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# Sun exposure and non-Hodgkin lymphoma: A population-based, case–control study

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ABSTRACT

To investigate the association between sun exposure and risk of non-Hodgkin lymphoma (NHL) by histologic subtypes and to explore whether or not vitamin D intake modify sun–NHL association, we analysed data from a population-based, case–control study conducted in Nebraska between 1999 and 2002. Information on sun exposure during the spring, summer, fall and winter was collected from 387 cases and 535 controls by telephone interview. We found no association between seasonal sun exposure and risk of NHL. Vitamin D intake was also not associated with NHL risk, nor does it modify the sun–NHL association. In contrast, total hours of sun exposure was inversely associated with the risk of NHL (odds ratio (OR) = 0.7 comparing >30 h/week to <14 h/week, 95% confidence interval (CI) = 0.5–1.1). Sun exposure was associated with a lower risk of NHL among farmers (OR = 0.8, 0.5–1.3 for 14–30 h/week; OR = 0.6, 0.3–0.9 for >30 h/week; *p*-trend = 0.02), but not among non-farmers. Total hours of sun exposure was also inversely associated with risk of diffuse large B-cell lymphoma and T-cell lymphoma. In conclusion, our data suggest that total hours of sun exposure is associated with a lower risk of NHL, and the inverse association is not modified by vitamin D intake, is stronger among farmer, and may vary by subtypes.



## 1. Introduction

Sun exposure has been postulated as a risk factor for non-Hodgkin lymphoma (NHL) due to the immunosuppressive effects of ultraviolet radiation.[1–4] However, the results of epidemiologic studies linking sun exposure and risk of NHL are inconsistent.[3,4] The ecologic studies have reported positive[5,6] as well as inverse[7,8] associations between sun exposure and risk of NHL. One study[9] found an inverse association between occupational sun exposure and risk of NHL, whereas two studies[10,11] found a positive association and two[12,13] reported no association. Recent epidemiologic studies used individual data to investigate the possible link between sunlight and risk of NHL. Three case–control studies[9,14,15] reported an inverse association between ultraviolet (UV) radiation exposure and risk of NHL, but a recent case–control study in Connecticut

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women showed a significant positive association between UV exposure and NHL risk.[11]

Age patterns and secular trends with respect to NHL incidence vary by histologic subtype,[16,17] suggesting different etiologies for the various NHL subtypes. However, only a handful of studies evaluated sun exposure and NHL association by histological subtype.[11,14,15] In general, no clear differences were found for different subtypes of NHL, although the inverse associations were somewhat stronger for B-cell than for T-cell lymphomas.[14,15] However, one case–control study[11] reported a positive association with B-cell lymphoma, particularly chronic lymphocytic leukaemia/small lymphocytic lymphoma.

Sun-induced synthesis of 1,25-dihydroxy vitamin D has been suggested as a potential mechanism for the association between sunlight exposure and risk of NHL. Hartge and colleagues[15] evaluated the effect modification of the sun–NHL association by the intake of vitamin D. However, they found no evidence for an association between vitamin D intake and risk of NHL, nor did the intake of vitamin D modify the sun–NHL association.

To further evaluate the association between sun exposure and risk of NHL, we analysed data from a population-based, case–control study conducted in Nebraska between 1999 and 2002. We also explored whether the association between sun exposure and NHL differs by NHL subtypes, vitamin D intake, and by farming status, since farmers receive higher annual solar UV exposure compared to indoor workers.[18]

## 2. Materials and methods

### 2.1. Study population

The study population and methods have been reported in detail elsewhere.[19,20] The Institutional Review Board of the University of Nebraska Medical Center approved the study. Briefly, eligible cases of NHL included men and women between the ages of 20 and 75 years who were residing in one of the 66 counties in eastern Nebraska and had newly-diagnosed and histologically-confirmed NHL between January 1999 and December 2002. New patients with NHL were identified weekly through the Nebraska Lymphoma Study Group and area hospitals using a rapid case ascertainment system. Cases were alive at the time of initial contact with no history of human immunodeficiency virus (HIV) infection or cancer. Of the 949 potential cases, 66 (7%) had died before contact and 354 (37%) were ineligible because they lived outside the study region ($n = 59$), were too young or too old ($n = 285$), had a previous diagnosis of cancer ($n = 8$), or did not speak English ($n = 2$). Of the 529 eligible cases, 387 participated in the study (73.2% participation rate). The main reasons for non-participation included subject refusal ($n = 92$), physician refusal ($n = 21$), subject could not be contacted ($n = 18$), or other reasons ($n = 11$).

