.33 to 1.53)	—	765 (17.2)	7 (30.4)	3.07 (0.60 to 15.57)	—	2160 (21.4)	49 (26.5)	1.08 (0.71 to 1.63)	—	2160 (21.4)	11 (20.4)	1.06 (0.46 to 2.48)	—	937 (18.1)	14 (17.1)	0.70 (0.34 to 1.42)	—
Q3	1975 (19.6)	8 (12.1)	0.54 (0.23 to 1.28)	—	945 (21.2)	4 (17.4)	1.13 (0.20 to 6.45)	—	1975 (19.6)	27 (14.6)	0.57 (0.35 to 0.94)	—	1975 (19.6)	8 (14.8)	0.74 (0.29 to 1.86)	—	1129 (21.8)	17 (20.7)	0.70 (0.35 to 1.39)	—
Q4 (high)	2799 (27.7)	14 (21.2)	0.69 (0.32 to 1.45)	—	941 (21.1)	6 (26.1)	1.34 (0.25 to 7.10)	—	2799 (27.7)	44 (23.8)	0.67 (0.44 to 1.03)	—	2799 (27.7)	13 (24.1)	0.95 (0.42 to 2.16)	—	1125 (21.8)	18 (22.0)	0.74 (0.37 to 1.47)	—
Lifetime cigarette exposure																				
Nonsmoker	6863 (42.5)	33 (36.3)	1.00 (Referent)	.024	3572 (40.5)	6 (15.4)	1.00 (Referent)	.091	6926 (42.5)	130 (43.8)	1.00 (Referent)	.79	6863 (42.5)	37 (31.9)	1.00 (Referent)	.015	2854 (39.4)	43 (50.0)	1.00 (Referent)	.68
1–10 pack-years	2736 (16.9)	17 (18.7)	1.51 (0.83 to 2.74)	—	1531 (17.3)	4 (10.3)	1.30 (0.36 to 4.69)	—	2736 (16.9)	42 (14.1)	0.84 (0.59 to 1.19)	—	2736 (16.9)	20 (17.2)	1.44 (0.82 to 2.51)	—	1316 (18.2)	19 (22.1)	0.87 (0.49 to 1.53)	—
11–20 pack-years	1739 (10.8)	3 (3.3)	0.41 (0.12 to 1.33)	—	906 (10.3)	1 (2.6)	—	—	1735 (10.8)	30 (10.1)	0.84 (0.56 to 1.26)	—	1735 (10.8)	11 (9.5)	1.21 (0.61 to 2.41)	—	747 (10.3)	6 (7.0)	0.57 (0.24 to 1.37)	—
21–35 pack-years	1754 (10.9)	17 (18.7)	2.23 (1.22 to 4.09)	—	869 (9.8)	7 (17.9)	2.35 (0.78 to 7.10)	—	1769 (10.9)	34 (11.4)	0.88 (0.60 to 1.31)	—	1754 (10.9)	17 (14.7)	1.88 (1.04 to 3.39)	—	684 (9.4)	7 (8.1)	0.90 (0.39 to 2.06)	—
>35 pack-years	1847 (11.4)	12 (13.2)	1.52 (0.76 to 3.05)	—	1064 (12.0)	14 (35.9)	2.72 (1.02 to 7.24)	—	1862 (11.4)	37 (12.5)	0.84 (0.57 to 1.24)	—	1847 (11.4)	23 (19.8)	2.47 (1.41 to 4.34)	—	871 (12.0)	5 (5.8)	0.82 (0.31 to 2.17)	—
Smoker, pack-years	291 (1.8)	2 (2.2)	1.54 (0.36 to 6.65)	—	148 (1.7)	2 (5.1)	3.26 (0.61 to 17.44)	—	292 (1.8)	8 (2.7)	1.26 (0.60 to 2.67)	—	291 (1.8)	0 (0.0)	—	—	117 (1.6)	4 (4.7)	1.80 (0.59 to 5.46)	—
unknown																				
Ever lived on a farm																				
No	4779 (56.3)	35 (64.8)	1.00 (Referent)	.25	3125 (66.3)	14 (73.7)	1.00 (Referent)	.30	4779 (56.3)	57 (59.4)	1.00 (Referent)	.94	4779 (56.3)	32 (64.0)	1.00 (Referent)	.33	2825 (67.6)	19 (67.9)	1.00 (Referent)	.038
Yes	3470 (40.9)	15 (27.8)	0.69 (0.36 to 1.31)	—	1526 (32.4)	5 (26.3)	0.58 (0.20 to 1.68)	—	3470 (40.9)	36 (37.5)	0.98 (0.63 to 1.53)	—	3470 (40.9)	15 (30.0)	0.73 (0.38 to 1.39)	—	1293 (30.9)	7 (25.0)	3.12 (1.12 to 8.70)	—
Inflammatory bowel disorder																				
No	14952 (97.5)	92 (95.8)	1.00 (Referent)	.11	7866 (98.3)	37 (100)	1.00 (Referent)	.24	15089 (97.5)	276 (95.5)	1.00 (Referent)	.0060	14952 (97.5)	102 (96.2)	1.00 (Referent)	.80	6133 (98.4)	55 (96.5)	1.00 (Referent)	.61
Yes	182 (1.2)	0 (0.0)	—	—	131 (1.6)	0 (0.0)	—	—	184 (1.2)	11 (3.8)	2.70 (1.44 to 5.05)	—	182 (1.2)	2 (1.9)	1.21 (0.29 to 4.96)	—	93 (1.5)	1 (1.8)	1.77 (0.23 to 13.39)	—
Duration of hair dye use																				
Never hair dye	1312 (13.4)	9 (14.5)	1.00 (Referent)	.89	—	—	—	—	1312 (13.4)	19 (10.7)	1.00 (Referent)	.14	1260 (13.6)	14 (17.9)	1.00 (Referent)	.26	571 (14.9)	11 (26.2)	1.00 (Referent)	<.001
1–8 y	830 (8.5)	7 (11.3)	1.10 (0.38 to 3.19)	—	—	—	—	—	830 (8.5)	13 (7.3)	1.75 (0.76 to 4.05)	—	756 (8.2)	4 (5.1)	1.24 (0.30 to 5.15)	—	336 (8.7)	7 (16.7)	0.58 (0.21 to 1.62)	—
9–19 y	608 (6.2)	4 (6.5)	0.80 (0.23 to 2.73)	—	—	—	—	—	608 (6.2)	3 (1.7)	0.52 (0.14 to 1.89)	—	565 (6.1)	6 (7.7)	2.33 (0.64 to 8.52)	—	302 (7.9)	1 (2.4)	0.15 (0.02 to 1.22)	—
≥20 y	751 (7.7)	9 (14.5)	1.38 (0.51 to 3.76)	—	—	—	—	—	751 (7.7)	15 (8.5)	1.87 (0.83 to 4.22)	—	668 (7.2)	6 (7.7)	1.83 (0.50 to 6.64)	—	375 (9.8)	11 (26.2)	4.97 (1.63 to 15.15)	—
Ever use, duration	518 (5.3)	4 (6.5)	1.44 (0.33 to 6.22)	—	—	—	—	—	518 (5.3)	13 (7.3)	1.10 (0.48 to 2.54)	—	518 (5.6)	6 (7.7)	0.41 (0.15 to 1.15)	—	24 (0.6)	0 (0.0)	—	—
unknown																				
Men	5516 (56.4)	27 (43.5)	—	—	—	—	—	—	5516 (56.4)	111 (62.7)	—	—	5235 (56.6)	38 (48.7)	—	—	2011 (52.4)	11 (26.2)	—	—
Used hair dyes before 1980																				
Never hair dye	1312 (13.4)	9 (14.5)	1.00 (Referent)	.26	—	—	—	—	1312 (13.4)	19 (10.7)	1.00 (Referent)	.63	1260 (13.6)	14 (17.9)	1.00 (Referent)	.17	571 (14.9)	11 (26.2)	1.00 (Referent)	.022
Ever hair dye use	854 (8.7)	5 (8.1)	0.61 (0.19 to 1.98)	—	—	—	—	—	854 (8.7)	17 (9.6)	1.77 (0.74 to 4.26)	—	854 (9.2)	10 (12.8)	2.28 (0.68 to 7.66)	—	594 (15.5)	10 (23.8)	2.75 (0.91 to 8.29)	—
<1980	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—
Hair dye use only	853 (8.7)	5 (8.1)	0.72 (0.22 to 2.32)	—	—	—	—	—	853 (8.7)	9 (5.1)	1.48 (0.55 to 3.97)	—	853 (9.2)	4 (5.1)	0.93 (0.23 to 3.83)	—	422 (11.0)	9 (21.4)	0.56 (0.22 to 1.45)	—
≥1980	1000 (10.2)	14 (22.6)	2.85 (0.82 to 9.95)	—	—	—	—	—	1000 (10.2)	18 (10.2)	1.05 (0.50 to 2.21)	—	800 (8.6)	8 (10.3)	0.50 (0.20 to 1.29)	—	21 (0.5)	0 (0.0)	—	—
Ever use, years	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—
unknown	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—
Missing/unknown	253 (2.6)	2 (3.2)	—	—	—	—	—	—	253 (2.6)	3 (1.7)	—	—	253 (2.7)	4 (5.1)	—	—	222 (5.8)	1 (2.4)	—	—
Men	5516 (56.4)	27 (43.5)	—	—	—	—	—	—	5516 (56.4)	111 (62.7)	—	—	5235 (56.6)	38 (48.7)	—	—	2011 (52.4)	11 (26.2)	—	—

* Odds ratio (OR) and 95% confidence interval (CI) adjusted for age, sex, race/ethnicity, and study. BMI = body mass index; CNS = central nervous system; HCV = hepatitis C virus; GI = gastrointestinal; HT = hormone therapy; NHL = non-Hodgkin lymphoma; OC = oral contraceptive; SES = socioeconomic status.

† Includes self-reported history of specific autoimmune diseases occurring ≥2 years before diagnosis/interview (except the New South Wales study, which did not ascertain date of onset). Autoimmune diseases were classified according to whether they are primarily mediated by B-cell or T-cell responses. 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.

‡ Includes self-reported history of atopic disorders including asthma, eczema, hay fever, or other allergies, excluding drug allergies, occurring ≥2 years prior to diagnosis/interview (except the New South Wales study, which did not ascertain date of onset).

§ Study specific quartiles among controls.

a farm (OR = 3.12), and hair dye use duration (OR = 4.97 for 20+ years versus never). Although none of the risk factors was unambiguously associated with all of these sites, there were consistent trends for family history for all sites, autoimmune disease for all sites except CNS, atopic disorders for all sites except cutaneous, young adult BMI for all sites except cutaneous.

Discussion

Our study provides strong evidence that many DLBCL risk factors previously recognized but assessed individually are independent of each other, supporting a complex and multifactorial etiology. Specifically, B-cell activating autoimmune diseases, HCV seropositivity, family history of NHL, and higher young adult BMI were associated with increased DLBCL risk, whereas higher SES, any atopic disorder, and greater recreational sun exposure were associated with decreased risk. Some risk factors were sex specific: OC use before 1970, HT use starting at age at least 50 years, and low usual adult BMI were all inversely associated with risk among women, whereas previous blood transfusion and lifetime alcohol consumption were both inversely associated with risk among men. Occupational associations were largely sex specific.

Several notable findings emerged from this analysis. Perhaps the most prominent was the robust link to risk factors associated with immune function, given the strong and independent associations of B-cell activating autoimmune diseases and HCV seropositivity with DLBCL risk, both of which mechanistically implicate chronic immune stimulation (14,16). In contrast, the immune impact of atopic disorders (with characteristic hypersensitivity reactions and associated release of inflammatory molecules) appears to play a role in decreasing DLBCL risk (18). The independent effects of each of these factors based on our multivariate results support a complex interaction of immune system function and DLBCL risk, which requires further research to understand the underlying mechanisms.

A second notable finding was the positive and independent association of young adult BMI with DLBCL risk, which was the same for both sexes. Although young adult BMI and usual adult BMI were correlated, 51% of the controls moved to a different BMI category (mainly gain) and with our large sample size we were able to model both simultaneously. The consistency of our findings with most previous data from cohort studies (29–34) strongly supports the robustness of excess body weight with DLBCL at younger ages, with implications for primary prevention. Whether BMI impacts DLBCL risk through immune, hormonal, or another mechanism remains to be determined (35). A role for hormonal factors was also supported by the protective effects of both OC and HT use in women, although positive impacts on immune function are also plausible (19).

The inverse association of sunlight with DLBCL risk was independent of physical activity, BMI, and other lifestyle factors including alcohol use. Basic biological and some epidemiological evidence suggests that either vitamin D or UV-induced immune alterations independent of vitamin D could be responsible for the observed inverse association (36–39), although circulating serum vitamin D levels evaluated a median of 5 years before DLBCL diagnosis were not associated with risk in a large pooling project

(36). UV radiation induction of regulatory T cells also is plausible but requires further investigation (40,41). Studies using intermediate biomarkers of exposure or effect will be needed to sort out this hypothesis.

An inverse association with transfusion history, significant only for men, will be more fully reported in a separate InterLymph publication; the findings here extend this association as independent of other immune and lifestyle factors. The inverse association is difficult to interpret in light of previous studies, which support a positive association (42), and raises concerns about bias or chance as primary explanations.

Many of the occupations associated with increased DLBCL risk may be related to carcinogenic exposures, but we were unable to pinpoint specific agents; likely candidates include pesticides, solvents, dyes, engine exhausts, wood dust and wood finishing chemicals, and microbes and other biological agents (43–47). Occupational associations were generally sex specific, and this may be due to actual exposure for men and women in the same jobs having different exposure levels or exposure patterns (48,49). A limitation of occupational titles is the high potential for misclassification of exposure status, which can dilute risk estimates.

Our finding of an increased DLBCL risk with family history of NHL was robust even when adjusted for other identified DLBCL risk factors. This is particularly relevant because family history reflects an interaction between shared exposures (both from shared environment and behaviors) and genetic susceptibility. The association between family history of NHL and DLBCL risk was not attenuated, and was even strengthened, by inclusion of environmental and lifestyle factors, suggesting that heritability is an independent risk factor for DLBCL. Further analyses are warranted to determine whether established genetic associations are independent of family history, or whether they help explain in part the association between family history of NHL and DLBCL.

We found little evidence for heterogeneity when we stratified these associations by age at diagnosis (<60 versus 60+ years), noting that 70% of the cases were aged 50–79 years at diagnosis, perhaps limiting our ability to identify age-related differences.

We aimed to explore whether risk factors identified for all DLBCL were common to selected sites (see Table 3), each of which has a somewhat unique descriptive (6–10) but little published risk factor epidemiology. For primary CNS lymphoma, the only established risk factors are congenital and acquired immunodeficiency (particularly HIV disease, which we excluded) (7). Consistent with the only comparable case-control study (50) were our observations of an inverse association with OC use, positive associations with family history of NHL and smoking, and null associations for farming and transfusion history; an inverse association with atopy in our study was null in that study, whereas we did not examine autoimmune disease (only six exposed cases) and did not assess tonsillectomy, reported to reduce risk in the previous study. For GI lymphoma, of which DLBCL is the most common histology (9,51), transplantation, HIV infection, and ulcerative colitis have been suggested as risk factors (52); we excluded HIV patients, whereas the reported association with ulcerative colitis is consistent with our finding for inflammatory bowel disease.

Autoimmune disease, atopy, family history of NHL, and perhaps young adult BMI showed consistent risk patterns across anatomical

sites, supporting a shared etiology. Intriguing site-specific patterns included associations for smoking with CNS, testicular and cutaneous DLBCL; inflammatory bowel disease with GI DLBCL; and ever having lived on a farm and hair dye use with mediastinal DLBCL. These findings suggest consideration of unique pathogenic mechanisms such as local inflammatory mechanisms in GI DLBCL and chemical exposure for mediastinal DLBCL. The approximately fourfold increase in CNS and mediastinal DLBCL risk with family history of NHL may suggest that heritability and genetics play even larger roles in these presentations. Nevertheless, caution is needed in interpreting these results due to small number of cases in these analyses, difficulty of diagnosing these rare entities, and the complexity of assigning a primary site for NHL in epidemiological studies. Furthermore, heterogeneity within some of the extranodal sites, particularly mediastinal (which will include true DLBCL but also primary mediastinal B-cell lymphoma), cutaneous (e.g., leg type versus other), and GI tract (e.g., some gastric cases are likely to be associated with *Helicobacter pylori* infection), could not be assessed.

Strengths specific to this analysis (beyond those of the entire initiative) (22) included the largest sample size of DLBCL cases yet assembled for a risk factor analysis and availability of data on anatomical sites. Specific limitations include the lack of data on DLBCL cell of origin (which may have unique etiologies) (11) and limited power to perform site-specific analyses. We did not adjust our results for multiple comparisons, although most of these exposures had a strong a priori probability. We had few cases above the age of 80 years, although this age group has the highest DLBCL incidence rates. Our analyses excluded HIV-associated DLBCL. Assignment to anatomical sites was limited to those studies that coded this information independent of stage. Beyond HCV, we did not have information on other infections. It will be important for future epidemiological studies to incorporate biological specimens to help elucidate the mechanisms underlying many of these observed associations.

In summary, this large pooled analysis has clarified multiple risk factors for DLBCL and has demonstrated that many previously reported factors act independently on DLBCL risk. These new findings will need to be incorporated into models of DLBCL epidemiology and pathogenesis, and support a complex biology that includes familial, medical, lifestyle, and occupational factors.

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Affiliations of authors: Department of Health Sciences Research, Mayo Clinic, Rochester, MN (JRC, SLS); Sydney School of Public Health, The University of Sydney, Sydney, Australia (AK); Department of Entomology, The Robert H. Smith Faculty of Agriculture, Koret School of Veterinary Medicine Veterinary Teaching Hospital, Hebrew University of Jerusalem, Jerusalem, Israel (OP); Winship Cancer Institute, Emory University, Atlanta, GA (CRF); Department of Cancer Etiology, Beckman Research Institute of the City of Hope, Duarte, CA (SSW, LB); Inserm, Centre for Research in Epidemiology and Population Health (CESP), U1018, Environmental Epidemiology of Cancer Group, F-94805, and Univ Paris Sud, UMRS 1018, F-94805, Villejuif, France (AM, JC); Registry of Hematological Malignancies in Gironde, Bergonié Institute, Bordeaux, France (AM); Division of Cancer Epidemiology and Genetics, National Cancer Institute, National Institutes of Health, Bethesda, MD (AB, NR, JNS, LMM); Unit of Epidemiology and Biostatistics, Centro di Riferimento Oncologico, IRCCS, Aviano, Italy (LDM); Epidemiology and Cancer Statistics Group, Department of Health Sciences, University of York, York, UK (EVK); Center for Chronic Immunodeficiency (CCI), University Medical Center Freiburg, Freiburg, Germany (AN); Department of Cancer Biology, Mayo Clinic Cancer Center, Jacksonville, FL (JMF); Unit of Occupational and Environmental Epidemiology, Cancer Prevention and Research Institute ISPO Florence, Florence, Italy (LM); Department of Epidemiology, School of Public Health, University of Alabama at Birmingham, Birmingham, AL (CFS).

Supplemental Table 1. Overall and sex-stratified results, with factors selected for multivariate modeling in bold

Exposure		All				Sex-stratified results											
						Males				Females					p-heterogeneity		
		Controls	Cases			Controls	Cases			Controls	Cases						
		No. (%)*	No. (%)*	OR (95% CI)†		P	No. (%)	No. (%)	OR (95% CI)†		P	No. (%)	No. (%)	OR (95% CI)†		P	
SOCIOECONOMIC STATUS (SES)																	
SES measure																	
Low		9266 (40.9)	1948 (41.7)	1.00 (referent)		<0.001	5235 (39.6)	1020 (39.6)	1.00 (referent)		<0.001	4031 (42.8)	928 (44.4)	1.00 (referent)		0.02	0.89
Medium		6577 (29.1)	1355 (29.0)	0.86 (0.79 to 0.93)			3763 (28.4)	735 (28.5)	0.85 (0.76 to 0.95)			2814 (29.9)	620 (29.7)	0.88 (0.78 to 0.99)			
High		6386 (28.2)	1296 (27.8)	0.83 (0.76 to 0.90)			3978 (30.1)	774 (30.0)	0.82 (0.74 to 0.92)			2408 (25.6)	522 (25.0)	0.85 (0.75 to 0.97)			
AUTOIMMUNE DISEASES																	
Sjogren Syndrome																	
No		9377 (97.9)	2280 (97.4)	1.00 (referent)		<0.001	1765 (99.9)	473 (99.8)	not estimated		0.08	4697 (98.1)	1077 (97.2)	1.00 (referent)		<0.001	0.96
Yes		9 (0.1)	19 (0.8)	9.35 (4.20 to 20.86)			0 (0.0)	1 (0.2)				9 (0.2)	18 (1.6)	9.08 (4.04 to 20.4)			
Systemic lupus erythematosus (SLE)																	
No		15987 (98.6)	3885 (98.4)	1.00 (referent)		0.002	4973 (99.8)	1092 (99.9)	1.00 (referent)		0.55	7389 (98.5)	1775 (98.3)	1.00 (referent)		<0.001	0.12
Yes		33 (0.2)	20 (0.5)	2.53 (1.44 to 4.43)			8 (0.2)	1 (0.1)	0.55 (0.07 to 4.46)			25 (0.3)	19 (1.1)	3.21 (1.75 to 5.87)			
Hemolytic anemia																	
No		7345 (99.7)	1382 (98.6)	1.00 (referent)		0.035	3057 (99.7)	497 (97.5)	1.00 (referent)		0.03	2522 (99.4)	596 (98.8)	1.00 (referent)		0.27	0.29
Yes		14 (0.2)	8 (0.6)	2.72 (1.13 to 6.57)			5 (0.2)	4 (0.8)	4.83 (1.22 to 19.1)			9 (0.4)	4 (0.7)	2.02 (0.61 to 6.69)			
Celiac disease																	
No		10045 (97.8)	2319 (97.5)	1.00 (referent)		0.042	3912 (99.5)	1008 (98.4)	1.00 (referent)		0.22	4612 (97.8)	999 (98.0)	1.00 (referent)		0.08	0.96
Yes		25 (0.2)	12 (0.5)	2.14 (1.07 to 4.28)			7 (0.2)	4 (0.4)	2.23 (0.65 to 7.68)			18 (0.4)	8 (0.8)	2.22 (0.95 to 5.15)			
Psoriasis																	
No		12961 (97.5)	2819 (97.2)	1.00 (referent)		0.67	7060 (97.5)	1465 (96.7)	1.00 (referent)		0.39	5901 (97.5)	1354 (97.7)	1.00 (referent)		0.67	0.20
Yes		305 (2.3)	79 (2.7)	1.06 (0.82 to 1.36)			166 (2.3)	48 (3.2)	1.16 (0.83 to 1.62)			139 (2.3)	31 (2.2)	0.92 (0.62 to 1.37)			
Rheumatoid arthritis																	
No		10896 (93.4)	2598 (90.3)	1.00 (referent)		<0.001	4620 (92.2)	1208 (88.4)	1.00 (referent)		0.01	4713 (92.5)	1113 (90.3)	1.00 (referent)		0.04	0.35
Yes		95 (0.8)	44 (1.5)	1.94 (1.35 to 2.79)			35 (0.7)	21 (1.5)	2.24 (1.29 to 3.90)			60 (1.2)	23 (1.9)	1.72 (1.05 to 2.81)			
Inflammatory bowel disorder																	
No		16231 (97.6)	3721 (97.5)	1.00 (referent)		0.49	7887 (97.5)	1824 (96.9)	1.00 (referent)		0.20	6948 (97.3)	1612 (97.8)	1.00 (referent)		0.61	0.19
Yes		199 (1.2)	53 (1.4)	1.12 (0.82 to 1.52)			91 (1.1)	29 (1.5)	1.33 (0.87 to 2.05)			108 (1.5)	24 (1.5)	0.89 (0.57 to 1.40)			
Crohn’s Disease																	
No		13634 (98.3)	3277 (98.3)	1.00 (referent)		0.33	6285 (98.1)	1575 (97.5)	1.00 (referent)		0.04	5953 (98.2)	1417 (99.0)	1.00 (referent)		0.31	0.04
Yes		37 (0.3)	13 (0.4)	1.39 (0.73 to 2.63)			15 (0.2)	10 (0.6)	2.38 (1.06 to 5.38)			22 (0.4)	3 (0.2)	0.56 (0.17 to 1.88)			
Ulcerative colitis																	
No		12944 (97.3)	3014 (97.4)	1.00 (referent)		0.97	7397 (97.6)	1708 (97.2)	1.00 (referent)		0.69	5547 (96.9)	1306 (97.7)	1.00 (referent)		0.59	0.55
Yes		162 (1.2)	38 (1.2)	1.01 (0.70 to 1.44)			74 (1.0)	19 (1.1)	1.11 (0.66 to 1.87)			88 (1.5)	19 (1.4)	0.87 (0.53 to 1.45)			
Type I diabetes																	
No		13185 (95.9)	2872 (93.1)	1.00 (referent)		0.64	7847 (96.3)	1647 (93.1)	1.00 (referent)		0.60	5146 (95.1)	1149 (92.6)	1.00 (referent)		0.72	0.94
Yes		84 (0.6)	16 (0.5)	0.88 (0.51 to 1.52)			50 (0.6)	9 (0.5)	0.83 (0.40 to 1.72)			34 (0.6)	7 (0.6)	0.86 (0.37 to 1.98)			
Sarcoidosis																	
No		11323 (99.6)	2845 (99.6)	1.00 (referent)		0.08	6466 (99.7)	1631 (99.5)	1.00 (referent)		0.27	3715 (99.4)	970 (99.7)	1.00 (referent)		0.15	0.63
Yes		28 (0.2)	3 (0.1)	0.39 (0.12 to 1.29)			15 (0.2)	2 (0.1)	0.47 (0.11 to 2.07)			13 (0.3)	1 (0.1)	0.29 (0.04 to 2.20)			
Pernicious anemia																	
No		6680 (99.8)	1573 (99.4)	1.00 (referent)		0.06	3900 (99.8)	851 (99.4)	1.00 (referent)		0.02	2780 (99.7)	722 (99.4)	1.00 (referent)		0.58	0.14

		All				Sex-stratified results										
						Males				Females						
		Controls	Cases			Controls	Cases			Controls	Cases			p-heterogeneity		
Exposure		No. (%)*	No. (%)*	OR (95% CI)†		P	No. (%)	No. (%)	OR (95% CI)†		P	No. (%)	No. (%)	OR (95% CI)†		P
Multiple Sclerosis	Yes	13 (0.2)	9 (0.6)	2.34	(0.99 to 5.53)		4 (0.1)	5 (0.6)	5.02	(1.32 to 19.0)		9 (0.3)	4 (0.6)	1.42	(0.43 to 4.69)	
	No	14107 (99.6)	3409 (99.4)	1.00 (referent)		0.69	4080 (99.8)	929 (99.8)	1.00 (referent)		0.69	5372 (99.3)	1348 (99.5)	1.00 (referent)		0.60
	Yes	22 (0.2)	5 (0.1)	0.82	(0.31 to 2.19)		6 (0.1)	2 (0.2)	1.41	(0.28 to 7.12)		16 (0.3)	3 (0.2)	0.72	(0.21 to 2.52)	
Systemic sclerosis or scleroderma	No	7906 (99.5)	1800 (99.6)	1.00 (referent)		0.67	2637 (99.7)	556 (99.8)	1.00 (referent)		0.88	2256 (99.0)	504 (99.4)	1.00 (referent)		0.62
	Yes	11 (0.1)	2 (0.1)	0.72	(0.16 to 3.31)		5 (0.2)	1 (0.2)	0.84	(0.10 to 7.48)		6 (0.3)	1 (0.2)	0.60	(0.07 to 5.07)	
Polymyositis or dermatomyositis	No	9978 (97.7)	2199 (97.8)	1.00 (referent)		0.71	603 (84.8)	90 (79.6)	not estimated		0.28	4291 (97.6)	949 (98.2)	1.00 (referent)		0.43
	Yes	18 (0.2)	4 (0.2)	1.24	(0.41 to 3.69)		5 (0.7)	0 (0.0)				13 (0.3)	4 (0.4)	1.61	(0.52 to 5.02)	
Immune thrombocytopenic purpura	No	4861 (100)	1023 (99.8)	1.00 (referent)		0.10	1565 (99.9)	279 (100)	not estimated		0.54	1978 (100)	472 (99.6)	not estimated		0.01
	Yes	1 (0.0)	2 (0.2)	7.29	(0.64 to 83.50)		1 (0.1)	0 (0.0)				0 (0.0)	2 (0.4)			0.93
Myasthenia gravis	No	7506 (99.5)	1927 (99.2)	1.00 (referent)		0.44	541 (99.4)	230 (100)	1.00 (referent)		0.35	2935 (99.2)	633 (99.1)	1.00 (referent)		0.24
	Yes	4 (0.1)	2 (0.1)	2.02	(0.36 to 11.26)		1 (0.2)	0 (0.0)	0.00	(0.00 to .)		3 (0.1)	2 (0.3)	3.15	(0.52 to 18.9)	
History of autoimmune disease‡																
	No autoimmune disease	19423 (95.9)	4286 (94.3)	1.00 (referent)		<0.001	11166 (96.6)	2379 (95.2)	1.00 (referent)		0.002	8257 (94.9)	1907 (93.2)	1.00 (referent)		<0.001
	B-cell activation	157 (0.8)	87 (1.9)	2.30	(1.76 to 3.00)		50 (0.4)	27 (1.1)	2.17	(1.35 to 3.50)		107 (1.2)	60 (2.9)	2.36	(1.71 to 3.27)	
	T-cell activation	664 (3.3)	159 (3.5)	1.01	(0.85 to 1.21)		336 (2.9)	90 (3.6)	1.12	(0.88 to 1.42)		328 (3.8)	69 (3.4)	0.88	(0.68 to 1.15)	
	Both	15 (0.1)	14 (0.3)	4.30	(2.06 to 8.97)		3 (0.0)	4 (0.2)	5.43	(1.21 to 24.5)		12 (0.1)	10 (0.5)	4.10	(1.74 to 9.63)	
ATOPIC DISORDERS																
Any atopic disorder§																
	No	15601 (68.9)	3262 (69.9)	1.00 (referent)		<0.001	9660 (73.0)	1865 (72.3)	1.00 (referent)		<0.001	5941 (63.1)	1397 (66.9)	1.00 (referent)		<0.001
	Yes	6442 (28.5)	1315 (28.2)	0.82	(0.76 to 0.88)		3187 (24.1)	658 (25.5)	0.83	(0.75 to 0.92)		3255 (34.6)	657 (31.5)	0.81	(0.73 to 0.91)	
Allergy§	No	10790 (72.1)	2534 (72.3)	1.00 (referent)		<0.001	6682 (76.8)	1525 (74.7)	1.00 (referent)		0.036	4108 (65.5)	1009 (68.9)	1.00 (referent)		<0.001
	Yes	3309 (22.1)	681 (19.4)	0.82	(0.74 to 0.90)		1556 (17.9)	346 (17.0)	0.87	(0.76 to 0.99)		1753 (28.0)	335 (22.9)	0.77	(0.67 to 0.89)	
Food Allergy	No	12757 (85.2)	2914 (83.1)	1.00 (referent)		0.002	6704 (86.1)	1500 (82.5)	1.00 (referent)		0.13	5141 (82.0)	1192 (81.4)	1.00 (referent)		0.006
	Yes	988 (6.6)	189 (5.4)	0.77	(0.65 to 0.91)		405 (5.2)	83 (4.6)	0.83	(0.65 to 1.06)		583 (9.3)	106 (7.2)	0.74	(0.59 to 0.92)	
Asthma	No	18448 (85.6)	3889 (84.4)	1.00 (referent)		0.024	10548 (86.3)	2144 (84.7)	1.00 (referent)		0.16	7900 (84.6)	1745 (84.1)	1.00 (referent)		0.081
	Yes	1698 (7.9)	335 (7.3)	0.87	(0.77 to 0.98)		909 (7.4)	177 (7.0)	0.89	(0.75 to 1.05)		789 (8.5)	158 (7.6)	0.85	(0.71 to 1.02)	
Hay fever	No	12467 (71.3)	2768 (70.3)	1.00 (referent)		<0.001	7000 (72.9)	1535 (70.8)	1.00 (referent)		<0.001	5467 (69.3)	1233 (69.5)	1.00 (referent)		0.002
	Yes	2958 (16.9)	587 (14.9)	0.78	(0.70 to 0.86)		1475 (15.4)	297 (13.7)	0.76	(0.66 to 0.87)		1483 (18.8)	290 (16.4)	0.79	(0.68 to 0.92)	
Eczema	No	14766 (86.1)	3299 (84.5)	1.00 (referent)		0.14	8722 (88.2)	1849 (85.5)	1.00 (referent)		0.22	6044 (83.3)	1450 (83.2)	1.00 (referent)		0.43
	Yes	1605 (9.4)	341 (8.7)	0.91	(0.80 to 1.03)		737 (7.5)	153 (7.1)	0.89	(0.74 to 1.07)		868 (12.0)	188 (10.8)	0.93	(0.79 to 1.11)	
HEPATITIS C VIRUS (HCV)																
HCV seropositivity																