Controls without a history of HIV infection or cancer were randomly selected from the same geographical area as the cases by 1.5:1 frequency matching by age (five-year age groups) to cases. Eligible controls were randomly selected by a two-stage, random digit dialing, as described by Waksberg.[21] Of the 697 live eligible controls, 535 participated in the study (76.8% participation rate). The main reasons for non-participation were subject refusal ($n = 116$), concern regarding blood collection ($n = 10$), subject could not be contacted ($n = 28$), or illness ($n = 8$).

### 2.2. Data collection

Information on non-dietary exposures was collected by telephone interview, followed by a mailed questionnaire for information on diet. Data collection for cases and controls was conducted concurrently. The telephone interview questionnaire included information on demographics, sunlight exposure, residential and water supply history, occupational history, past medical history, and family history of cancer. Information on sun exposure during the spring, summer, fall and winter was obtained from the following question: 'Before two years ago (the date of interview), how many hours per day were you usually exposed to sunlight in the spring?' The question was repeated for summer, fall and winter. Participants responded by quantifying the hours per day or hours per week of exposure.

After the completion of the telephone interview, subjects were sent a self-administered, semi-quantitative 117-item food frequency questionnaire that was derived from the Block 1995 Revision of the Health Habits and History Questionnaire.[22] The instrument was validated against multiple diet records with correlations for most nutrients in a 0.5–0.6 range.[23] Subjects were instructed to answer the questions based on 'usual eating habits, as an adult, before one year ago and not including any recent dietary changes'. For the current study, we combined vitamin D intake from food sources and multivitamin supplements to obtain the total dietary intake of vitamin D.

### 2.3. Data analysis

Sun exposure in the spring, summer, and fall was divided into tertiles according to the distribution among controls. There was little variation in sun exposure during the winter and, thus, sun exposure was grouped into two categories ($\leqslant$median and >median). Each season was arbitrarily defined as having 91.25 days (365 days per year divided by four seasons). Total hours of sun exposure per year were then calculated by multiplying the hours of sun exposure per day in each season by 91.25 days and then summed across seasons. Total hours of sun exposure was grouped into tertiles based on the distribution among controls. Subjects who had never lived or worked on a farm as an adult were defined as non-farmers.

The histological subtypes of NHL were defined according to the new World Health Organization (WHO) classification.[24] Six subtypes with a large enough sample size were evaluated in the current study: (1) diffuse large B-cell lymphoma (all types); (2) follicular lymphoma (including follicular lymphoma grades 1–3 and diffuse follicle centre lymphoma grades 1/2); (3) small lymphocytic lymphoma (including B-cell chronic lymphocytic leukaemia); (4) marginal zone lymphoma (including splenic marginal zone B-cell lymphoma, extranodal marginal zone B-cell lymphoma, and nodal marginal zone B-cell lymphoma); (5) other miscellaneous B-cell

NHLs (including mantle cell lymphoma, precursor B-lymphoblastic lymphoma, lymphoplasmacytic lymphoma, Burkitt lymphoma, and unclassified B-cell lymphoma); and (6) T-cell lymphoma (all types).

The maximum likelihood estimate of the odds ratio (OR)[25] and 95% confidence interval (CI) were used as the measure of association between sun exposure and risk of NHL. The reported *p*-values are two-sided. Age and sex were included in the final model because controls were frequency matched by these variables to cases in the case–control study. A family history of cancer (yes/no) was included in the model because it is a risk factor for NHL in the current study. Other potential confounders were considered based on prior knowledge of risk factors for NHL, as well as change-in-estimate criteria.[26] Factors such as tobacco use, alcohol use, and marital status were not included in the final models because they did not change the risk estimates by more than 10%. Tests for trend across the tertiles were performed by logistic regression classifying the first to third tertiles as an ordinal variable. We also tested for trend by modelling sun exposure variables as continuous variables. No meaningful differences were noted between the two methods. Therefore, we present the *p*-trend values derived from ordinal variables. Analysis was conducted using SAS software programs version 9.1 (SAS Institute, Care, NC, USA).

## 3. Results

Table 1 shows the characteristics of the NHL cases and population-based controls. Cases and controls were similar with respect to ethnicity and education. However, compared with controls, cases were more likely to be currently married or have a positive family history of heamatopoietic cancer (including Hodgkin lymphoma, NHL, or multiple myeloma) among first-degree relatives.

We found an inverse association between the length of sun exposure in the fall and risk of NHL (Table 2). Sun exposure in the spring, summer, and winter was not associated with NHL risk. There was an inverse association between total hours of sun exposure and risk of NHL. Compared to individuals exposed to sunlight less than 14 h per week, the risk of NHL was 0.9 (0.6–1.2) for those exposed 14–30 h per week and 0.7 (0.5–1.1) for those exposed longer than 30 h per week (*p*-trend = 0.1). Intake of vitamin D was not associated with risk of NHL. We also found no effect modification by the intake of vitamin D for the sun–NHL association (data not shown). The pattern of association between sun exposure and NHL risk was similar for men and women (data not shown).

Table 3 shows the results for sun exposure and risk of NHL according to farming status. Among non-farmers, sun exposure was not associated with risk of NHL. Conversely, sun exposure was inversely associated with risk of NHL among farmers, irrespective of seasons. Compared to farmers who were exposed to the sun less than 14 h per week, the risk of NHL was 0.8 (0.5–1.3) for farmers exposed 14–30 h per week and 0.6 (0.3–0.9) for farmers exposed longer than 30 h per week (*p*-trend = 0.02). Intake of vitamin D was not associated with risk of NHL in either farmers or non-farmers. The inverse association seen in farmers remained unchanged after further adjustment for the use of insecticides and herbicides (data not shown). Because farmers may have different dietary habits than non-farmers, we further adjusted for total caloric intake, body mass index, and vegetable consumption. We found that the point estimates were not materially changed (data not shown).

Sun exposure was weakly and inversely associated with the risk of diffuse large B-cell lymphoma, but not the other

**Table 1 – Characteristics of NHL cases and control subjects in Nebraska, 1999–2002**[a]

| | Cases (*n* = 387) | | Controls (*n* = 535) | |
|---|---|---|---|---|
| | *n* | (%) | *n* | (%) |
| *Sex* | | | | |
| Males | 214 | (55.3) | 281 | (52.5) |
| Females | 173 | (44.7) | 254 | (47.5) |
| *Ethnicity* | | | | |
| White | 369 | (95.6) | 512 | (95.7) |
| Non-white | 17 | (4.4) | 23 | (4.3) |
| *Education* | | | | |
| <High school | 18 | (4.7) | 15 | (2.8) |
| High school | 146 | (38.1) | 226 | (42.2) |
| >High school | 219 | (57.2) | 294 | (55.0) |
| *Marital status* | | | | |
| Never | 23 | (6.0) | 59 | (11.0) |
| Former | 69 | (17.9) | 114 | (21.3) |
| Current | 294 | (76.2) | 362 | (67.7) |
| *Family history of cancer* | | | | |
| None | 173 | (45.1) | 260 | (48.8) |
| Non-heamatopoietic cancer | 168 | (43.8) | 232 | (43.5) |
| Heamatopoietic cancer | 43 | (11.2) | 41 | (7.7) |

a Number of cases and controls may not sum to 387 and 535, respectively, due to missing data.