Exposure		All				Sex-stratified results											
						Males				Females				p-heterogeneity			
						Controls	Cases	OR (95% CI)†	P	Controls	Cases	OR (95% CI)†	P				
		No. (%)*	No. (%)*	OR (95% CI)†		P	No. (%)	No. (%)	OR (95% CI)†		P	No. (%)	No. (%)	OR (95% CI)†		P	
		No	6746 (66.8)	1591 (66.8)	1.00 (referent)		<0.001	3871 (66.3)	937 (68.9)	1.00 (referent)		<0.001	2033 (71.7)	425 (60.6)	1.00 (referent)		0.008
		Yes	152 (1.5)	63 (2.6)	2.33 (1.71 to 3.19)			97 (1.7)	38 (2.8)	2.42 (1.62 to 3.61)			55 (1.9)	25 (3.6)	2.04 (1.23 to 3.39)		
BLOOD TRANSFUSIONS																	
Any history of blood Transfusion																	
		No	10742 (76.7)	2654 (81.3)	1.00 (referent)		0.004	6085 (75.1)	1440 (82.1)	1.00 (referent)		<0.001	4657 (78.9)	1214 (80.5)	1.00 (referent)		0.35
		Yes	1966 (14.0)	411 (12.6)	0.84 (0.75 to 0.95)			878 (10.8)	146 (8.3)	0.73 (0.61 to 0.88)			1088 (18.4)	265 (17.6)	0.93 (0.80 to 1.08)		0.046
Age at first transfusion																	
No transfusion		10742 (76.7)	2654 (81.3)	1.00 (referent)		0.013	6085 (75.1)	1440 (82.1)	1.00 (referent)		<0.001	4657 (78.9)	1214 (80.5)	1.00 (referent)		0.83	0.10
<25 years		483 (3.4)	102 (3.1)	0.85 (0.68 to 1.06)			215 (2.7)	40 (2.3)	0.79 (0.56 to 1.12)			268 (4.5)	62 (4.1)	0.91 (0.68 to 1.21)			
25-39 years		579 (4.1)	143 (4.4)	0.95 (0.79 to 1.16)			178 (2.2)	37 (2.1)	0.88 (0.61 to 1.26)			401 (6.8)	106 (7.0)	0.99 (0.79 to 1.24)			
40-54 years		449 (3.2)	77 (2.4)	0.69 (0.54 to 0.88)			212 (2.6)	21 (1.2)	0.42 (0.27 to 0.67)			237 (4.0)	56 (3.7)	0.91 (0.67 to 1.23)			
55+ years		455 (3.2)	89 (2.7)	0.84 (0.66 to 1.07)			273 (3.4)	48 (2.7)	0.84 (0.61 to 1.17)			182 (3.1)	41 (2.7)	0.85 (0.60 to 1.21)			
Total number of blood transfusions																	
No transfusion		10742 (76.7)	2654 (81.3)	1.00 (referent)		0.005	6085 (75.1)	1440 (82.1)	1.00 (referent)		0.008	4657 (78.9)	1214 (80.5)	1.00 (referent)		0.19	0.18
1 transfusion		1306 (9.3)	296 (9.1)	0.91 (0.80 to 1.05)			572 (7.1)	101 (5.8)	0.77 (0.61 to 0.96)			734 (12.4)	195 (12.9)	1.02 (0.86 to 1.21)			
2 transfusions		361 (2.6)	64 (2.0)	0.70 (0.53 to 0.92)			151 (1.9)	20 (1.1)	0.57 (0.35 to 0.91)			210 (3.6)	44 (2.9)	0.79 (0.56 to 1.10)			
3+ transfusions		229 (1.6)	44 (1.3)	0.80 (0.57 to 1.11)			106 (1.3)	20 (1.1)	0.89 (0.54 to 1.46)			123 (2.1)	24 (1.6)	0.74 (0.47 to 1.15)			
Unknown		70 (0.5)	7 (0.2)	0.44 (0.20 to 0.96)			49 (0.6)	5 (0.3)	0.48 (0.19 to 1.23)			21 (0.4)	2 (0.1)	0.37 (0.08 to 1.58)			
Number of years from 1st transfusion to date of diagnosis																	
No transfusion		10742 (76.7)	2654 (81.3)	1.00 (referent)		0.017	6085 (75.1)	1440 (82.1)	1.00 (referent)		0.010	4657 (78.9)	1214 (80.5)	1.00 (referent)		0.15	0.12
<20 years		878 (6.3)	174 (5.3)	0.83 (0.70 to 0.98)			492 (6.1)	83 (4.7)	0.75 (0.59 to 0.96)			386 (6.5)	91 (6.0)	0.91 (0.71 to 1.15)			
20-39 years		748 (5.3)	174 (5.3)	0.91 (0.77 to 1.09)			274 (3.4)	42 (2.4)	0.68 (0.49 to 0.95)			474 (8.0)	132 (8.7)	1.05 (0.86 to 1.29)			
40+ years		340 (2.4)	63 (1.9)	0.73 (0.55 to 0.96)			112 (1.4)	21 (1.2)	0.77 (0.48 to 1.24)			228 (3.9)	42 (2.8)	0.70 (0.50 to 0.99)			
Transfusion before 1990																	
No transfusion		10742 (76.7)	2654 (81.3)	1.00 (referent)		0.027	6085 (75.1)	1440 (82.1)	1.00 (referent)		0.004	4657 (78.9)	1214 (80.5)	1.00 (referent)		0.79	0.20
Transfusion <1990		1457 (10.4)	317 (9.7)	0.87 (0.76 to 0.99)			610 (7.5)	106 (6.0)	0.79 (0.63 to 0.98)			847 (14.4)	211 (14.0)	0.92 (0.78 to 1.09)			
Transfusion 1990+		404 (2.9)	79 (2.4)	0.80 (0.62 to 1.03)			226 (2.8)	36 (2.1)	0.66 (0.46 to 0.95)			178 (3.0)	43 (2.8)	0.97 (0.69 to 1.37)			
Year unknown		105 (0.7)	15 (0.5)	0.67 (0.37 to 1.20)			42 (0.5)	4 (0.2)	0.38 (0.13 to 1.12)			63 (1.1)	11 (0.7)	1.04 (0.50 to 2.20)			
HISTORY OF ULCERS																	
Peptic ulcer																	
No		9049 (87.9)	2039 (84.2)	1.00 (referent)		0.65	5264 (87.7)	1164 (84.0)	1.00 (referent)		0.90	3785 (88.3)	875 (84.5)	1.00 (referent)		0.51	0.54
Yes		729 (7.1)	174 (7.2)	1.04 (0.87 to 1.24)			472 (7.9)	105 (7.6)	1.02 (0.81 to 1.27)			257 (6.0)	69 (6.7)	1.10 (0.83 to 1.46)			
Gastric ulcer																	
No		3219 (72.0)	671 (70.1)	1.00 (referent)		0.14	1704 (70.2)	360 (69.5)	1.00 (referent)		0.28	1515 (74.2)	311 (70.8)	1.00 (referent)		0.32	0.93
Yes		362 (8.1)	60 (6.3)	0.81 (0.60 to 1.08)			226 (9.3)	38 (7.3)	0.82 (0.57 to 1.19)			136 (6.7)	22 (5.0)	0.79 (0.49 to 1.27)			
CHILDREN/REPRODUCTION																	
Number of children																	
0												985 (17.1)	231 (17.0)	0.96 (0.76 to 1.21)			
1												668 (11.6)	164 (12.0)	1.00 (referent)		0.36	
2												1510 (26.2)	337 (24.8)	0.85 (0.69 to 1.06)			
3+												2118 (36.7)	486 (35.7)	0.86 (0.70 to 1.06)			
Male																	

Exposure		All				Sex-stratified results									p-heterogeneity		
						Males				Females							
						Controls	Cases	OR (95% CI)†	P	Controls	Cases	OR (95% CI)†	P				
No. (%)*	No. (%)*	No. (%)	No. (%)	No. (%)	No. (%)												
No livebirhts										985 (17.1)	231 (17.0)	1.00 (referent)		0.43			
<20 years										618 (10.7)	125 (9.2)	0.89	(0.68 to 1.17)				
20-29 years										676 (11.7)	171 (12.6)	1.02	(0.78 to 1.33)				
30+ years										1423 (24.6)	289 (21.2)	0.84	(0.66 to 1.07)				
Children, but time unknown										1579 (27.3)	402 (29.5)	0.96	(0.74 to 1.25)				
Male																	
Ever used oral contraceptives (OC)																	
No										2817 (62.6)	638 (65.0)	1.00 (referent)		0.06			
Yes										1541 (34.3)	289 (29.4)	0.84	(0.70 to 1.00)				
Male																	
Year of first oral contraceptive (OC) use																	
No OC use										2817 (62.6)	638 (65.0)	1.00 (referent)		0.02			
<1970										765 (17.0)	128 (13.0)	0.71	(0.57 to 0.90)				
1970+										757 (16.8)	155 (15.8)	0.99	(0.78 to 1.26)				
Unknown date										19 (0.4)	6 (0.6)	1.42	(0.56 to 3.62)				
Male																	
Ever used hormone therapy (HT)																	
No										2399 (62.0)	582 (65.2)	1.00 (referent)		0.01			
Yes										1191 (30.8)	244 (27.4)	0.78	(0.65 to 0.94)				
Age at first HT use																	
No HT use										2399 (62.0)	582 (65.2)	1.00 (referent)		0.01			
<50 years										584 (15.1)	137 (15.4)	0.88	(0.71 to 1.10)				
50+ years										569 (14.7)	97 (10.9)	0.65	(0.50 to 0.83)				
Unknown age (female)										38 (1.0)	10 (1.1)	1.06	(0.52 to 2.18)				
Male																	
FAMILY HISTORY IN A FIRST DEGREE RELATIVE																	
Any hematologic malignancy																	
No		14346 (81.5)	2796 (77.8)	1.00 (referent)		<0.001	8704 (84.1)	1521 (78.4)	1.00 (referent)		<0.001	5642 (77.9)	1275 (77.2)	1.00 (referent)	<0.001	0.98	
Yes		769 (4.4)	245 (6.8)	1.57	(1.34 to 1.83)		416 (4.0)	118 (6.1)	1.53	(1.23 to 1.91)		353 (4.9)	127 (7.7)	1.59	(1.28 to 1.98)		
Any hematologic malignancy, male relative																	
No		11543 (80.5)	2238 (77.8)	1.00 (referent)		0.009	6870 (82.9)	1189 (77.4)	1.00 (referent)		0.068	4673 (77.2)	1049 (78.2)	1.00 (referent)		0.078	1.00
Yes		329 (2.3)	91 (3.2)	1.40	(1.10 to 1.79)		187 (2.3)	48 (3.1)	1.38	(0.99 to 1.94)		142 (2.3)	43 (3.2)	1.39	(0.97 to 1.98)		
Any hematologic malignancy, female relative																	
No		11560 (80.6)	2231 (77.5)	1.00 (referent)		0.001	6898 (83.3)	1193 (77.7)	1.00 (referent)		0.031	4662 (77.0)	1038 (77.3)	1.00 (referent)		0.016	0.99
Yes		312 (2.2)	98 (3.4)	1.51	(1.19 to 1.92)		159 (1.9)	44 (2.9)	1.50	(1.05 to 2.14)		153 (2.5)	54 (4.0)	1.52	(1.09 to 2.11)		
Hodgkin lymphoma																	
No		14149 (94.5)	2786 (93.5)	1.00 (referent)		<0.001	8371 (95.6)	1413 (93.1)	1.00 (referent)		0.005	5296 (94.3)	1217 (94.4)	1.00 (referent)		0.087	0.69
Yes		84 (0.6)	34 (1.1)	2.09	(1.38 to 3.15)		53 (0.6)	21 (1.4)	2.24	(1.32 to 3.79)		31 (0.6)	13 (1.0)	1.85	(0.94 to 3.62)		
Hodgkin lymphoma, male relative																	
No		10916 (93.4)	2037 (92.3)	1.00 (referent)		0.17	6491 (94.8)	1094 (92.5)	1.00 (referent)		0.83	4289 (93.4)	917 (93.3)	1.00 (referent)		0.069	0.24
Yes		39 (0.3)	12 (0.5)	1.64	(0.83 to 3.22)		26 (0.4)	5 (0.4)	1.12	(0.41 to 3.03)		13 (0.3)	7 (0.7)	2.53	(0.98 to 6.57)		
Hodgkin lymphoma, female relative																	

Exposure		All				Sex-stratified results												
						Males				Females				p-heterogeneity				
						Controls	Cases	OR (95% CI)†		P	Controls	Cases	OR (95% CI)†		P			
		No. (%)*	No. (%)*	OR (95% CI)†		P	No. (%)	No. (%)	OR (95% CI)†		P	No. (%)	No. (%)	OR (95% CI)†		P		
		No	10316 (94.6)	2127 (94.3)	1.00 (referent)		0.32	5895 (94.5)	1120 (92.4)	1.00 (referent)		0.041	3011 (98.2)	690 (98.6)	1.00 (referent)		0.17	0.050
		Yes	29 (0.3)	9 (0.4)	1.50 (0.69 to 3.28)			15 (0.2)	8 (0.7)	2.69 (1.09 to 6.64)			14 (0.5)	1 (0.1)	0.29 (0.04 to 2.33)			
Non-Hodgkin lymphoma		No	14116 (83.6)	2758 (80.7)	1.00 (referent)		<0.001	8544 (86.2)	1482 (80.8)	1.00 (referent)		<0.001	5572 (80.0)	1276 (80.5)	1.00 (referent)		<0.001	0.68
		Yes	278 (1.6)	110 (3.2)	1.84 (1.46 to 2.33)			132 (1.3)	51 (2.8)	1.89 (1.34 to 2.66)			146 (2.1)	59 (3.7)	1.76 (1.28 to 2.42)			
Non-Hodgkin lymphoma, male relative		No	12021 (83.8)	2338 (81.2)	1.00 (referent)		<0.001	7149 (86.3)	1250 (81.4)	1.00 (referent)		0.002	4872 (80.5)	1088 (81.1)	1.00 (referent)		0.11	0.33
		Yes	113 (0.8)	45 (1.6)	1.90 (1.33 to 2.73)			54 (0.7)	25 (1.6)	2.27 (1.37 to 3.75)			59 (1.0)	20 (1.5)	1.56 (0.93 to 2.63)			
Non-Hodgkin lymphoma, female relative		No	11746 (81.9)	2290 (79.6)	1.00 (referent)		0.078	6661 (83.9)	1165 (78.7)	1.00 (referent)		0.24	4744 (78.3)	1069 (79.7)	1.00 (referent)		0.25	0.92
		Yes	126 (0.9)	39 (1.4)	1.41 (0.97 to 2.05)			55 (0.7)	16 (1.1)	1.43 (0.80 to 2.55)			71 (1.2)	23 (1.7)	1.34 (0.82 to 2.19)			
Leukemia		No	13831 (92.4)	2726 (91.5)	1.00 (referent)		0.21	8373 (93.7)	1467 (92.1)	1.00 (referent)		0.86	5458 (90.5)	1259 (90.8)	1.00 (referent)		0.06	0.18
		Yes	402 (2.7)	94 (3.2)	1.16 (0.92 to 1.47)			234 (2.6)	41 (2.6)	0.97 (0.69 to 1.37)			168 (2.8)	53 (3.8)	1.38 (1.00 to 1.91)			
Leukemia, male relative		No	11634 (92.6)	2275 (92.1)	1.00 (referent)		0.69	6927 (94.0)	1213 (92.3)	1.00 (referent)		0.33	4707 (90.6)	1062 (91.8)	1.00 (referent)		0.73	0.33
		Yes	197 (1.6)	36 (1.5)	0.93 (0.64 to 1.34)			114 (1.5)	16 (1.2)	0.77 (0.44 to 1.33)			83 (1.6)	20 (1.7)	1.09 (0.66 to 1.81)			
Leukemia, female relative		No	11680 (92.9)	2263 (91.6)	1.00 (referent)		0.005	6951 (94.3)	1208 (91.9)	1.00 (referent)		0.26	4729 (91.0)	1055 (91.2)	1.00 (referent)		0.005	0.22
		Yes	151 (1.2)	48 (1.9)	1.66 (1.18 to 2.33)			90 (1.2)	21 (1.6)	1.34 (0.82 to 2.21)			61 (1.2)	27 (2.3)	2.04 (1.27 to 3.30)			
Multiple myeloma		No	11831 (82.5)	2316 (80.5)	1.00 (referent)		0.38	6420 (83.8)	1060 (77.7)	1.00 (referent)		0.26	3646 (74.2)	840 (76.5)	1.00 (referent)		0.72	0.44
		Yes	41 (0.3)	13 (0.5)	1.35 (0.71 to 2.57)			14 (0.2)	5 (0.4)	1.92 (0.64 to 5.73)			27 (0.5)	8 (0.7)	1.16 (0.52 to 2.60)			
Multiple myeloma, male relative		No	7676 (75.8)	1601 (74.5)	1.00 (referent)		0.88	3235 (73.6)	588 (68.1)	1.00 (referent)		0.82	2773 (87.0)	550 (87.7)	1.00 (referent)		0.99	0.88
		Yes	16 (0.2)	3 (0.1)	0.91 (0.26 to 3.18)			6 (0.1)	1 (0.1)	0.78 (0.09 to 6.86)			10 (0.3)	2 (0.3)	1.01 (0.22 to 4.74)			
Multiple myeloma, female relative		No	9387 (79.0)	1804 (76.4)	1.00 (referent)		0.37	4643 (93.3)	637 (87.9)	1.00 (referent)		0.25	2833 (71.6)	774 (76.4)	1.00 (referent)		0.69	0.44
		Yes	25 (0.2)	9 (0.4)	1.45 (0.66 to 3.18)			8 (0.2)	3 (0.4)	2.42 (0.58 to 10.21)			17 (0.4)	6 (0.6)	1.22 (0.47 to 3.13)			
ANTHROPOMETRICS AND ENERGY BALANCE																		
Usual adult height																		
Quartile 1 (low)		4131 (24.1)	827 (22.5)	1.00 (referent)		0.23	2360 (24.2)	415 (20.9)	1.00 (referent)		0.13	1771 (24.1)	412 (24.4)	1.00 (referent)		0.47	0.14	
Quartile 2		3852 (22.5)	807 (22.0)	1.05 (0.94 to 1.17)			2235 (22.9)	468 (23.6)	1.18 (1.01 to 1.37)			1617 (22.0)	339 (20.1)	0.97 (0.83 to 1.15)				
Quartile 3		4169 (24.3)	903 (24.6)	1.07 (0.96 to 1.20)			2436 (24.9)	499 (25.1)	1.08 (0.93 to 1.26)			1733 (23.6)	404 (23.9)	1.04 (0.89 to 1.22)				
Quartile 4 (high)		4352 (25.4)	972 (26.5)	1.12 (1.01 to 1.25)			2413 (24.7)	510 (25.7)	1.17 (1.00 to 1.36)			1939 (26.4)	462 (27.4)	1.10 (0.94 to 1.29)				
Usual adult weight [¶]																		
Quartile 1 (low)		4115 (24.0)	795 (21.7)	1.00 (referent)		0.002	2341 (24.0)	387 (19.5)	1.00 (referent)		0.095	1774 (24.1)	408 (24.2)	1.00 (referent)		<0.001	0.075	
Quartile 2		3953 (23.1)	783 (21.3)	1.01 (0.90 to 1.13)			2359 (24.2)	456 (23.0)	1.12 (0.96 to 1.31)			1594 (21.7)	327 (19.4)	0.90 (0.77 to 1.06)				
Quartile 3		4335 (25.3)	907 (24.7)	1.03 (0.92 to 1.15)			2396 (24.5)	494 (24.9)	1.13 (0.97 to 1.31)			1939 (26.4)	413 (24.5)	0.93 (0.80 to 1.09)				
Quartile 4 (high)		4101 (24.0)	1024 (27.9)	1.20 (1.07 to 1.33)			2348 (24.0)	555 (28.0)	1.21 (1.04 to 1.41)			1753 (23.8)	469 (27.8)	1.21 (1.03 to 1.41)				
Usual adult body mass index (kg/m ²)																		