**Table 2 – Association of sun exposure and risk of non-Hodgkin lymphoma (NHL), Nebraska, 1999–2002**

| Sun exposure | Controls[a], *n* (%) | | Cases[a], *n* (%) | | OR[b] | 95%CI[b] |
|---|---|---|---|---|---|---|
| *Spring (h/day)* | | | | | | |
| <2 | 110 | (20.6) | 76 | (19.7) | 1.0 | (referent) |
| 2–4 | 242 | (45.2) | 181 | (47.0) | 1.0 | (0.7–1.5) |
| >4 | 183 | (34.2) | 128 | (41.2) | 0.9 | (0.6–1.4) |
| | | | | | | *p*-trend = 0.6 |
| *Summer (h/day)* | | | | | | |
| <3 | 157 | (29.4) | 114 | (29.6) | 1.0 | (referent) |
| 3–5 | 170 | (31.8) | 129 | (33.5) | 1.0 | (0.7–1.4) |
| >5 | 208 | (38.9) | 142 | (36.9) | 0.9 | (0.6–1.2) |
| | | | | | | *p*-trend = 0.4 |
| *Fall (h/day)* | | | | | | |
| <2 | 112 | (20.9) | 85 | (22.1) | 1.0 | (referent) |
| 2–4 | 238 | (44.5) | 186 | (48.3) | 1.0 | (0.7–1.4) |
| >4 | 185 | (34.6) | 114 | (29.6) | 0.7 | (0.5–1.0) |
| | | | | | | *p*-trend = 0.07 |
| *Winter (h/day)* | | | | | | |
| ⩽1 | 263 | (49.2) | 189 | (49.1) | 1.0 | (referent) |
| >1 | 272 | (50.8) | 196 | (50.9) | 0.9 | (0.7–1.2) |
| *Total (h/week)* | | | | | | |
| <14 | 179 | (33.5) | 139 | (36.1) | 1.0 | (referent) |
| 14–30 | 176 | (32.9) | 125 | (32.5) | 0.9 | (0.6–1.2) |
| >30 | 180 | (33.6) | 121 | (31.4) | 0.7 | (0.5–1.1) |
| | | | | | | *p*-trend = 0.1 |
| *Vitamin D (IU/day)* | | | | | | |
| <114.3 | 156 | (33.2) | 108 | (30.9) | 1.0 | (referent) |
| 114.3–213.6 | 157 | (33.4) | 140 | (40.0) | 1.3 | (0.9–1.8) |
| >213.6 | 157 | (33.4) | 102 | (29.1) | 0.9 | (0.7–1.3) |
| | | | | | | *p*-trend = 0.7 |

a Numbers may not sum to overall total due to missing data.
b Odds ratios (ORs) and 95% confidence intervals (CIs) were estimated relative to controls adjusted for age (20–44, 45–54, 55–64, ⩾65 years), sex, and a family history of cancer.

B-cell subtypes evaluated (Table 4). There was also an inverse association between sun exposure and risk of T-cell NHL, particularly sun exposure in the fall and total hours of sun exposure. The risks of T-cell NHL among subjects exposed to sun 14–30 h per week and greater than 30 h per week were 0.5 (0.2–1.5) and 0.3 (0.1–1.3), respectively, compared with those who were exposed less than 14 h per week. However, these numbers are too small for confident analysis.

## 4. Discussion

In this population-based, case–control study with data on the length of sun exposure during different seasons, seasonal sun exposure was not clearly associated with risk of NHL, whereas total hours of sun exposure was weakly associated with a lower risk of NHL. We also found a significant inverse association between sun exposure and risk of NHL among farmers, regardless of season. There was also a suggestive inverse association of sun exposure with diffuse large B-cell lymphoma and T-cell lymphoma. Finally, we found no association between vitamin D intake and risk of NHL.

Four epidemiologic studies of sun exposure and NHL risk collected sun exposure data for individuals by questionnaire.[9,11,14,15] A population-based, case–control study in Australia found a significant inverse association between total sun exposure and risk of NHL.[9] Compared with individuals in the lowest quartile of total sun exposure, the risks of NHL for successively higher quartiles were 0.72 (95% CI 0.53–0.98), 0.66 (0.48–0.91) and 0.65 (0.46–0.91), (*p*-trend = 0.01). A large population-based, case–control study in Denmark and Sweden[14] found that a history of high UV exposure was associated with reduced risk of NHL. In that study, frequent sun bathing and sunburns at age 20 years and 5–10 years before the interview, and sun vacations abroad, were associated with a 30–40% lower risk of NHL. Hartge and colleagues[15] also reported a weak protective effect of sunlight in a population-based, case–control study in the United States. In that study, ORs were in the range of 0.73–0.78 for participants reporting more than 28 hours per week in the mid-day summer sun. In contrast, a population-based, case–control study of Connecticut women[11] reported a threefold increased risk of NHL among women who reported having had a suntan for less than 3 months per year or a suntan history of more than 60 years (OR = 2.8; 95% CI 1.6–4.9) compared with those who reported never having had a suntan. In addition, there was a 70% higher risk of NHL among women who reported having spent time in strong sunlight between 9 a.m. and 3 p.m. during the summer (OR = 1.7 comparing the highest tertile of duration with the lowest; 95% CI 1.2–2.4). In the current study, we found no association between sun exposure in a particular