		All				Sex-stratified results									
		Controls		Cases		Males				Females				p-hetero geneity	
		No. (%) [*]		No. (%) [*]		Controls		Cases		Controls		Cases			
Exposure		No. (%) [*]	No. (%) [*]	OR (95% CI) [†]	<i>P</i>	No. (%)	No. (%)	OR (95% CI) [†]	<i>P</i>	No. (%)	No. (%)	OR (95% CI) [†]	<i>P</i>		
	15-<18.5	267 (1.6)	33 (0.9)	0.60 (0.41 to 0.88)	0.002	68 (0.7)	12 (0.6)	1.10 (0.57 to 2.13)	0.47	199 (2.7)	21 (1.2)	0.47 (0.29 to 0.74)	<0.001	0.20	
	18.5-<22.5	3481 (20.3)	722 (19.7)	1.00 (referent)		1458 (14.9)	248 (12.5)	1.00 (referent)		2023 (27.5)	474 (28.1)	1.00 (referent)			
	22.5-<25	4276 (25.0)	850 (23.1)	0.96 (0.85 to 1.07)		2552 (26.1)	474 (23.9)	1.01 (0.85 to 1.20)		1724 (23.4)	376 (22.3)	0.93 (0.80 to 1.09)			
	25-<30	6112 (35.7)	1310 (35.7)	1.03 (0.93 to 1.15)		4107 (42.1)	851 (42.9)	1.09 (0.93 to 1.28)		2005 (27.3)	459 (27.2)	1.01 (0.87 to 1.17)			
	30-<35	1760 (10.3)	419 (11.4)	1.09 (0.94 to 1.25)		991 (10.1)	239 (12.0)	1.19 (0.97 to 1.46)		769 (10.5)	180 (10.7)	1.03 (0.84 to 1.25)			
	35-50	608 (3.6)	175 (4.8)	1.26 (1.04 to 1.53)		268 (2.7)	68 (3.4)	1.19 (0.87 to 1.63)		340 (4.6)	107 (6.3)	1.36 (1.06 to 1.74)			
Body mass index as a young adult (kg/															
	15-<18.5	384 (2.4)	64 (1.8)	0.83 (0.62 to 1.10)	<0.001	100 (1.2)	25 (1.3)	1.24 (0.78 to 1.99)	<0.001	284 (3.9)	39 (2.3)	0.66 (0.46 to 0.95)	<0.001	0.023	
	18.5-<22.5	2804 (17.3)	517 (14.2)	1.00 (referent)		1378 (17.0)	232 (12.0)	1.00 (referent)		1405 (19.3)	285 (17.0)	1.00 (referent)			
	22.5-<25	1394 (8.6)	276 (7.6)	1.17 (0.99 to 1.38)		975 (12.0)	168 (8.7)	1.05 (0.84 to 1.31)		389 (5.3)	108 (6.5)	1.42 (1.10 to 1.84)			
	25-<30	839 (5.2)	226 (6.2)	1.64 (1.36 to 1.97)		635 (7.8)	172 (8.9)	1.67 (1.33 to 2.09)		185 (2.5)	54 (3.2)	1.57 (1.11 to 2.20)			
	30-50	173 (1.1)	54 (1.5)	1.84 (1.32 to 2.56)		102 (1.3)	33 (1.7)	2.00 (1.30 to 3.07)		66 (0.9)	21 (1.3)	1.68 (0.99 to 2.86)			
Physical activity															
	None	716 (10.1)	173 (10.3)	1.00 (referent)	0.23	319 (9.5)	85 (10.1)	1.00 (referent)	0.13	397 (10.7)	88 (10.5)	1.00 (referent)	0.59	0.17	
	Mild	474 (6.7)	112 (6.7)	0.89 (0.67 to 1.18)		210 (6.2)	63 (7.5)	0.98 (0.66 to 1.45)		264 (7.1)	49 (5.8)	0.85 (0.56 to 1.30)			
	Moderate	934 (13.2)	240 (14.3)	1.00 (0.78 to 1.27)		424 (12.6)	121 (14.4)	0.95 (0.68 to 1.34)		510 (13.8)	119 (14.1)	1.09 (0.77 to 1.55)			
	Vigorous	3037 (43.0)	627 (37.3)	0.85 (0.70 to 1.04)		1380 (41.0)	272 (32.4)	0.76 (0.57 to 1.01)		1657 (44.8)	355 (42.2)	0.96 (0.72 to 1.28)			
CIGARETTE SMOKING															
History of cigarette smoking [‡]															
	No	8879 (40.7)	1823 (41.0)	1.00 (referent)	0.80	3934 (30.8)	792 (32.6)	1.00 (referent)	0.64	4945 (54.9)	1031 (51.1)	1.00 (referent)	0.41	0.29	
	Yes	11690 (53.6)	2316 (52.1)	1.01 (0.94 to 1.08)		8047 (63.0)	1458 (59.9)	0.98 (0.88 to 1.08)		3643 (40.4)	858 (42.6)	1.05 (0.94 to 1.16)			
Smoking status as of ~1 year prior to															
	Non-smoker	8879 (40.7)	1823 (41.0)	1.00 (referent)	0.19	3934 (30.8)	792 (32.6)	1.00 (referent)	0.20	4945 (54.9)	1031 (51.1)	1.00 (referent)	0.84	0.64	
	Former smoker	6327 (29.0)	1280 (28.8)	1.01 (0.93 to 1.09)		4452 (34.8)	814 (33.5)	0.98 (0.87 to 1.10)		1875 (20.8)	466 (23.1)	1.04 (0.92 to 1.18)			
	Current smoker	4829 (22.2)	890 (20.0)	0.98 (0.90 to 1.08)		3183 (24.9)	531 (21.8)	0.94 (0.83 to 1.07)		1646 (18.3)	359 (17.8)	1.04 (0.91 to 1.19)			
	Smoker, status unknown	534 (2.5)	146 (3.3)	1.26 (1.01 to 1.57)		412 (3.2)	113 (4.6)	1.25 (0.96 to 1.64)		122 (1.4)	33 (1.6)	1.14 (0.74 to 1.76)			
Age started smoking cigarettes regularly															
	Non-smoker	8879 (40.7)	1823 (41.0)	1.00 (referent)	0.53	3934 (30.8)	792 (32.6)	1.00 (referent)	0.38	4945 (54.9)	1031 (51.1)	1.00 (referent)	0.65	0.42	
	<14 years	1068 (4.9)	214 (4.8)	1.00 (0.85 to 1.17)		841 (6.6)	163 (6.7)	0.99 (0.82 to 1.19)		227 (2.5)	51 (2.5)	0.99 (0.72 to 1.36)			
	14-17 years	4348 (20.0)	892 (20.0)	1.01 (0.92 to 1.10)		3108 (24.3)	572 (23.5)	0.94 (0.83 to 1.06)		1240 (13.8)	320 (15.9)	1.13 (0.98 to 1.31)			
	18-19 years	2352 (10.8)	453 (10.2)	0.98 (0.87 to 1.10)		1578 (12.3)	272 (11.2)	0.95 (0.81 to 1.11)		774 (8.6)	181 (9.0)	1.03 (0.86 to 1.23)			
	20+ years	3251 (14.9)	607 (13.6)	1.00 (0.90 to 1.11)		1989 (15.6)	330 (13.6)	1.01 (0.88 to 1.17)		1262 (14.0)	277 (13.7)	0.98 (0.84 to 1.14)			
	Smoker, age start unknown	671 (3.1)	150 (3.4)	1.23 (1.00 to 1.52)		531 (4.2)	121 (5.0)	1.25 (0.97 to 1.60)		140 (1.6)	29 (1.4)	1.11 (0.73 to 1.71)			
Frequency of cigarette smoking															
	Non-smoker	8879 (40.7)	1823 (41.0)	1.00 (referent)	0.093	3934 (30.8)	792 (32.6)	1.00 (referent)	0.066	4945 (54.9)	1031 (51.1)	1.00 (referent)	0.66	0.42	
	Smoker, 1-10 cigarettes/day	3910 (17.9)	763 (17.1)	0.93 (0.85 to 1.03)		2149 (16.8)	372 (15.3)	0.88 (0.76 to 1.01)		1761 (19.5)	391 (19.4)	0.98 (0.86 to 1.12)			
	Smoker, 11-20 cigarettes/day	4766 (21.9)	965 (21.7)	1.05 (0.96 to 1.15)		3424 (26.8)	636 (26.1)	1.01 (0.90 to 1.14)		1342 (14.9)	329 (16.3)	1.10 (0.95 to 1.27)			
	Smoker, 21-30 cigarettes/day	1248 (5.7)	277 (6.2)	1.17 (1.01 to 1.35)		985 (7.7)	213 (8.8)	1.17 (0.99 to 1.40)		263 (2.9)	64 (3.2)	1.07 (0.80 to 1.43)			
	Smoker, >30 cigarettes/day	1339 (6.1)	231 (5.2)	0.99 (0.84 to 1.15)		1158 (9.1)	179 (7.4)	0.91 (0.76 to 1.10)		181 (2.0)	52 (2.6)	1.22 (0.88 to 1.68)			
	Smoker, frequency unknown	427 (2.0)	80 (1.8)	1.00 (0.77 to 1.29)		331 (2.6)	58 (2.4)	0.98 (0.72 to 1.33)		96 (1.1)	22 (1.1)	1.05 (0.65 to 1.70)			
Duration of cigarette smoking															
	Non-smoker	8879 (40.7)	1823 (41.0)	1.00 (referent)	0.44	3934 (30.8)	792 (32.6)	1.00 (referent)	0.50	4945 (54.9)	1031 (51.1)	1.00 (referent)	0.32	0.68	
	1-20 years	3917 (18.0)	774 (17.4)	0.99 (0.90 to 1.09)		2475 (19.4)	459 (18.9)	0.99 (0.87 to 1.12)		1442 (16.0)	315 (15.6)	0.98 (0.85 to 1.14)			
	21-30 years	2341 (10.7)	470 (10.6)	0.99 (0.88 to 1.11)		1644 (12.9)	317 (13.0)	0.99 (0.85 to 1.15)		697 (7.7)	153 (7.6)	0.95 (0.78 to 1.15)			

		All				Sex-stratified results									
						Males				Females				p-heterogeneity	
		Controls	Cases			Controls	Cases			Controls	Cases				
Exposure		No. (%) [*]	No. (%) [*]	OR (95% CI) [†]	P	No. (%)	No. (%)	OR (95% CI) [†]	P	No. (%)	No. (%)	OR (95% CI) [†]	P		
	30-39 years	2392 (11.0)	502 (11.3)	1.02	(0.91 to 1.14)	1641 (12.8)	306 (12.6)	0.94	(0.81 to 1.09)	751 (8.3)	196 (9.7)	1.13	(0.94 to 1.35)		
	40+ years	2749 (12.6)	517 (11.6)	1.02	(0.91 to 1.14)	2055 (16.1)	337 (13.9)	0.95	(0.81 to 1.10)	694 (7.7)	180 (8.9)	1.13	(0.94 to 1.37)		
	Smoker, duration unknown	291 (1.3)	53 (1.2)	1.42	(1.04 to 1.95)	232 (1.8)	39 (1.6)	1.39	(0.96 to 2.02)	59 (0.7)	14 (0.7)	1.57	(0.85 to 2.90)		
Years since quit cigarette smoking															
	Non-smoker	8879 (40.7)	1823 (41.0)	1.00 (referent)	<0.001	3934 (30.8)	792 (32.6)	1.00 (referent)	0.15	4945 (54.9)	1031 (51.1)	1.00 (referent)	<0.001	0.25	
	Quit >25 years ago	1622 (7.4)	333 (7.5)	0.93	(0.81 to 1.07)	1143 (8.9)	226 (9.3)	0.95	(0.80 to 1.12)	479 (5.3)	107 (5.3)	0.90	(0.72 to 1.12)		
	Quit 16-25 years ago	1498 (6.9)	340 (7.6)	1.04	(0.91 to 1.18)	1062 (8.3)	234 (9.6)	1.05	(0.89 to 1.24)	436 (4.8)	106 (5.3)	0.98	(0.78 to 1.24)		
	Quit 6-15 years ago	1743 (8.0)	333 (7.5)	0.93	(0.81 to 1.06)	1199 (9.4)	198 (8.1)	0.88	(0.74 to 1.05)	544 (6.0)	135 (6.7)	0.99	(0.81 to 1.21)		
	Quit ≤5 years ago	1049 (4.8)	194 (4.4)	1.00	(0.85 to 1.18)	734 (5.7)	113 (4.6)	0.95	(0.76 to 1.18)	315 (3.5)	81 (4.0)	1.08	(0.84 to 1.40)		
	Unknown when quit	415 (1.9)	80 (1.8)	2.20	(1.65 to 2.95)	314 (2.5)	43 (1.8)	1.59	(1.06 to 2.39)	101 (1.1)	37 (1.8)	3.37	(2.19 to 5.17)		
	Current smoker	4829 (22.2)	890 (20.0)	0.98	(0.90 to 1.08)	3183 (24.9)	531 (21.8)	0.94	(0.83 to 1.06)	1646 (18.3)	359 (17.8)	1.04	(0.91 to 1.19)		
Lifetime cigarette exposure															
	Non-smoker	8879 (40.7)	1823 (41.0)	1.00 (referent)	0.065	3934 (30.8)	792 (32.6)	1.00 (referent)	0.51	4945 (54.9)	1031 (51.1)	1.00 (referent)	0.043	0.39	
	1-10 pack-years	3473 (15.9)	663 (14.9)	0.93	(0.84 to 1.03)	1960 (15.3)	348 (14.3)	0.92	(0.80 to 1.06)	1513 (16.8)	315 (15.6)	0.93	(0.81 to 1.08)		
	11-20 pack-years	2272 (10.4)	441 (9.9)	0.95	(0.85 to 1.07)	1501 (11.7)	271 (11.1)	0.93	(0.80 to 1.09)	771 (8.6)	170 (8.4)	0.96	(0.80 to 1.15)		
	21-35 pack-years	2369 (10.9)	528 (11.9)	1.10	(0.98 to 1.23)	1650 (12.9)	337 (13.9)	1.05	(0.91 to 1.22)	719 (8.0)	191 (9.5)	1.17	(0.98 to 1.40)		
	>35 pack-years	3038 (13.9)	580 (13.0)	1.07	(0.96 to 1.20)	2523 (19.7)	428 (17.6)	0.99	(0.86 to 1.14)	515 (5.7)	152 (7.5)	1.28	(1.04 to 1.56)		
	Smoker, pack-years unknown	538 (2.5)	104 (2.3)	1.16	(0.92 to 1.46)	413 (3.2)	74 (3.0)	1.12	(0.85 to 1.48)	125 (1.4)	30 (1.5)	1.26	(0.83 to 1.92)		
ALCOHOL CONSUMPTION															
History of alcohol consumption															
	Non-drinker	4277 (21.7)	975 (23.6)	1.00 (referent)	<0.001	1995 (17.1)	391 (17.4)	1.00 (referent)	<0.001	2282 (28.5)	584 (31.1)	1.00 (referent)	0.024	0.020	
	Drinker (≥1 drink/month)	10994 (55.9)	2059 (49.9)	0.81	(0.73 to 0.89)	7245 (62.2)	1235 (54.9)	0.73	(0.63 to 0.83)	3749 (46.8)	824 (43.9)	0.86	(0.76 to 0.98)		
Alcohol consumption status as of ~2 years prior to diagnosis/interview															
	Non-drinker	4277 (21.7)	975 (23.6)	1.00 (referent)	<0.001	1995 (17.1)	391 (17.4)	1.00 (referent)	<0.001	2282 (28.5)	584 (31.1)	1.00 (referent)	0.010	0.011	
	Former drinker	609 (3.1)	143 (3.5)	0.97	(0.78 to 1.20)	326 (2.8)	68 (3.0)	0.78	(0.56 to 1.07)	283 (3.5)	75 (4.0)	1.12	(0.83 to 1.51)		
	Current drinker	5010 (25.5)	976 (23.7)	0.71	(0.63 to 0.80)	3122 (26.8)	563 (25.0)	0.63	(0.52 to 0.76)	1888 (23.6)	413 (22.0)	0.79	(0.66 to 0.93)		
	Drinker, status unknown	5375 (27.3)	940 (22.8)	0.90	(0.79 to 1.03)	3797 (32.6)	604 (26.9)	0.82	(0.68 to 0.99)	1578 (19.7)	336 (17.9)	0.92	(0.75 to 1.12)		
Age at first alcohol consumption															
	Non-drinker	4277 (21.7)	975 (23.6)	1.00 (referent)	<0.001	1995 (17.1)	391 (17.4)	1.00 (referent)	<0.001	2282 (28.5)	584 (31.1)	1.00 (referent)	0.054	0.001	
	<20 years	2281 (11.6)	456 (11.1)	0.87	(0.75 to 1.01)	1441 (12.4)	273 (12.1)	0.70	(0.56 to 0.86)	840 (10.5)	183 (9.8)	1.02	(0.83 to 1.27)		
	20-29 years	2908 (14.8)	543 (13.2)	0.71	(0.62 to 0.82)	1881 (16.1)	304 (13.5)	0.58	(0.48 to 0.71)	1027 (12.8)	239 (12.7)	0.87	(0.72 to 1.05)		
	30+ years	768 (3.9)	171 (4.1)	0.82	(0.68 to 1.00)	313 (2.7)	72 (3.2)	0.77	(0.57 to 1.05)	455 (5.7)	99 (5.3)	0.79	(0.62 to 1.02)		
	Drinker, age start unknown	5037 (25.6)	889 (21.6)	0.85	(0.73 to 0.98)	3610 (31.0)	586 (26.1)	0.85	(0.70 to 1.04)	1427 (17.8)	303 (16.2)	0.78	(0.63 to 0.98)		
Duration of alcohol consumption															
	Non-drinker	4277 (21.7)	975 (23.6)	1.00 (referent)	<0.001	1995 (17.1)	391 (17.4)	1.00 (referent)	<0.001	2282 (28.5)	584 (31.1)	1.00 (referent)	0.012	<.0001	
	1-20 years	1307 (6.6)	209 (5.1)	0.79	(0.65 to 0.95)	813 (7.0)	93 (4.1)	0.57	(0.43 to 0.76)	494 (6.2)	116 (6.2)	1.11	(0.86 to 1.43)		
	21-30 years	1085 (5.5)	162 (3.9)	0.74	(0.60 to 0.91)	692 (5.9)	85 (3.8)	0.62	(0.46 to 0.84)	393 (4.9)	77 (4.1)	0.89	(0.66 to 1.19)		
	30-39 years	1247 (6.3)	225 (5.5)	0.82	(0.68 to 0.99)	751 (6.4)	138 (6.1)	0.86	(0.66 to 1.12)	496 (6.2)	87 (4.6)	0.73	(0.55 to 0.96)		
	40+ years	1900 (9.7)	309 (7.5)	0.71	(0.60 to 0.85)	1163 (10.0)	177 (7.9)	0.72	(0.56 to 0.92)	737 (9.2)	132 (7.0)	0.71	(0.56 to 0.90)		
	Drinker, duration unknown	5455 (27.7)	1154 (28.0)	0.86	(0.75 to 0.98)	3826 (32.8)	742 (33.0)	0.75	(0.63 to 0.90)	1629 (20.3)	412 (22.0)	0.90	(0.75 to 1.09)		
Servings of alcohol per week as an adult															
	Non-drinker	4277 (21.7)	975 (23.6)	1.00 (referent)	<0.001	1995 (17.1)	391 (17.4)	1.00 (referent)	<0.001	2282 (28.5)	584 (31.1)	1.00 (referent)	0.008	0.079	
	<1 drink/week	955 (4.9)	255 (6.2)	0.97	(0.82 to 1.14)	331 (2.8)	93 (4.1)	0.92	(0.70 to 1.20)	624 (7.8)	162 (8.6)	0.98	(0.80 to 1.20)		
	1-6 drinks/week	3738 (19.0)	727 (17.6)	0.81	(0.73 to 0.91)	2104 (18.0)	362 (16.1)	0.76	(0.64 to 0.89)	1634 (20.4)	365 (19.5)	0.83	(0.71 to 0.97)		

		All				Sex-stratified results									
						Males				Females				p-hetero geneity	
		Controls	Cases			Controls	Cases			Controls	Cases				
Exposure		No. (%)*	No. (%)*	OR (95% CI)†	P	No. (%)	No. (%)	OR (95% CI)†	P	No. (%)	No. (%)	OR (95% CI)†	P		
7-13 drinks/week		2216 (11.3)	403 (9.8)	0.76	(0.67 to 0.87)	1448 (12.4)	259 (11.5)	0.74	(0.62 to 0.89)	768 (9.6)	144 (7.7)	0.74	(0.60 to 0.91)		
14-27 drinks/week		2137 (10.9)	374 (9.1)	0.77	(0.67 to 0.89)	1596 (13.7)	261 (11.6)	0.66	(0.55 to 0.80)	541 (6.8)	113 (6.0)	0.99	(0.78 to 1.25)		
28+ drinks/week or binge		1918 (9.8)	299 (7.3)	0.77	(0.66 to 0.90)	1750 (15.0)	259 (11.5)	0.68	(0.57 to 0.83)	168 (2.1)	40 (2.1)	1.11	(0.76 to 1.62)		
Drinker, drinks/week unknown		30 (0.2)	1 (0.0)	0.15	(0.02 to 1.10)	16 (0.1)	1 (0.0)	0.23	(0.03 to 1.74)	14 (0.2)	0 (0.0)	*	(0.00 to *)		
Servings of beer per week as an adult															
Non-drinker		4277 (21.7)	975 (23.6)	1.00 (referent)	0.003	1995 (17.1)	391 (17.4)	1.00 (referent)	0.002	2282 (28.5)	584 (31.1)	1.00 (referent)	0.51	0.35	
<1 drink/week		1430 (7.3)	330 (8.0)	0.80	(0.69 to 0.92)	773 (6.6)	170 (7.6)	0.72	(0.58 to 0.89)	657 (8.2)	160 (8.5)	0.85	(0.69 to 1.04)		
1-6 drinks/week		2789 (14.2)	523 (12.7)	0.82	(0.72 to 0.94)	2193 (18.8)	383 (17.0)	0.77	(0.65 to 0.91)	596 (7.4)	140 (7.5)	0.86	(0.69 to 1.07)		
7-13 drinks/week		915 (4.7)	161 (3.9)	0.75	(0.62 to 0.92)	797 (6.8)	134 (6.0)	0.69	(0.55 to 0.87)	118 (1.5)	27 (1.4)	0.85	(0.54 to 1.32)		
14-27 drinks/week		638 (3.2)	112 (2.7)	0.77	(0.61 to 0.97)	598 (5.1)	104 (4.6)	0.72	(0.56 to 0.92)	40 (0.5)	8 (0.4)	0.72	(0.33 to 1.57)		
28+ drinks/week or binge		357 (1.8)	56 (1.4)	0.77	(0.56 to 1.04)	337 (2.9)	54 (2.4)	0.72	(0.52 to 1.00)	20 (0.2)	2 (0.1)	0.46	(0.11 to 2.04)		
Drinker, drinks/week unknown		1080 (5.5)	173 (4.2)	0.85	(0.62 to 1.16)	621 (5.3)	101 (4.5)	0.81	(0.51 to 1.28)	459 (5.7)	72 (3.8)	0.84	(0.55 to 1.30)		
Drinker, liquor & wine (no beer)		3785 (19.2)	704 (17.1)	0.81	(0.72 to 0.91)	1926 (16.5)	289 (12.9)	0.68	(0.57 to 0.82)	1859 (23.2)	415 (22.1)	0.88	(0.76 to 1.02)		
Servings of liquor per week as an adult															
Non-drinker		4277 (21.7)	975 (23.6)	1.00 (referent)	<0.001	1995 (17.1)	391 (17.4)	1.00 (referent)	0.002	2282 (28.5)	584 (31.1)	1.00 (referent)	0.003	0.027	
<1 drink/week		1910 (9.7)	425 (10.3)	0.71	(0.62 to 0.82)	1089 (9.3)	250 (11.1)	0.67	(0.55 to 0.83)	821 (10.2)	175 (9.3)	0.69	(0.56 to 0.85)		
1-6 drinks/week		2095 (10.7)	353 (8.6)	0.78	(0.67 to 0.90)	1540 (13.2)	227 (10.1)	0.72	(0.60 to 0.88)	555 (6.9)	126 (6.7)	0.79	(0.63 to 1.00)		
7-13 drinks/week		552 (2.8)	88 (2.1)	0.81	(0.63 to 1.03)	454 (3.9)	70 (3.1)	0.83	(0.63 to 1.11)	98 (1.2)	18 (1.0)	0.65	(0.39 to 1.09)		
14-27 drinks/week		322 (1.6)	50 (1.2)	0.87	(0.63 to 1.20)	287 (2.5)	36 (1.6)	0.75	(0.52 to 1.10)	35 (0.4)	14 (0.7)	1.31	(0.69 to 2.48)		
28+ drinks/week or binge		152 (0.8)	19 (0.5)	0.79	(0.48 to 1.31)	136 (1.2)	18 (0.8)	0.90	(0.53 to 1.53)	16 (0.2)	1 (0.1)	0.21	(0.03 to 1.58)		
Drinker, drinks/week unknown		1080 (5.5)	173 (4.2)	0.85	(0.63 to 1.17)	621 (5.3)	101 (4.5)	0.81	(0.51 to 1.28)	459 (5.7)	72 (3.8)	0.85	(0.55 to 1.31)		
Drinker, beer & wine (no liquor)		4883 (24.8)	951 (23.1)	0.84	(0.76 to 0.94)	3118 (26.7)	533 (23.7)	0.71	(0.60 to 0.83)	1765 (22.0)	418 (22.3)	0.98	(0.84 to 1.14)		
Servings of wine per week as an adult															
Non-drinker		4277 (21.7)	975 (23.6)	1.00 (referent)	<0.001	1995 (17.1)	391 (17.4)	1.00 (referent)	<0.001	2282 (28.5)	584 (31.1)	1.00 (referent)	0.007	0.012	
<1 drink/week		1281 (6.5)	340 (8.2)	0.88	(0.76 to 1.02)	619 (5.3)	171 (7.6)	0.87	(0.69 to 1.09)	662 (8.3)	169 (9.0)	0.86	(0.70 to 1.06)		
1-6 drinks/week		2869 (14.6)	570 (13.8)	0.75	(0.66 to 0.85)	1677 (14.4)	302 (13.4)	0.70	(0.58 to 0.84)	1192 (14.9)	268 (14.3)	0.77	(0.64 to 0.92)		
7-13 drinks/week		1129 (5.7)	200 (4.8)	0.70	(0.58 to 0.83)	612 (5.3)	108 (4.8)	0.61	(0.48 to 0.78)	517 (6.5)	92 (4.9)	0.75	(0.58 to 0.96)		
14-27 drinks/week		1241 (6.3)	214 (5.2)	0.78	(0.65 to 0.93)	806 (6.9)	128 (5.7)	0.58	(0.45 to 0.74)	435 (5.4)	86 (4.6)	1.09	(0.83 to 1.43)		
28+ drinks/week or binge		(5.7)	171 (4.1)	0.75	(0.61 to 0.92)	1036 (8.9)	143 (6.4)	0.56	(0.44 to 0.72)	92 (1.1)	28 (1.5)	1.50	(0.94 to 2.38)		
Drinker, drinks/week unknown		1080 (5.5)	173 (4.2)	0.85	(0.62 to 1.15)	621 (5.3)	101 (4.5)	0.79	(0.50 to 1.24)	459 (5.7)	72 (3.8)	0.84	(0.54 to 1.30)		
Drinker, beer & liquor (no wine)		2266 (11.5)	391 (9.5)	0.91	(0.79 to 1.04)	1874 (16.1)	282 (12.5)	0.83	(0.69 to 0.99)	392 (4.9)	109 (5.8)	0.98	(0.77 to 1.25)		
Grams of ethanol per week as an adult, consumed from any type of alcoholic beverage															
Non-drinker		4277 (21.7)	975 (23.6)	1.00 (referent)	<0.001	1995 (17.1)	391 (17.4)	1.00 (referent)	<0.001	2282 (28.5)	584 (31.1)	1.00 (referent)	0.085	0.076	
Quartile 1 (low)		2421 (12.3)	544 (13.2)	0.84	(0.75 to 0.96)	1135 (9.7)	218 (9.7)	0.76	(0.62 to 0.92)	1286 (16.1)	326 (17.4)	0.88	(0.75 to 1.04)		
Quartile 2		2471 (12.6)	484 (11.7)	0.79	(0.70 to 0.90)	1449 (12.4)	269 (12.0)	0.76	(0.63 to 0.91)	1022 (12.8)	215 (11.5)	0.79	(0.66 to 0.95)		
Quartile 3		2488 (12.6)	459 (11.1)	0.77	(0.68 to 0.88)	1759 (15.1)	308 (13.7)	0.70	(0.59 to 0.83)	729 (9.1)	151 (8.1)	0.86	(0.70 to 1.06)		
Quartile 4 (high)		2534 (12.9)	399 (9.7)	0.78	(0.67 to 0.90)	2281 (19.6)	339 (15.1)	0.68	(0.57 to 0.82)	253 (3.2)	60 (3.2)	1.12	(0.82 to 1.54)		
Drinker, grams unknown		1080 (5.5)	173 (4.2)	0.85	(0.62 to 1.15)	621 (5.3)	101 (4.5)	0.81	(0.51 to 1.29)	459 (5.7)	72 (3.8)	0.84	(0.55 to 1.30)		
Grams of ethanol per week as an adult, consumed from beer															
Non-drinker		4277 (21.7)	975 (23.6)	1.00 (referent)	<0.001	1995 (17.1)	391 (17.4)	1.00 (referent)	<0.001	2282 (28.5)	584 (31.1)	1.00 (referent)	0.47	0.19	
Quartile 1 (low)		1430 (7.3)	330 (8.0)	0.80	(0.69 to 0.92)	773 (6.6)	170 (7.6)	0.72	(0.58 to 0.89)	657 (8.2)	160 (8.5)	0.85	(0.69 to 1.04)		
Quartile 2		1576 (8.0)	277 (6.7)	0.78	(0.66 to 0.91)	1201 (10.3)	186 (8.3)	0.70	(0.57 to 0.85)	375 (4.7)	91 (4.9)	0.87	(0.67 to 1.13)		
Quartile 3		1535 (7.8)	312 (7.6)	0.87	(0.75 to 1.02)	1263 (10.8)	253 (11.2)	0.84	(0.70 to 1.02)	272 (3.4)	59 (3.1)	0.80	(0.59 to 1.10)		
Quartile 4 (high)		1588 (8.1)	263 (6.4)	0.75	(0.63 to 0.88)	1461 (12.5)	236 (10.5)	0.69	(0.57 to 0.84)	127 (1.6)	27 (1.4)	0.82	(0.53 to 1.27)		
Drinker, grams unknown		1080 (5.5)	173 (4.2)	0.85	(0.62 to 1.16)	621 (5.3)	101 (4.5)	0.81	(0.51 to 1.28)	459 (5.7)	72 (3.8)	0.84	(0.55 to 1.30)		