**Table 3 – Association of sun exposure and risk of non-Hodgkin lymphoma (NHL), Nebraska, 1999–2002**

| Sun exposure | Non-farmers | | | | Farmers | | | |
|---|---|---|---|---|---|---|---|---|
| | Controls | Cases | OR[a] | 95%CI | Controls | Cases | OR[a] | 95%CI |
| *Spring (h/day)* | | | | | | | | |
| <2 | 73 | 42 | 1.0 | (referent) | 37 | 34 | 1.0 | (referent) |
| 2–4 | 113 | 90 | 1.2 | (0.7–1.9) | 110 | 91 | 0.8 | (0.5–1.5) |
| >4 | 67 | 50 | 1.3 | (0.7–2.3) | 116 | 78 | 0.6 | (0.3–1.1) |
| | | | | *p*-trend = 0.4 | | | | *p*-trend = 0.06 |
| *Summer (h/day)* | | | | | | | | |
| <3 | 98 | 60 | 1.0 | (referent) | 59 | 54 | 1.0 | (referent) |
| 3–5 | 90 | 61 | 1.1 | (0.7–1.8) | 80 | 68 | 0.9 | (0.5–1.5) |
| >5 | 84 | 61 | 1.2 | (0.7–2.0) | 124 | 81 | 0.6 | (0.4–1.0) |
| | | | | *p*-trend = 0.5 | | | | *p*-trend = 0.04 |
| *Fall (h/day)* | | | | | | | | |
| <2 | 71 | 47 | 1.0 | (referent) | 41 | 38 | 1.0 | (referent) |
| 2–4 | 131 | 91 | 1.1 | (0.7–1.7) | 107 | 95 | 0.9 | (0.5–1.5) |
| >4 | 70 | 44 | 0.9 | (0.5–1.6) | 115 | 70 | 0.5 | (0.3–0.9) |
| | | | | *p*-trend = 0.8 | | | | *p*-trend = 0.01 |
| *Winter (h/day)* | | | | | | | | |
| ⩽1 | 152 | 94 | 1.0 | (referent) | 111 | 95 | 1.0 | (referent) |
| >1 | 120 | 88 | 1.2 | (0.8–1.8) | 152 | 108 | 0.7 | (0.5–1.1) |
| *Total (h/week)* | | | | | | | | |
| <14 | 108 | 73 | 1.0 | (referent) | 71 | 66 | 1.0 | (referent) |
| 14–30 | 99 | 62 | 0.9 | (0.6–1.4) | 77 | 63 | 0.8 | (0.5–1.3) |
| >30 | 65 | 47 | 1.1 | (0.6–1.8) | 115 | 74 | 0.6 | (0.3–0.9) |
| | | | | *p*-trend = 0.9 | | | | *p*-trend = 0.02 |
| *Vitamin D (IU/day)* | | | | | | | | |
| <114.3 | 69 | 54 | 1.0 | (referent) | 87 | 54 | 1.0 | (referent) |
| 114.3–213.6 | 84 | 62 | 0.9 | (0.9–1.8) | 73 | 78 | 1.7 | (1.1–2.7) |
| >213.6 | 73 | 46 | 0.8 | (0.7–1.3) | 84 | 56 | 1.1 | (0.6–1.7) |
| | | | | *p*-trend = 0.7 | | | | *p*-trend = 0.8 |

a Odds ratios (ORs) and 95% confidence intervals (CIs) were estimated relative to controls adjusted for age (20–44, 45–54, 55–64, ⩾65), sex, and a family history of cancer (yes/no).

season, but total annual sun exposure was inversely associated with risk of NHL. These findings suggest that total hours of sun exposure may be more important than high sun exposure in any given season. It is also possible that our instrument is rather crude in estimating seasonal sun exposure.