Exposure	All				Sex-stratified results											
					Males				Females					p-hetero geneity		
	Controls	Cases	OR (95% CI)†		P	Controls	Cases	OR (95% CI)†		P	Controls	Cases	OR (95% CI)†		P	
	No. (%)*	No. (%)*				No. (%)	No. (%)				No. (%)	No. (%)				
Drinker, wine & liquor (no beer)	3785 (19.2)	704 (17.1)	0.81	(0.72 to 0.91)	1926 (16.5)	289 (12.9)	0.68	(0.57 to 0.82)	1859 (23.2)	415 (22.1)	0.88	(0.76 to 1.02)				
Grams of ethanol per week as an adult, consumed from liquor																
Non-drinker	4277 (21.7)	975 (23.6)	1.00 (referent)	<0.001	1995 (17.1)	391 (17.4)	1.00 (referent)	<0.001	2282 (28.5)	584 (31.1)	1.00 (referent)	0.002	0.001			
Quartile 1 (low)	1242 (6.3)	288 (7.0)	0.70	(0.59 to 0.83)	712 (6.1)	166 (7.4)	0.65	(0.51 to 0.82)	530 (6.6)	122 (6.5)	0.72	(0.56 to 0.91)				
Quartile 2	1255 (6.4)	254 (6.2)	0.79	(0.67 to 0.93)	803 (6.9)	174 (7.7)	0.85	(0.68 to 1.06)	452 (5.6)	80 (4.3)	0.60	(0.46 to 0.79)				
Quartile 3	1253 (6.4)	205 (5.0)	0.74	(0.62 to 0.89)	922 (7.9)	121 (5.4)	0.64	(0.51 to 0.81)	331 (4.1)	84 (4.5)	0.87	(0.67 to 1.14)				
Quartile 4 (high)	1281 (6.5)	188 (4.6)	0.81	(0.68 to 0.98)	1069 (9.2)	140 (6.2)	0.78	(0.62 to 0.97)	212 (2.6)	48 (2.6)	0.85	(0.61 to 1.20)				
Drinker, grams unknown	1080 (5.5)	173 (4.2)	0.85	(0.63 to 1.17)	621 (5.3)	101 (4.5)	0.81	(0.51 to 1.29)	459 (5.7)	72 (3.8)	0.85	(0.55 to 1.31)				
Drinker, wine & beer (no liquor)	4883 (24.8)	951 (23.1)	0.84	(0.76 to 0.94)	3118 (26.7)	533 (23.7)	0.71	(0.61 to 0.83)	1765 (22.0)	418 (22.3)	0.98	(0.84 to 1.14)				
Grams of ethanol per week as an adult, consumed from wine																
non-drinker	4277 (21.7)	975 (23.6)	1.00 (referent)	<0.001	1995 (17.1)	391 (17.4)	1.00 (referent)	<0.001	2282 (28.5)	584 (31.1)	1.00 (referent)	0.015	0.049			
Quartile 1 (low)	1879 (9.6)	406 (9.8)	0.78	(0.68 to 0.90)	1013 (8.7)	202 (9.0)	0.72	(0.59 to 0.88)	866 (10.8)	204 (10.9)	0.82	(0.68 to 0.99)				
Quartile 2	1885 (9.6)	408 (9.9)	0.78	(0.68 to 0.90)	1057 (9.1)	212 (9.4)	0.74	(0.60 to 0.90)	828 (10.3)	196 (10.5)	0.80	(0.65 to 0.97)				
Quartile 3	1717 (8.7)	338 (8.2)	0.75	(0.65 to 0.86)	989 (8.5)	191 (8.5)	0.67	(0.55 to 0.83)	728 (9.1)	147 (7.8)	0.78	(0.63 to 0.96)				
Quartile 4 (high)	2167 (11.0)	343 (8.3)	0.78	(0.66 to 0.91)	1691 (14.5)	247 (11.0)	0.58	(0.47 to 0.73)	476 (5.9)	96 (5.1)	1.20	(0.92 to 1.57)				
Drinker, grams unknown	1080 (5.5)	173 (4.2)	0.85	(0.62 to 1.16)	621 (5.3)	101 (4.5)	0.80	(0.50 to 1.25)	459 (5.7)	72 (3.8)	0.84	(0.55 to 1.30)				
Drinker, liquor & beer (no wine)	2266 (11.5)	391 (9.5)	0.91	(0.79 to 1.04)	1874 (16.1)	282 (12.5)	0.82	(0.69 to 0.98)	392 (4.9)	109 (5.8)	0.98	(0.77 to 1.25)				
Lifetime alcohol consumption																
Non-Drinker	4277 (21.7)	975 (23.6)	1.00 (referent)	<0.001	1995 (17.1)	391 (17.4)	1.00 (referent)	<0.001	2282 (28.5)	584 (31.1)	1.00 (referent)	0.16	0.0029			
1-100 kg	1444 (7.3)	305 (7.4)	0.80	(0.68 to 0.94)	628 (5.4)	104 (4.6)	0.70	(0.53 to 0.92)	816 (10.2)	201 (10.7)	0.85	(0.68 to 1.05)				
101-200 kg	641 (3.3)	134 (3.2)	0.79	(0.64 to 0.99)	394 (3.4)	76 (3.4)	0.78	(0.57 to 1.06)	247 (3.1)	58 (3.1)	0.79	(0.58 to 1.09)				
201-400 kg	651 (3.3)	121 (2.9)	0.69	(0.55 to 0.86)	467 (4.0)	82 (3.6)	0.68	(0.50 to 0.91)	184 (2.3)	39 (2.1)	0.68	(0.47 to 1.00)				
>400 kg	759 (3.9)	137 (3.3)	0.65	(0.52 to 0.82)	677 (5.8)	110 (4.9)	0.62	(0.47 to 0.82)	82 (1.0)	27 (1.4)	1.04	(0.65 to 1.66)				
Drinker, lifetime unknown	7499 (38.1)	1362 (33.0)	0.85	(0.75 to 0.96)	5079 (43.6)	863 (38.4)	0.75	(0.64 to 0.89)	2420 (30.2)	499 (26.6)	0.89	(0.75 to 1.06)				
Lifetime beer consumption																
Non-Drinker	4277 (21.7)	975 (23.6)	1.00 (referent)	<0.001	1995 (17.1)	391 (17.4)	1.00 (referent)	<0.001	2282 (28.5)	584 (31.1)	1.00 (referent)	0.13	<0.001			
1-100 kg	1328 (6.8)	261 (6.3)	0.78	(0.66 to 0.92)	926 (7.9)	147 (6.5)	0.68	(0.53 to 0.86)	402 (5.0)	114 (6.1)	1.02	(0.80 to 1.30)				
101-200 kg	325 (1.7)	69 (1.7)	0.85	(0.64 to 1.13)	276 (2.4)	59 (2.6)	0.87	(0.63 to 1.21)	49 (0.6)	10 (0.5)	0.78	(0.39 to 1.55)				
201-400 kg	237 (1.2)	38 (0.9)	0.63	(0.44 to 0.91)	213 (1.8)	34 (1.5)	0.63	(0.42 to 0.93)	24 (0.3)	4 (0.2)	0.61	(0.21 to 1.79)				
>400 kg	171 (0.9)	36 (0.9)	0.84	(0.57 to 1.22)	164 (1.4)	33 (1.5)	0.76	(0.50 to 1.14)	7 (0.1)	3 (0.2)	1.54	(0.39 to 6.10)				
Drinker, lifetime unknown	5148 (26.2)	951 (23.1)	0.82	(0.72 to 0.93)	3740 (32.1)	673 (29.9)	0.76	(0.64 to 0.90)	1408 (17.6)	278 (14.8)	0.77	(0.64 to 0.93)				
Drinker, wine & liquor (no beer)	3785 (19.2)	704 (17.1)	0.81	(0.72 to 0.91)	1926 (16.5)	289 (12.9)	0.68	(0.57 to 0.82)	1859 (23.2)	415 (22.1)	0.88	(0.76 to 1.03)				
Lifetime liquor consumption																
Non-Drinker	4277 (21.7)	975 (23.6)	1.00 (referent)	<0.001	1995 (17.1)	391 (17.4)	1.00 (referent)	0.002	2282 (28.5)	584 (31.1)	1.00 (referent)	0.014	0.006			
1-100 kg	1136 (5.8)	221 (5.4)	0.74	(0.62 to 0.89)	581 (5.0)	93 (4.1)	0.71	(0.54 to 0.94)	555 (6.9)	128 (6.8)	0.80	(0.63 to 1.01)				
101-200 kg	303 (1.5)	60 (1.5)	0.77	(0.57 to 1.04)	201 (1.7)	35 (1.6)	0.74	(0.50 to 1.11)	102 (1.3)	25 (1.3)	0.84	(0.53 to 1.34)				
201-400 kg	244 (1.2)	42 (1.0)	0.67	(0.47 to 0.94)	183 (1.6)	29 (1.3)	0.67	(0.44 to 1.03)	61 (0.8)	13 (0.7)	0.72	(0.39 to 1.34)				
>400 kg	164 (0.8)	34 (0.8)	0.78	(0.53 to 1.15)	131 (1.1)	28 (1.2)	0.87	(0.55 to 1.36)	33 (0.4)	6 (0.3)	0.61	(0.25 to 1.48)				
Drinker, lifetime unknown	4264 (21.7)	751 (18.2)	0.79	(0.69 to 0.89)	3031 (26.0)	517 (23.0)	0.74	(0.62 to 0.88)	1233 (15.4)	234 (12.5)	0.72	(0.58 to 0.88)				
Drinker, beer & wine (no liquor)	4883 (24.8)	951 (23.1)	0.85	(0.76 to 0.95)	3118 (26.7)	533 (23.7)	0.72	(0.61 to 0.84)	1765 (22.0)	418 (22.3)	0.99	(0.85 to 1.15)				
Lifetime wine consumption																
Non-Drinker	4277 (21.7)	975 (23.6)	1.00 (referent)	<0.001	1995 (17.1)	391 (17.4)	1.00 (referent)	<0.001	2282 (28.5)	584 (31.1)	1.00 (referent)	0.009	<0.001			
1-100 kg	1730 (8.8)	333 (8.1)	0.74	(0.63 to 0.86)	894 (7.7)	152 (6.8)	0.75	(0.59 to 0.96)	836 (10.4)	181 (9.7)	0.71	(0.57 to 0.87)				
101-200 kg	363 (1.8)	68 (1.6)	0.70	(0.53 to 0.92)	229 (2.0)	39 (1.7)	0.65	(0.45 to 0.95)	134 (1.7)	29 (1.5)	0.72	(0.47 to 1.11)				

		All				Sex-stratified results									
		Controls		Cases	OR (95% CI)†	P	Males				Females				p-heterogeneity
							Controls	Cases	OR (95% CI)†	P	Controls	Cases	OR (95% CI)†	P	
Exposure		No. (%)*	No. (%)*		No. (%)	No. (%)					No. (%)	No. (%)			
	201-400 kg	278 (1.4)	56 (1.4)	0.71	(0.52 to 0.98)	202 (1.7)	36 (1.6)	0.62	(0.41 to 0.93)	76 (0.9)	20 (1.1)	0.84	(0.49 to 1.43)		
	>400 kg	303 (1.5)	52 (1.3)	0.56	(0.40 to 0.79)	283 (2.4)	38 (1.7)	0.45	(0.30 to 0.69)	20 (0.2)	14 (0.7)	2.07	(0.99 to 4.31)		
	Drinker, lifetime unknown	6054 (30.8)	1159 (28.1)	0.83	(0.74 to 0.94)	3763 (32.3)	688 (30.6)	0.70	(0.59 to 0.84)	2291 (28.6)	471 (25.1)	0.92	(0.78 to 1.09)		
	Drinker, wine & liquor (no wine)	2266 (11.5)	391 (9.5)	0.91	(0.79 to 1.04)	1874 (16.1)	282 (12.5)	0.82	(0.69 to 0.98)	392 (4.9)	109 (5.8)	0.97	(0.76 to 1.23)		
SUN EXPOSURE															
Total sun exposure (hrs/week) [¶]															
	Quartile 1 (low)	1508 (18.7)	387 (19.2)	1.00 (referent)	0.057	483 (12.3)	132 (13.2)	1.00 (referent)	0.28	1025 (24.9)	255 (25.0)	1.00 (referent)	0.22	0.80	
	Quartile 2	1594 (19.8)	419 (20.7)	1.03	(0.88 to 1.20)	654 (16.6)	169 (16.9)	0.94	(0.73 to 1.23)	940 (22.8)	250 (24.5)	1.09	(0.89 to 1.33)		
	Quartile 3	1633 (20.3)	354 (17.5)	0.85	(0.72 to 1.01)	825 (21.0)	178 (17.8)	0.80	(0.62 to 1.03)	808 (19.6)	176 (17.3)	0.90	(0.72 to 1.12)		
	Quartile 4 (high)	1714 (21.3)	387 (19.2)	0.88	(0.74 to 1.03)	1135 (28.8)	264 (26.4)	0.85	(0.67 to 1.08)	579 (14.1)	123 (12.1)	0.88	(0.69 to 1.12)		
Recreational sun exposure (hrs/week) [¶]															
	Quartile 1 (low)	2234 (20.6)	649 (22.7)	1.00 (referent)	0.003	1003 (18.1)	303 (19.8)	1.00 (referent)	0.071	1231 (23.3)	346 (26.0)	1.00 (referent)	0.037	0.47	
	Quartile 2	2332 (21.6)	619 (21.6)	0.91	(0.80 to 1.03)	1112 (20.1)	291 (19.0)	0.84	(0.70 to 1.01)	1220 (23.1)	328 (24.7)	0.99	(0.83 to 1.17)		
	Quartile 3	2159 (20.0)	512 (17.9)	0.82	(0.71 to 0.93)	1121 (20.2)	277 (18.1)	0.80	(0.67 to 0.97)	1038 (19.7)	235 (17.7)	0.83	(0.69 to 1.00)		
	Quartile 4 (high)	2983 (27.6)	714 (24.9)	0.81	(0.72 to 0.92)	1745 (31.5)	449 (29.3)	0.82	(0.69 to 0.96)	1238 (23.5)	265 (19.9)	0.80	(0.67 to 0.97)		
HAIR DYE USE															
Ever used hair dyes															
	Never hair dye	1873 (15.7)	367 (14.0)	1.00 (referent)	0.66					1873 (32.9)	367 (29.2)	1.00 (referent)	0.66		
	Ever hair dye	3570 (29.9)	788 (30.0)	1.03	(0.90 to 1.19)					3570 (62.7)	788 (62.7)	1.03	(0.90 to 1.19)		
	Male	6241 (52.3)	1367 (52.1)												
Type of hair dye used															
	Never hair dye	1873 (15.7)	367 (14.0)	1.00 (referent)	0.88					1873 (32.9)	367 (29.2)	1.00 (referent)	0.88		
	Temporary only	429 (3.6)	67 (2.6)	1.00	(0.74 to 1.34)					429 (7.5)	67 (5.3)	1.00	(0.74 to 1.34)		
	Permanent	2838 (23.8)	655 (25.0)	1.03	(0.89 to 1.19)					2838 (49.8)	655 (52.1)	1.03	(0.89 to 1.19)		
	Ever hair dye, type unknown	303 (2.5)	66 (2.5)	1.17	(0.80 to 1.71)					303 (5.3)	66 (5.3)	1.17	(0.80 to 1.71)		
	Male	6241 (52.3)	1367 (52.1)												
Color of hair dye used															
	Never hair dye	1873 (15.7)	367 (14.0)	1.00 (referent)	0.042					1873 (32.9)	367 (29.2)	1.00 (referent)	0.042		
	Light	1036 (8.7)	246 (9.4)	1.07	(0.89 to 1.29)					1036 (18.2)	246 (19.6)	1.07	(0.89 to 1.29)		
	Dark	2090 (17.5)	432 (16.5)	0.94	(0.80 to 1.11)					2090 (36.7)	432 (34.4)	0.94	(0.80 to 1.11)		
	Ever hair dye, color unknown	444 (3.7)	110 (4.2)	1.41	(1.07 to 1.87)					444 (7.8)	110 (8.8)	1.41	(1.07 to 1.87)		
	Male	6241 (52.3)	1367 (52.1)												
Duration of hair dye use															
	Never hair dye	1873 (15.7)	367 (14.0)	1.00 (referent)	0.82					1873 (32.9)	367 (29.2)	1.00 (referent)	0.82		
	1-8 years	1164 (9.8)	249 (9.5)	1.03	(0.85 to 1.26)					1164 (20.4)	249 (19.8)	1.03	(0.85 to 1.26)		
	9-19 years	849 (7.1)	184 (7.0)	1.01	(0.82 to 1.24)					849 (14.9)	184 (14.6)	1.01	(0.82 to 1.24)		
	20+ years	983 (8.2)	243 (9.3)	1.12	(0.92 to 1.36)					983 (17.3)	243 (19.3)	1.12	(0.92 to 1.36)		
	Ever hair dye, duration unknown	574 (4.8)	112 (4.3)	0.96	(0.72 to 1.27)					574 (10.1)	112 (8.9)	0.96	(0.72 to 1.27)		
	Male	6241 (52.3)	1367 (52.1)												
Frequency of hair dye use															
	Never hair dye	1873 (15.7)	367 (14.0)	1.00 (referent)	0.88					1873 (32.9)	367 (29.2)	1.00 (referent)	0.88		
	1-5 times/year	1067 (8.9)	234 (8.9)	1.06	(0.87 to 1.29)					1067 (18.7)	234 (18.6)	1.06	(0.87 to 1.29)		
	6-11 times/year	1024 (8.6)	242 (9.2)	0.97	(0.80 to 1.18)					1024 (18.0)	242 (19.3)	0.97	(0.80 to 1.18)		
	12+ times/year	736 (6.2)	148 (5.6)	1.01	(0.81 to 1.26)					736 (12.9)	148 (11.8)	1.01	(0.81 to 1.26)		

		All				Sex-stratified results												
		Controls		Cases			Males				Females				p-hetero geneity			
		OR (95% CI)†		P			Controls		Cases			Controls		Cases				P
Exposure		No. (%)*	No. (%)*			No. (%)	No. (%)	OR (95% CI)†	P	No. (%)	No. (%)	OR (95% CI)†	P	No. (%)		No. (%)	OR (95% CI)†	P
	Frequency unknown	743 (6.2)	164 (6.3)	1.09	(0.87 to 1.36)									743 (13.0)	164 (13.1)	1.09	(0.87 to 1.36)	
	Male	6241 (52.3)	1367 (52.1)															
Used hair dyes prior to 1980																		
	Never hair dye	1873 (15.7)	367 (14.0)	1.00 (referent)	0.68									1873 (32.9)	367 (29.2)	1.00 (referent)	0.68	
	Ever hair dye use <1980	1400 (11.7)	335 (12.8)	1.11	(0.92 to 1.34)									1400 (24.6)	335 (26.7)	1.11	(0.92 to 1.34)	
	Hair dye use only 1980+	1127 (9.4)	260 (9.9)	1.03	(0.84 to 1.26)									1127 (19.8)	260 (20.7)	1.03	(0.84 to 1.26)	
	Time period unknown	1043 (8.7)	193 (7.4)	0.94	(0.74 to 1.21)									1043 (18.3)	193 (15.4)	0.94	(0.74 to 1.21)	
	Male	6241 (52.3)	1367 (52.1)															
FARMING																		
Ever lived or worked on a farm																		
	No	11106 (58.6)	2372 (64.3)	1.00 (referent)	0.98	6091 (54.3)	1226 (61.0)	1.00 (referent)	0.89	5015 (65.0)	1146 (68.3)	1.00 (referent)	0.91				0.70	
	Yes	7558 (39.9)	1257 (34.1)	1.00	(0.92 to 1.09)	4964 (44.3)	742 (36.9)	1.01	(0.90 to 1.13)	2594 (33.6)	515 (30.7)	0.99	(0.87 to 1.13)					
Ever lived on a farm																		
	No	4779 (56.3)	1109 (57.6)	1.00 (referent)	0.88	2800 (57.6)	617 (58.1)	1.00 (referent)	0.92	1979 (54.7)	492 (57.0)	1.00 (referent)	0.89				0.85	
	Yes	3470 (40.9)	767 (39.8)	1.01	(0.91 to 1.12)	1925 (39.6)	410 (38.6)	1.01	(0.87 to 1.17)	1545 (42.7)	357 (41.4)	1.01	(0.86 to 1.19)					
Ever worked on a farm																		
	No	11675 (80.0)	2648 (81.1)	1.00 (referent)	0.98	6348 (76.5)	1404 (77.1)	1.00 (referent)	0.47	5327 (84.6)	1244 (86.0)	1.00 (referent)	0.52				0.96	
	Yes	2717 (18.6)	575 (17.6)	1.00	(0.90 to 1.11)	1832 (22.1)	386 (21.2)	1.05	(0.92 to 1.20)	885 (14.1)	189 (13.1)	0.94	(0.79 to 1.13)					
OCCUPATIONS																		
Bakers and millers																		
	No	11857 (96.1)	3028 (98.1)	1.00 (referent)	0.93	6124 (93.7)	1580 (97.5)	1.00 (referent)	0.93	5481 (98.8)	1406 (98.8)	1.00 (referent)	0.85				0.87	
	Yes	158 (1.3)	38 (1.2)	0.99	(0.69 to 1.41)	97 (1.5)	24 (1.5)	1.02	(0.65 to 1.61)	61 (1.1)	14 (1.0)	0.95	(0.53 to 1.70)					
Chemists and chemical workers																		
	No	11315 (95.8)	2927 (98.1)	1.00 (referent)	0.36	5804 (92.8)	1517 (97.2)	1.00 (referent)	0.21	4541 (99.2)	1172 (98.9)	1.00 (referent)	0.65				0.19	
	Yes	167 (1.4)	36 (1.2)	0.85	(0.59 to 1.22)	136 (2.2)	26 (1.7)	0.77	(0.50 to 1.17)	31 (0.7)	10 (0.8)	1.19	(0.58 to 2.45)					
Cleaners																		
	No	11427 (92.6)	2894 (93.8)	1.00 (referent)	0.067	6008 (91.9)	1539 (94.9)	1.00 (referent)	0.15	5419 (93.4)	1355 (92.5)	1.00 (referent)	0.26				0.93	
	Yes	588 (4.8)	172 (5.6)	1.18	(0.99 to 1.41)	213 (3.3)	65 (4.0)	1.24	(0.93 to 1.65)	375 (6.5)	107 (7.3)	1.14	(0.91 to 1.44)					
Cleaners and related workers																		
	No	11608 (94.1)	2942 (95.3)	1.00 (referent)	0.031	5863 (93.7)	1513 (97.0)	1.00 (referent)	0.12	5464 (94.2)	1368 (93.4)	1.00 (referent)	0.18				0.53	
	Yes	395 (3.2)	122 (4.0)	1.27	(1.03 to 1.57)	73 (1.2)	28 (1.8)	1.44	(0.93 to 2.25)	322 (5.6)	94 (6.4)	1.19	(0.93 to 1.52)					
Drivers																		
	No	11116 (90.1)	2824 (91.5)	1.00 (referent)	0.74	5393 (82.5)	1373 (84.7)	1.00 (referent)	0.26	5723 (98.7)	1451 (99.0)	1.00 (referent)	0.055				0.057	
	Yes	899 (7.3)	242 (7.8)	1.03	(0.88 to 1.20)	828 (12.7)	231 (14.3)	1.10	(0.94 to 1.29)	71 (1.2)	11 (0.8)	0.56	(0.29 to 1.06)					
Drivers: material handling equipment																		
	No	11925 (96.7)	3031 (98.2)	1.00 (referent)	0.042	5695 (93.5)	1425 (96.5)	1.00 (referent)	0.036	2760 (99.8)	687 (99.7)	1.00 (referent)	0.90				0.57	
	Yes	78 (0.6)	33 (1.1)	1.56	(1.03 to 2.37)	73 (1.2)	32 (2.2)	1.60	(1.05 to 2.46)	5 (0.2)	1 (0.1)	0.87	(0.10 to 7.64)					
Dry Cleaners																		
	No	11890 (96.4)	3034 (98.3)	1.00 (referent)	0.68	5512 (94.1)	1403 (98.3)	1.00 (referent)	0.99	5700 (98.3)	1437 (98.1)	1.00 (referent)	0.64				0.65	
	Yes	125 (1.0)	32 (1.0)	1.09	(0.73 to 1.61)	31 (0.5)	7 (0.5)	1.00	(0.43 to 2.30)	94 (1.6)	25 (1.7)	1.12	(0.71 to 1.75)					
Electrical and electronics workers																		
	No	11266 (91.3)	2874 (93.1)	1.00 (referent)	0.86	5618 (85.9)	1451 (89.5)	1.00 (referent)	0.98	5648 (97.4)	1423 (97.1)	1.00 (referent)	0.99				0.74	

Exposure		All				Sex-stratified results									
						Males				Females				p-heterogeneity	
		Controls		Cases	OR (95% CI)†	P	Controls		Cases	OR (95% CI)†	P				
		No. (%)*	No. (%)*	No. (%)			No. (%)								
Yes	749 (6.1)	192 (6.2)	0.99	(0.83 to 1.16)			603 (9.2)	153 (9.4)	1.00			(0.83 to 1.21)	146 (2.5)		39 (2.7)
Electrical fitters	No	9816 (95.8)	2534 (98.4)	1.00 (referent)		5402 (93.0)	1376 (97.2)	1.00 (referent)		3012 (99.6)	763 (99.6)	1.00 (referent)		0.069	0.96
	Yes	92 (0.9)	20 (0.8)	0.83	(0.51 to 1.36)	85 (1.5)	20 (1.4)	0.90	(0.55 to 1.48)	7 (0.2)	0 (0.0)	*	(0.00 to *)		
	Electrical fitters and related electrical and electronics workers														
Engine mechanic	No	8729 (95.9)	2231 (98.5)	1.00 (referent)		4388 (92.6)	1105 (97.3)	1.00 (referent)		2136 (99.1)	528 (99.4)	1.00 (referent)		0.58	0.48
	Yes	48 (0.5)	14 (0.6)	1.06	(0.58 to 1.94)	37 (0.8)	12 (1.1)	1.21	(0.63 to 2.36)	11 (0.5)	2 (0.4)	0.66	(0.14 to 3.05)		
	Farm workers, any type														
Animal farm workers	No	10583 (85.8)	2696 (87.4)	1.00 (referent)		5271 (80.6)	1363 (84.1)	1.00 (referent)		5312 (91.6)	1333 (91.0)	1.00 (referent)		0.34	0.29
	Yes	1432 (11.6)	370 (12.0)	1.03	(0.91 to 1.17)	950 (14.5)	241 (14.9)	1.00	(0.85 to 1.17)	482 (8.3)	129 (8.8)	1.11	(0.90 to 1.37)		
	Crop farm workers														
Field crop and vegetable farm workers	No	11699 (94.8)	3000 (97.2)	1.00 (referent)		5549 (91.1)	1412 (95.7)	1.00 (referent)		5701 (98.3)	1443 (98.5)	1.00 (referent)		0.40	0.97
	Yes	316 (2.6)	66 (2.1)	0.82	(0.62 to 1.08)	223 (3.7)	47 (3.2)	0.82	(0.59 to 1.14)	93 (1.6)	19 (1.3)	0.81	(0.49 to 1.34)		
	Crop farm workers														
Field crop and vegetable farm workers	No	11442 (92.7)	2907 (94.2)	1.00 (referent)		5864 (89.7)	1502 (92.7)	1.00 (referent)		5326 (96.0)	1363 (95.8)	1.00 (referent)		0.47	0.89
	Yes	573 (4.6)	159 (5.2)	1.15	(0.95 to 1.38)	357 (5.5)	102 (6.3)	1.19	(0.94 to 1.50)	216 (3.9)	57 (4.0)	1.12	(0.83 to 1.53)		
	Field crop and vegetable farm workers														
Mixed and unspecified farm workers	No	10392 (94.8)	2664 (96.3)	1.00 (referent)		5362 (92.3)	1359 (96.0)	1.00 (referent)		5030 (97.6)	1305 (96.7)	1.00 (referent)		0.004	0.33
	Yes	233 (2.1)	79 (2.9)	1.49	(1.14 to 1.94)	125 (2.2)	37 (2.6)	1.30	(0.89 to 1.90)	108 (2.1)	42 (3.1)	1.75	(1.21 to 2.54)		
	Mixed and unspecified farm workers														
General farm workers	No	11318 (91.7)	2884 (93.5)	1.00 (referent)		5737 (87.7)	1484 (91.5)	1.00 (referent)		5329 (96.1)	1358 (95.4)	1.00 (referent)		0.22	0.14
	Yes	697 (5.6)	182 (5.9)	1.01	(0.85 to 1.20)	484 (7.4)	120 (7.4)	0.93	(0.75 to 1.15)	213 (3.8)	62 (4.4)	1.21	(0.90 to 1.63)		
	General farm workers														
Fire fighter	No	11600 (94.0)	2958 (95.9)	1.00 (referent)		5961 (91.2)	1539 (94.9)	1.00 (referent)		4482 (96.6)	1152 (96.3)	1.00 (referent)		0.16	0.22
	Yes	403 (3.3)	106 (3.4)	1.09	(0.87 to 1.37)	256 (3.9)	63 (3.9)	1.00	(0.74 to 1.33)	147 (3.2)	43 (3.6)	1.30	(0.91 to 1.85)		
	Fire fighter														
Forestry worker	No	11220 (96.5)	2864 (98.9)	1.00 (referent)		6143 (94.0)	1591 (98.1)	1.00 (referent)							
	Yes	78 (0.7)	13 (0.4)	0.63	(0.35 to 1.13)	78 (1.2)	13 (0.8)	0.63	(0.35 to 1.13)						
	Forestry worker														
Hair dresser	No	10694 (96.4)	2755 (98.6)	1.00 (referent)		5875 (93.9)	1526 (97.8)	1.00 (referent)		2504 (99.7)	609 (99.5)	1.00 (referent)		0.49	0.68
	Yes	71 (0.6)	19 (0.7)	1.13	(0.68 to 1.89)	65 (1.0)	17 (1.1)	1.11	(0.65 to 1.90)	6 (0.2)	2 (0.3)	1.82	(0.36 to 9.15)		
	Hair dresser														
Women’s hairdresser	No	11857 (96.1)	3008 (97.5)	1.00 (referent)		6186 (94.6)	1593 (98.3)	1.00 (referent)		5671 (97.8)	1415 (96.6)	1.00 (referent)		0.016	0.46
	Yes	158 (1.3)	58 (1.9)	1.49	(1.10 to 2.03)	35 (0.5)	11 (0.7)	1.18	(0.59 to 2.34)	123 (2.1)	47 (3.2)	1.55	(1.10 to 2.19)		
	Women’s hairdresser														
General unspecified labourer	No	11357 (96.2)	2915 (97.7)	1.00 (referent)		5922 (94.6)	1537 (98.5)	1.00 (referent)		5435 (98.0)	1378 (96.8)	1.00 (referent)		0.011	0.44
	Yes	113 (1.0)	46 (1.5)	1.62	(1.14 to 2.30)	14 (0.2)	4 (0.3)	1.06	(0.35 to 3.26)	99 (1.8)	42 (3.0)	1.65	(1.14 to 2.38)		
	General unspecified labourer														

Exposure		All				Sex-stratified results											
						Males				Females				p-heterogeneity			
		Controls	Cases	OR (95% CI)†		P	Controls	Cases	OR (95% CI)†		P	Controls	Cases		OR (95% CI)†		P
		No. (%)*	No. (%)*				No. (%)	No. (%)				No. (%)	No. (%)				
	No	11369 (92.1)	2869 (93.0)	1.00 (referent)		0.17	5753 (88.0)	1467 (90.5)	1.00 (referent)		0.32	5616 (96.8)	1402 (95.7)	1.00 (referent)		0.24	0.52
	Yes	646 (5.2)	197 (6.4)	1.13	(0.95 to 1.33)		468 (7.2)	137 (8.5)	1.11	(0.91 to 1.36)		178 (3.1)	60 (4.1)	1.20	(0.89 to 1.63)		
Leather worker																	
	No	10610 (95.7)	2738 (98.0)	1.00 (referent)		0.89	5865 (93.7)	1525 (97.8)	1.00 (referent)		0.92	3838 (97.8)	957 (97.9)	1.00 (referent)		0.97	0.90
	Yes	155 (1.4)	36 (1.3)	0.98	(0.67 to 1.41)		75 (1.2)	18 (1.2)	0.97	(0.58 to 1.64)		80 (2.0)	18 (1.8)	1.01	(0.60 to 1.70)		
Meat worker																	
	No	11907 (96.5)	3034 (98.3)	1.00 (referent)		0.55	6143 (94.0)	1574 (97.1)	1.00 (referent)		0.093	5764 (99.4)	1460 (99.7)	1.00 (referent)		0.033	0.030
	Yes	108 (0.9)	32 (1.0)	1.13	(0.76 to 1.69)		78 (1.2)	30 (1.9)	1.46	(0.95 to 2.24)		30 (0.5)	2 (0.1)	0.28	(0.07 to 1.16)		
Medical worker																	
	No	11120 (90.1)	2865 (92.8)	1.00 (referent)		0.044	5996 (91.7)	1545 (95.3)	1.00 (referent)		0.92	5124 (88.3)	1320 (90.1)	1.00 (referent)		0.016	0.20
	Yes	895 (7.3)	201 (6.5)	0.85	(0.72 to 1.00)		225 (3.4)	59 (3.6)	1.02	(0.76 to 1.37)		670 (11.6)	142 (9.7)	0.79	(0.65 to 0.96)		
Metal processor																	
	No	11884 (96.3)	3021 (97.9)	1.00 (referent)		0.071	6109 (93.4)	1562 (96.4)	1.00 (referent)		0.027	4319 (99.4)	1063 (99.4)	1.00 (referent)		0.52	0.25
	Yes	131 (1.1)	45 (1.5)	1.39	(0.98 to 1.96)		112 (1.7)	42 (2.6)	1.53	(1.06 to 2.20)		19 (0.4)	3 (0.3)	0.68	(0.20 to 2.32)		
Metal worker																	
	No	11284 (91.5)	2896 (93.8)	1.00 (referent)		0.36	5602 (85.7)	1456 (89.8)	1.00 (referent)		0.67	5286 (97.8)	1367 (98.2)	1.00 (referent)		0.32	0.61
	Yes	731 (5.9)	170 (5.5)	0.92	(0.77 to 1.10)		619 (9.5)	148 (9.1)	0.96	(0.79 to 1.16)		112 (2.1)	22 (1.6)	0.80	(0.50 to 1.27)		
Painter																	
	No	11795 (95.6)	3009 (97.5)	1.00 (referent)		0.89	6033 (92.3)	1554 (95.9)	1.00 (referent)		0.67	5510 (99.3)	1413 (99.3)	1.00 (referent)		0.73	0.72
	Yes	220 (1.8)	57 (1.8)	1.02	(0.76 to 1.37)		188 (2.9)	50 (3.1)	1.07	(0.78 to 1.48)		32 (0.6)	7 (0.5)	0.87	(0.38 to 1.97)		
Spray-painter (except construction)																	
	No	10596 (96.7)	2730 (98.7)	1.00 (referent)		0.10	5465 (94.1)	1386 (98.0)	1.00 (referent)		0.11	4854 (99.6)	1277 (99.5)	1.00 (referent)		0.59	0.80
	Yes	29 (0.3)	13 (0.5)	1.79	(0.93 to 3.46)		22 (0.4)	10 (0.7)	1.90	(0.90 to 4.04)		7 (0.1)	3 (0.2)	1.47	(0.38 to 5.71)		
Pulp and paper worker																	
	No	7403 (99.5)	1788 (99.3)	1.00 (referent)		0.90	3679 (99.4)	934 (98.9)	1.00 (referent)		0.34	3047 (99.5)	720 (99.6)	1.00 (referent)		0.030	0.95
	Yes	24 (0.3)	6 (0.3)	0.95	(0.39 to 2.33)		14 (0.4)	6 (0.6)	1.63	(0.62 to 4.27)		10 (0.3)	0 (0.0)	*	(0.00 to *)		
Petroleum worker																	
	No	10558 (96.9)	2697 (99.0)	1.00 (referent)		0.59	5758 (94.5)	1491 (98.5)	1.00 (referent)		0.62						
	Yes	18 (0.2)	6 (0.2)	1.30	(0.51 to 3.29)		18 (0.3)	6 (0.4)	1.27	(0.50 to 3.24)							
Printer																	
	No	11786 (95.5)	3014 (97.7)	1.00 (referent)		0.38	6075 (92.9)	1572 (97.0)	1.00 (referent)		0.47	5711 (98.5)	1442 (98.4)	1.00 (referent)		0.70	0.76
	Yes	229 (1.9)	52 (1.7)	0.87	(0.64 to 1.19)		146 (2.2)	32 (2.0)	0.87	(0.59 to 1.28)		83 (1.4)	20 (1.4)	0.91	(0.55 to 1.49)		
University and higher education teachers																	
	No	11729 (95.1)	2999 (97.2)	1.00 (referent)		0.078	6063 (92.7)	1564 (96.5)	1.00 (referent)		0.37	5666 (97.7)	1435 (98.0)	1.00 (referent)		0.13	0.60
	Yes	274 (2.2)	65 (2.1)	0.78	(0.59 to 1.03)		154 (2.4)	38 (2.3)	0.85	(0.59 to 1.23)		120 (2.1)	27 (1.8)	0.73	(0.47 to 1.11)		
Secondary education teachers																	
	No	11126 (94.2)	2891 (96.9)	1.00 (referent)		0.050	5792 (92.6)	1512 (96.9)	1.00 (referent)		0.18	5334 (96.1)	1379 (96.9)	1.00 (referent)		0.12	0.80
	Yes	344 (2.9)	70 (2.3)	0.77	(0.59 to 1.01)		144 (2.3)	29 (1.9)	0.76	(0.50 to 1.15)		200 (3.6)	41 (2.9)	0.77	(0.54 to 1.08)		
Pre-primary education teachers																	
	No	11860 (96.1)	3031 (98.2)	1.00 (referent)		0.64	4470 (93.3)	1128 (98.3)	1.00 (referent)		0.93	5653 (97.5)	1432 (97.7)	1.00 (referent)		0.52	0.75
	Yes																

Exposure		All				Sex-stratified results									p-heterogeneity
						Males				Females					
		Controls		Cases		OR (95% CI)†	P	Controls		Cases		OR (95% CI)†	P		
		No. (%)*	No. (%)*	No. (%)	No. (%)			No. (%)	No. (%)						
	Yes	143 (1.2)	33 (1.1)	0.91	(0.62 to 1.34)	10 (0.2)	3 (0.3)	1.07	(0.29 to 3.94)	133 (2.3)	30 (2.0)	0.88	(0.59 to 1.31)		
Textile worker	No	11244 (91.1)	2848 (92.3)	1.00 (referent)	0.035	5761 (92.1)	1496 (95.9)	1.00 (referent)	0.67	5202 (89.7)	1291 (88.1)	1.00 (referent)	0.038	0.42	
	Yes	771 (6.2)	218 (7.1)	1.20	(1.02 to 1.41)	179 (2.9)	47 (3.0)	1.08	(0.77 to 1.50)	592 (10.2)	171 (11.7)	1.23	(1.01 to 1.49)		
Fiber preparers	No	6729 (99.2)	1628 (98.4)	1.00 (referent)	0.013	3670 (99.2)	891 (98.3)	1.00 (referent)	0.064	2782 (99.0)	670 (98.4)	1.00 (referent)	0.11	0.93	
	Yes	30 (0.4)	17 (1.0)	2.21	(1.21 to 4.03)	15 (0.4)	9 (1.0)	2.28	(0.99 to 5.26)	15 (0.5)	8 (1.2)	2.10	(0.88 to 5.00)		
Sewers and embroiderers	No	11771 (95.4)	2981 (96.6)	1.00 (referent)	0.003	3775 (99.4)	1021 (99.2)	1.00 (referent)	0.93	5563 (95.9)	1381 (94.3)	1.00 (referent)	0.005	0.44	
	Yes	232 (1.9)	83 (2.7)	1.50	(1.15 to 1.94)	9 (0.2)	2 (0.2)	0.93	(0.20 to 4.40)	223 (3.8)	81 (5.5)	1.48	(1.13 to 1.94)		
Undertakers and embalmers	No	7419 (95.4)	1916 (98.9)	1.00 (referent)	0.022	4151 (92.3)	1041 (98.2)	1.00 (referent)	0.073	830 (99.3)	230 (100.0)	1.00 (referent)	0.089	0.95	
	Yes	36 (0.5)	2 (0.1)	0.26	(0.06 to 1.07)	30 (0.7)	2 (0.2)	0.33	(0.08 to 1.38)	6 (0.7)	0 (0.0)	0.00	(0.00 to .		
Welders and famecutters	No	11817 (95.8)	2999 (97.2)	1.00 (referent)	0.053	6059 (92.7)	1553 (95.8)	1.00 (referent)	0.16	5362 (99.2)	1373 (98.6)	1.00 (referent)	0.11	0.37	
	Yes	198 (1.6)	67 (2.2)	1.33	(1.00 to 1.77)	162 (2.5)	51 (3.1)	1.27	(0.92 to 1.75)	36 (0.7)	16 (1.1)	1.65	(0.91 to 3.00)		
Woodworkers	No	11663 (94.5)	2966 (96.1)	1.00 (referent)	0.35	5901 (90.3)	1511 (93.2)	1.00 (referent)	0.28	5114 (99.3)	1340 (99.3)	1.00 (referent)	0.81	0.63	
	Yes	352 (2.9)	100 (3.2)	1.12	(0.89 to 1.41)	320 (4.9)	93 (5.7)	1.14	(0.90 to 1.45)	32 (0.6)	7 (0.5)	0.91	(0.40 to 2.06)		
General carpenter	No	11212 (96.5)	2850 (98.4)	1.00 (referent)	0.63	6143 (94.0)	1578 (97.3)	1.00 (referent)	0.76	289 (97.3)	97 (99.0)	1.00 (referent)	0.073	0.95	
	Yes	74 (0.6)	25 (0.9)	1.12	(0.71 to 1.78)	74 (1.1)	24 (1.5)	1.08	(0.67 to 1.73)	0 (0.0)	1 (1.0)	*	(0.00 to *		

*The counts do not add up to the total # of cases/controls due to data missing by design or report
†Odds Ratio (OR) and 95% Confidence Interval (95% CI), adjusted for age, sex, race/ethncity, and study.