In our study, the significant inverse association between sun exposure and risk of NHL was limited to farmers, but no such association was found among non-farmers. A hospital-based, case–control study also found a weak inverse association between UV exposure in farmers and risk of NHL.[27] In that study, farmers exposed to UV had an OR of 0.79 (95% CI = 0.47–1.32) compared with other non-manual workers not exposed to UV. Farmers are a homogenous group that differs from the general population in several ways. Our findings are unlikely to be explained by a healthier lifestyle of farmers because the inverse association remained unchanged after further adjustment for total caloric intake, body mass index, and vegetable consumption. The inverse association among farmers was also not materially changed after additional adjustment for the use of pesticides. In the current study, farmers have higher sun exposure levels than the rest of the study participants, with more than one-third of farmers in the highest sun exposure category compared to less than one-quarter of non-farmers. These findings suggest that the amount of sun exposure in the general population may not be high enough to have a protective effect. It is also possible that farmers recall sun exposure better than non-farmers, thus, less misclassification for exposure assessment.

We found an inverse association between sun exposure and the risk of T-cell NHL and, to a lesser extent, diffuse large B-cell lymphoma. In a large population-based, case–control study in Denmark and Sweden, Smedby and colleagues[14] found that the inverse association between sun exposure and risk of NHL appeared to be stronger for B-cell NHL (including chronic lymphocytic leukaemia, diffuse large B-cell, and follicular NHL) than for T-cell NHL. In a case–control study conducted in four Surveillance, Epidemiology, and End Results (SEER) registries in the United States, Hartge and colleagues[15] reported an inverse association between UV radiation exposure and risk of diffuse large B-cell lymphoma and follicular lymphoma. In contrast, a population-based, case–control study in Connecticut[11] found a positive association between the longer duration of having a suntan and the duration of time spent in strong sunlight during summer and the risk of B-cell lymphoma, particularly for chronic lymphocytic leukaemia/small lymphocytic lymphoma. In that study,[11] women who reported having vacationed in the

**Table 4 – Association of sun exposure and risk of non-Hodgkin lymphoma (NHL) by histological subtypes, Nebraska, 1999–2002**

| Sun exposure | Ctls | CLL/SLL[a] | | MZL | | FL | | DLBCL | | All B-cell NHLs | | All T-cell NHLs | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | Cases | OR[b] (95% CI) | Cases | OR (95% CI) | Cases | OR (95% CI) | Cases | OR (95% CI) | Cases | OR (95% CI) | Cases | OR (95% CI) |
| *Spring (h/day)* | | | | | | | | | | | | | |
| <2 | 110 | 3 | 1.0 (referent) | 3 | 1.0 (referent) | 34 | 1.0 (referent) | 25 | 1.0 (referent) | 72 | 1.0 (referent) | 4 | 1.0 (referent) |
| 2–4 | 242 | 13 | 2.1 (0.5–9.7) | 22 | 3.2 (0.9–10.9) | 47 | 0.6 (0.4–1.0) | 43 | 0.7 (0.4–1.2) | 170 | 1.0 (0.7–1.5) | 11 | 1.4 (0.4–4.5) |
| >4 | 183 | 12 | 2.2 (0.4–10.8) | 10 | 1.9 (0.5–7.4) | 42 | 0.7 (0.4–1.2) | 35 | 0.7 (0.4–1.2) | 125 | 0.9 (0.6–1.4) | 3 | 0.5 (0.1–2.7) |
| | | | *p*-trend = 0.4 | | *p*-trend = 0.6 | | *p*-trend = 0.3 | | *p*-trend = 0.2 | | *p*-trend = 0.7 | | *p*-trend = 0.5 |
| *Summer (h/day)* | | | | | | | | | | | | | |
| <3 | 157 | 8 | 1.0 (referent) | 7 | 1.0 (referent) | 35 | 1.0 (referent) | 36 | 1.0 (referent) | 106 | 1.0 (referent) | 8 | 1.0 (referent) |
| 3–5 | 170 | 10 | 1.1 (0.4–3.1) | 15 | 2.1 (0.8–5.2) | 41 | 1.1 (0.7–1.8) | 32 | 0.8 (0.5–1.3) | 123 | 1.1 (0.8–1.5) | 6 | 0.7 (0.2–2.2) |
| >5 | 208 | 10 | 0.8 (0.3–2.3) | 13 | 1.5 (0.5–4.1) | 47 | 1.0 (0.6–1.7) | 35 | 0.6 (0.3–1.0) | 138 | 0.9 (0.6–1.3) | 4 | 0.4 (0.1–1.5) |
| | | | *p*-trend = 0.6 | | *p*-trend = 0.5 | | *p*-trend = 0.07 | | *p*-trend = 0.9 | | *p*-trend = 0.6 | | *p*-trend = 0.2 |
| *Fall (h/day)* | | | | | | | | | | | | | |
| <2 | 112 | 7 | 1.0 (referent) | 7 | 1.0 (referent) | 28 | 1.0 (referent) | 24 | 1.0 (referent) | 77 | 1.0 (referent) | 8 | 1.0 (referent) |
| 2–4 | 238 | 9 | 0.5 (0.2–1.6) | 19 | 1.3 (0.5–3.1) | 59 | 1.0 (0.6–1.6) | 48 | 0.8 (0.5–1.5) | 179 | 1.1 (0.7–1.5) | 7 | 0.4 (0.1–1.2) |
| >4 | 185 | 12 | 0.7 (0.2–2.2) | 9 | 0.7 (0.2–2.2) | 36 | 0.7 (0.4–1.3) | 31 | 0.6 (0.3–1.1) | 111 | 0.8 (0.5–1.1) | 3 | 0.2 (0.1–1.0) |
| | | | *p*-trend = 0.7 | | *p*-trend = 0.5 | | *p*-trend = 0.3 | | *p*-trend = 0.1 | | *p*-trend = 0.1 | | *p*-trend = 0.04 |
| *Winter (h/day)* | | | | | | | | | | | | | |
| ⩽1 | 263 | 12 | 1.0 (referent) | 20 | 1.0 (referent) | 61 | 1.0 (referent) | 48 | 1.0 (referent) | 175 | 1.0 (referent) | 14 | 1.0 (referent) |
| >1 | 272 | 16 | 1.0 (0.4–2.2) | 15 | 0.7 (0.3–1.4) | 62 | 1.0 (0.6–1.5) | 55 | 1.0 (0.6–1.5) | 192 | 1.0 (0.7–1.3) | 4 | 0.3 (0.1–0.9) |
| *Total (h/week)* | | | | | | | | | | | | | |
| <14 | 179 | 9 | 1.0 (referent) | 9 | 1.0 (referent) | 44 | 1.0 (referent) | 41 | 1.0 (referent) | 129 | 1.0 (referent) | 10 | 1.0 (referent) |
| 14–30 | 176 | 9 | 1.0 (0.4–2.6) | 17 | 2.0 (0.8–4.6) | 39 | 0.9 (0.6–1.5) | 29 | 0.7 (0.4–1.1) | 120 | 0.9 (0.7–1.3) | 5 | 0.5 (0.2–1.5) |
| >30 | 180 | 10 | 0.9 (0.3–2.4) | 9 | 1.0 (0.3–2.8) | 40 | 0.9 (0.5–1.5) | 33 | 0.6 (0.4–1.1) | 118 | 0.8 (0.6–1.2) | 3 | 0.3 (0.1–1.3) |
| | | | *p*-trend = 0.8 | | *p*-trend = 0.9 | | *p*-trend = 0.6 | | *p*-trend = 0.1 | | *p*-trend = 0.3 | | *p*-trend = 0.08 |
| *Vitamin D (IU/day)* | | | | | | | | | | | | | |
| <114.3 | 156 | 10 | 1.0 (referent) | 10 | 1.0 (referent) | 34 | 1.0 (referent) | 26 | 1.0 (referent) | 103 | 1.0 (referent) | 5 | 1.0 (referent) |
| 114.3–213.6 | 157 | 9 | 1.0 (0.4–2.6) | 14 | 1.4 (0.6–3.3) | 44 | 1.3 (0.8–2.2) | 42 | 1.6 (0.9–2.8) | 133 | 1.3 (0.9–1.8) | 7 | 1.4 (0.4–4.6) |
| >213.6 | 157 | 9 | 0.8 (0.3–2.2) | 8 | 0.8 (0.3–2.1) | 33 | 1.0 (0.6–1.6) | 23 | 0.8 (0.5–1.5) | 95 | 0.9 (0.6–1.3) | 7 | 1.5 (0.5–5.0) |
| | | | *p*-trend = 0.7 | | *p*-trend = 0.7 | | *p*-trend = 0.9 | | *p*-trend = 0.6 | | *p*-trend = 0.6 | | *p*-trend = 0.5 |