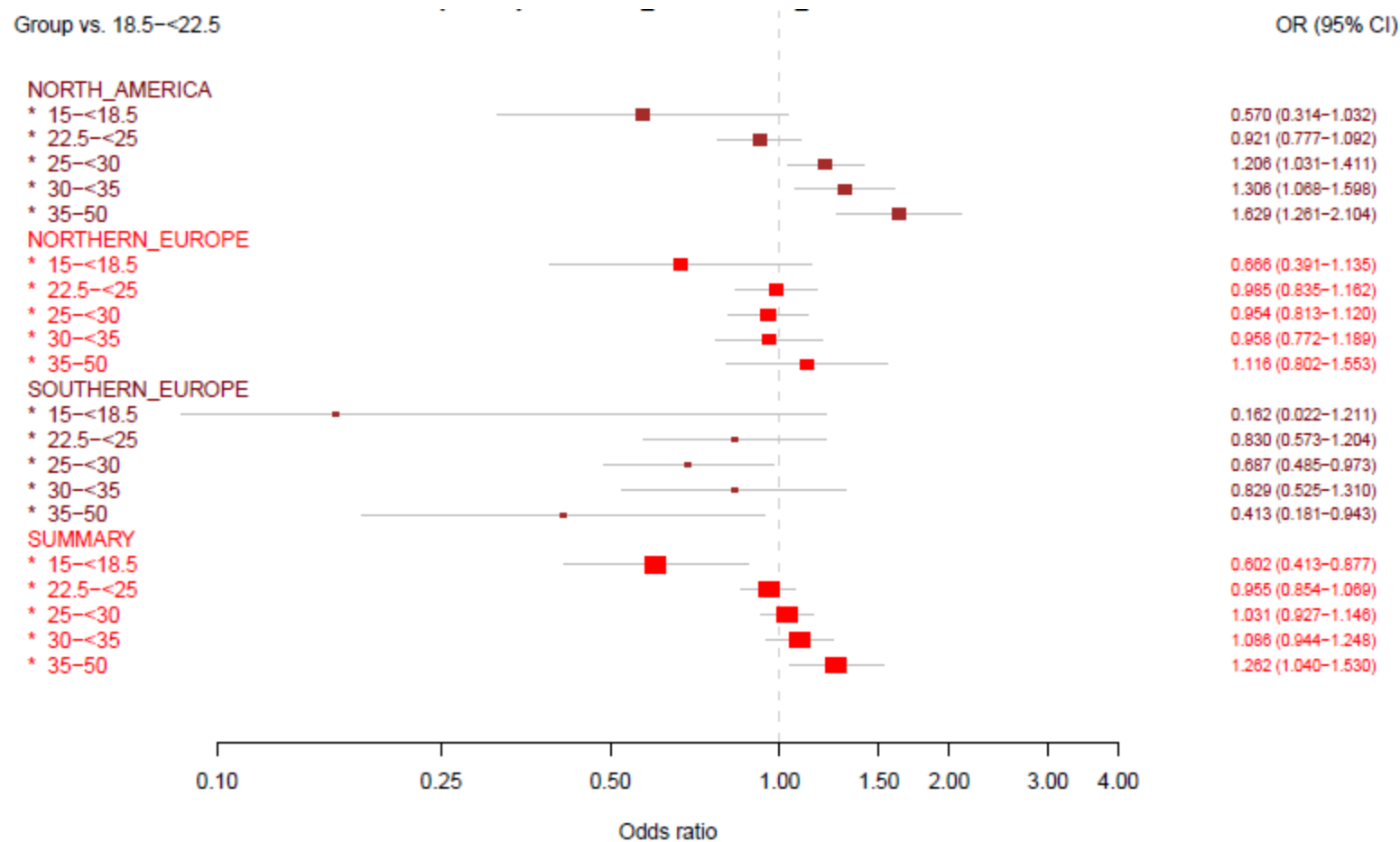
‡Includes self-reported history of specific autoimmune diseases occurring ≥2 years prior to diagnosis/interview (except the New South Wales study, which did not ascertain date of onset). Autoimmune diseases were classified according to whether they are primarily mediated by B-cell or T-cell responses. 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.

§Includes self-reported history of atopic disorders including asthma, eczema, hay fever, or other allergies, excluding drug allergies, occurring ≥2 years prior to diagnosis/interview (except the New South Wales study, which did not ascertain date of onset).

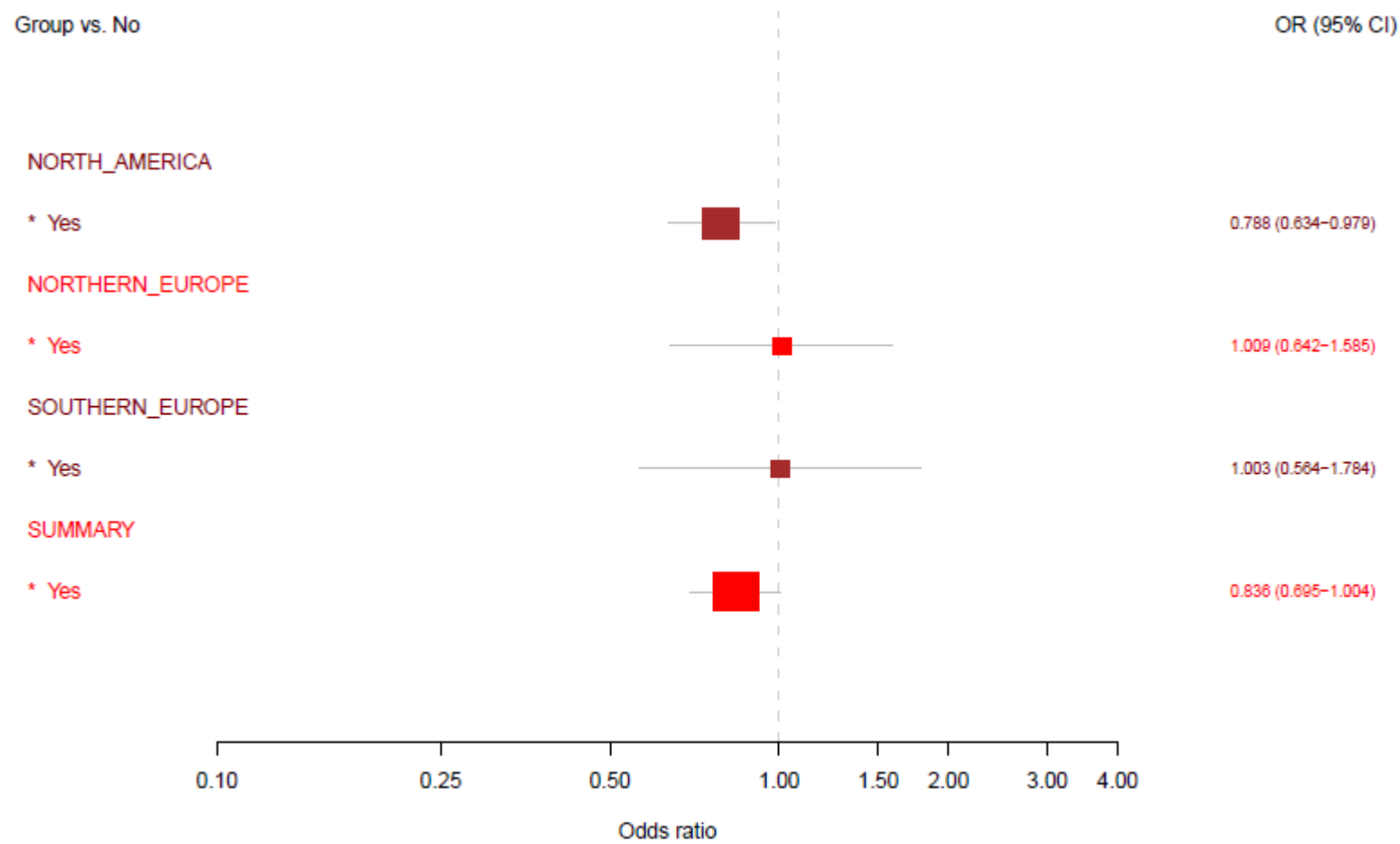
|| Smoked longer than 6 months or more than 100 cigarettes in lifetime.

¶Study specific quartiles among controls

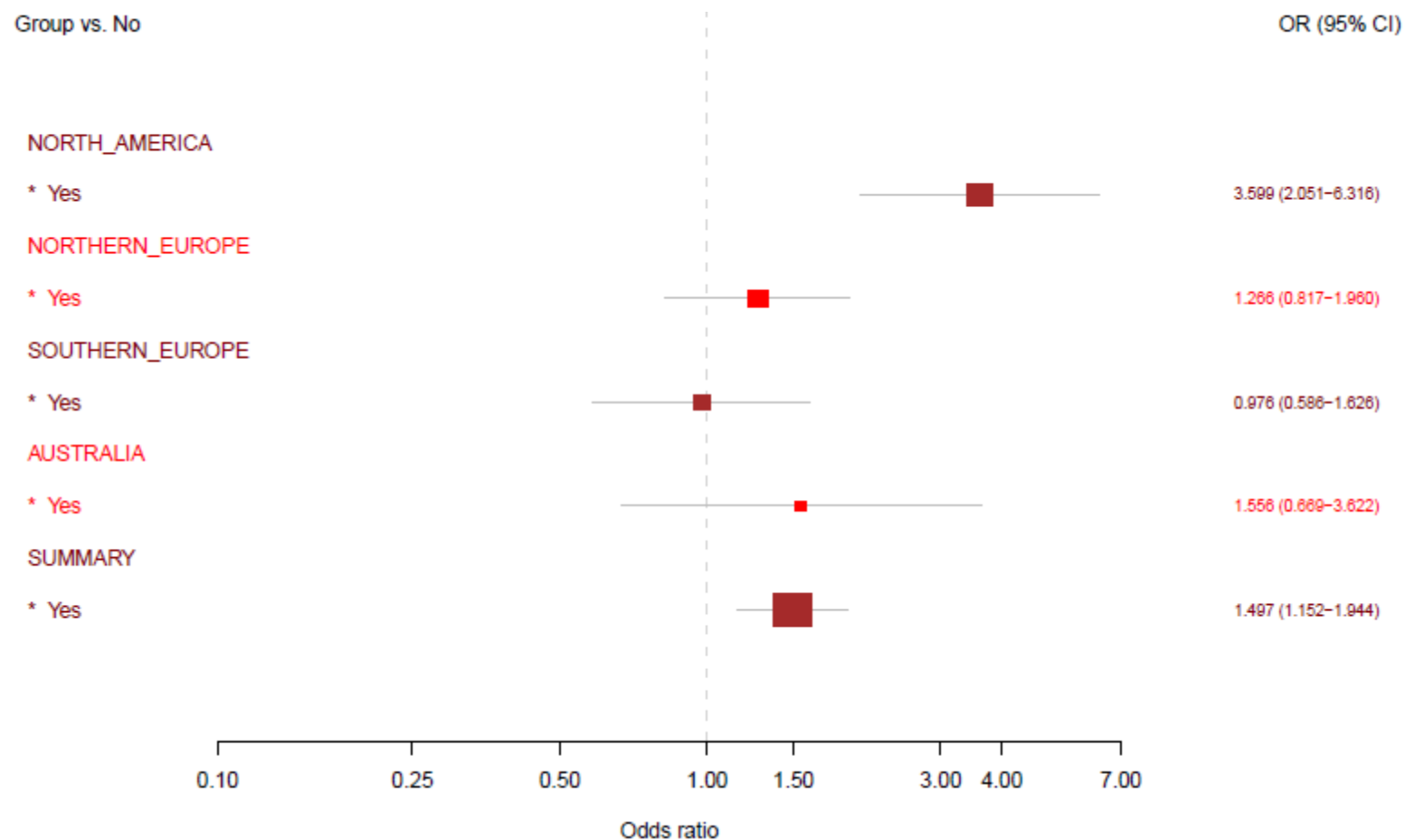
Supplemental Figure 1. DLBCL Risk Estimates for Usual Adult BMI by Region (ORs adjusted for age, sex, race/ethnicity, and center).



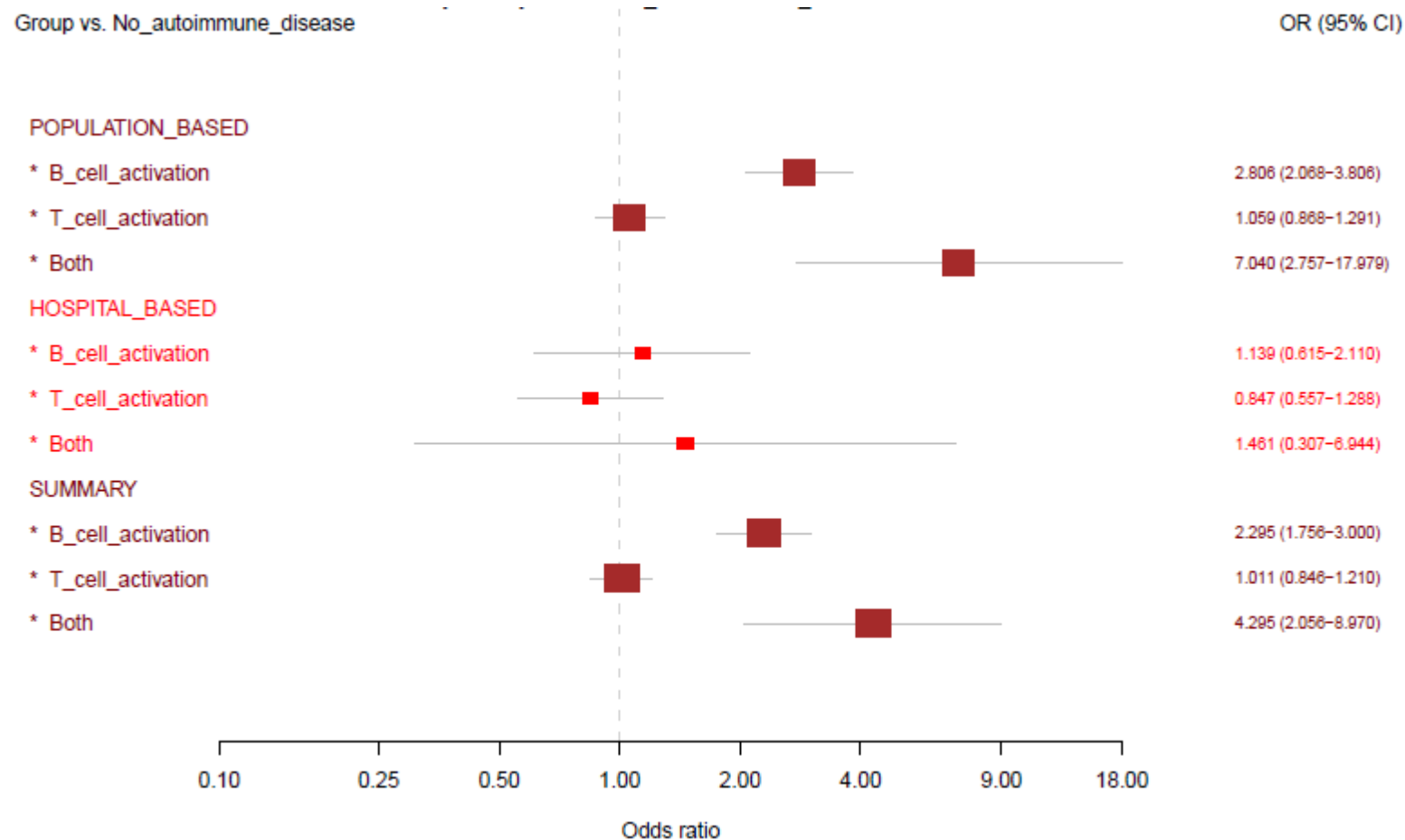
Supplemental Figure 2. DLBCL Risk Estimates for OC Use Before 1970 by Region (ORs adjusted for age, , race/ethnicity, and center).



Supplemental Figure 3. DLBCL Risk Estimates for Seamstresses/Embroiders by Region (ORs adjusted for age, sex, race/ethnicity, and center).



Supplemental Figure 4. DLBCL Risk Estimates for Autoimmune Disease by Study Design (ORs adjusted for age, sex, race/ethnicity, and center).



Supplemental Figure 5. DLBCL Risk Estimates for Recreational Sun Exposure by Region (ORs adjusted for age, sex, race/ethnicity, and center).