a Ctls: controls; CLL/SLL: B-cell chronic lymphocytic leukaemia/small lymphocytic lymphoma; MZL: marginal zone lymphoma; FL: follicular lymphoma; DLBCL: diffuse large B-cell lymphoma.
b Odds ratios (ORs) and 95% confidence intervals (CIs) were estimated relative to controls adjusted for age, sex, and a family history of cancer (yes/no).

tropics also had a 60% higher risk of diffuse large B-cell lymphoma (OR = 1.6; 95% CI 1.1–2.3). UV radiation has been shown to induce local and systemic immune suppression.[28] Possible mechanisms include mitogen-stimulated protein kinase activation of platelet activating factor synthesis with the production of down stream mediators (e.g., IL4 and IL10) that induce immune suppression, increased effect on Th2 anti-inflammatory response, and the toxic and immunosuppressive effects of reactive oxygen species that are created following UV exposure.[29] However, it remains to be determined as to how UV-induced systemic immune modulation could confer a lower risk of NHL or how the risk would differ by histological subtype.[30]

In the present study, there was no association between the intake of vitamin D and risk of NHL. In addition, the associations between sun exposure and risk of NHL were not modified by vitamin D intake. These findings are consistent with those reported in a multi-SEER registry case–control study by Hartge and colleagues.[15] Vitamin D has been shown to promote cell differentiation and inhibit proliferation,[31] and may reduce the risk of prostate, colon and other cancers.[32] Many non-renal cells contain 1-α-hydroxylase resulting in local production of $1,25(OH)_2D$ in tissues such as lymph nodes.[33] Findings from the current study and that of Hartge and colleagues[15] suggest that sun exposure may be associated with a lowered risk of NHL through mechanisms other than vitamin D.

One limitation of our study is that the sample size is too small to study uncommon histologic subtypes of NHL in depth. Thus, our findings should be interpreted cautiously. Another limitation is that our questions on sun exposure were not comprehensive. For example, we used self-reported sun exposure data and we did not have information on the skin type, the amount of exposed skin, the type of recreational activities, or sun protective clothing. We also did not have information on sun exposure during different periods in life. Finally, farmers were defined as those who had ever lived or worked on a farm as an adult. It is possible that some of them may no longer farm during the time period at which sun exposure was ascertained. However, such a misclassification is likely to be random.

A strength of the study is quantifying seasonal sun exposure for individuals as an estimate of sun exposure rather than relying on geographic latitude of residence or occupational title to estimate sun exposure. Other strengths of the study include the use of the new WHO classification, high response rates (73.2% for cases and 76.8% for controls), inclusion of only newly-diagnosed, histologically-confirmed cases of NHL that occurred in a defined time period in a single geographic area, and randomly-selected control subjects representative of the population at large in the targeted geographic area.

In conclusion, we found an inverse association between total sun exposure and risk of NHL, in particular for T-cell lymphoma and, to a lesser extent, diffuse large B-cell lymphoma. We also found a significant inverse association between sun exposure and risk of NHL among farmers. Future studies with detailed information on sun exposure during different periods in life to better understand the potential protective effects of UV for NHL are warranted.

## Conflict of interest statement

None declared.

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