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Sun sensitivity, indoor tanning and B-cell non-Hodgkin lymphoma (NHL) risk among Caucasian women in Los Angeles County

Sophia S. Wang^{1,+}, Jianning Luo¹, Wendy Cozen², Yani Lu¹, Jane Halley-Sullivan¹, Jenna Voutsinas¹, Charlie Zhong¹, Joo Song³, Dennis Weisenburger³, and Leslie Bernstein¹

¹Division of Cancer Etiology, Department of Population Sciences, City of Hope and the Beckman Research Institute, Duarte, California

²Division of Preventive Medicine, University of Southern California, Los Angeles, California

³Division of Pathology, City of Hope Medical Center, Duarte, California

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Exposure to ultraviolet (UV) radiation continues to be a public health concern, particularly with the rising prevalence in exposure to artificially administered UV via indoor tanning salons (Wehner *et al* 2014). In contrast to outdoor sun exposure, which proportionally emits more UVB radiation, indoor tanning appliances (defined as tanning booths, solariums, sun lamps) proportionally emit more UVA radiation (International Agency for Research on Cancer [IARC] 2007). Both are classified as Group 1 carcinogens by the IARC and both are definitively associated with increased risk of skin cancers (Colantonio *et al* 2014, Veierod *et al* 2014).

Given that the geographical and racial Non-Hodgkin lymphoma (NHL) incidence patterns parallel those of melanoma, it was hypothesized that the risk association between UV and NHL would similarly parallel that observed for melanoma. However, international pooling efforts among NHL case-control studies have linked outdoor/recreational sun exposure with a reduced NHL risk (Krickler *et al* 2008). Results from prospective cohort studies, however, remain equivocal (Chang *et al* 2011, Bertrand *et al* 2011). Efforts to evaluate artificial sources of UV radiation with NHL risk have been similarly equivocal, with reduced NHL risk from tanning booth usage reported in one U.S. case-control study (Hartge *et al* 2006) and no associations identified in two prospective cohort studies (Zhang *et al* 2013, Veierod *et al* 2010).

Here, we investigate the relationship between use of tanning booths, UV treatment and risk of B-cell NHL among women in the Los Angeles County NHL Case-Control Study (see

*To whom correspondence should be addressed: Sophia S. Wang, Ph.D., Division of Cancer Etiology, Department of Population Sciences, Beckman Research Institute and the City of Hope, 1500 East Duarte Road, Duarte, CA 91010, Phone: (626) 471-7316, FAX: (626) 471-7308, sowang@coh.org.

Appendix S1). Briefly, the study comprised women of Los Angeles County between the ages of 20–79 years old with no prior diagnosis of any haematological malignancy who were diagnosed with primary B-cell NHL between 1 May 2004 and 31 March 2008. In all, the study included 1006 female B-cell NHL cases and 1038 controls. As part of the study questionnaire, participants were queried if they had ever used a tanning booth (including sun lamps) at least 15 times in their life prior to the date of diagnosis). Those who answered affirmatively were further queried regarding the age, average number of times, and total duration of use. Participants were also asked to provide their eye colour and natural hair colour, history of sunburns that required medical attention for blistering and if they had ever undergone UV skin treatment. Other characteristics evaluated as potential confounders included family history of haematological malignancies or skin cancer, smoking status, alcohol consumption, and body mass index.

As shown in Table SI, tanning booth use and sun sensitivity was highest among non-Hispanic Caucasians (with very low or no use reported among Black, Asian and Hispanic women [Table SII]); therefore, we conducted statistical analyses among the 628 cases and 662 controls reported as non-Hispanic Caucasians. We used conditional logistic regression to calculate odds ratios (ORs) and corresponding 95% confidence intervals (CI) for evaluating NHL risk and unconditional logistic regression for evaluating major NHL subtypes and NHL/NHL subtype risk. Final multivariate models included socioeconomic status, age and family history of haematological malignancy.

Among non-Hispanic Caucasian women, those reported ever having a sunburn requiring medical attention for blistering had a 38% lower risk for B-cell NHL (OR=0.62; 95% CI=0.49–0.80) with a strong trend of decreasing risk with increasing number of total reported sunburns (p-trend = 0.001) (Table I). We did not observe any association between tanning booth use or UV treatment and B-cell NHL risk (Table I) or by subtype (Table SIII). However, when stratified by site, we observed a 7.8-fold increased risk for cutaneous B-cell NHL (95% CI=1.71–35.8) among those reporting ever using a tanning booth (Table II). We further observed a $p_{\text{homogeneity}} = 0.013$, when comparing the observed risk by site (cutaneous vs. systemic). While the decreased NHL risk among those reporting a history of sunburns remained present for both cutaneous (OR=0.67) and systemic B-cell NHL (OR=0.66), among those who reported having used a tanning booth and also having a sunburn, the increased risk for cutaneous B-cell lymphoma remained (OR: 15.7, 95% CI=2.56–96.9; p-interaction=0.019). The four women with cutaneous B-cell NHL who reported using a tanning booth began use at ages 18–49 years (3 had begun use by age 35 years) and their NHLs occurred from 8 to 33 years later. Two cutaneous B-cell NHL cases reported more than 150 visits to use a tanning booth extending for more than a 5 year time period.

Although cutaneous NHL is a relatively rare entity among B-cell NHL, data from the Los Angeles County NHL Case-Control Study suggest that an association between use of indoor tanning booths and cutaneous B-cell NHL may exist. Our population of non-Hispanic Caucasian female participants is the primary population of interest for evaluating the long-term effects of tanning, but our age group of women (median age of controls: 63 years) clearly precedes the dramatic rise in tanning booth use that ranges from 19% among

adolescents to 55% in university students (Wehner *et al* 2014). Our study results could thus be an early indicator of a potential rise in incidence of cutaneous lymphomas due to indoor tanning usage.

Curiously, both outdoor sun exposure and indoor tanning increase the risk for skin cancers, such as melanoma, but associations with NHL remain equivocal and even protective for recreational sun exposure (IARC, 2007; Colantonio *et al* 2014; Veirod *et al* 2014; Zhang *et al* 2013). Our results, that skin sensitivity measures are associated with decreased NHL risk, appear to be consistent with these studies, but our evaluation of tanning booths does not support an extended protective association with UV exposure. Biologically, distinct effects of outdoor sun exposure and indoor tanning on NHL risk may be plausible, as UVA and UVB radiation do alter the immune response in different ways. Specifically, UVB induces immunosuppression at both the local and systemic levels, while UVA induces DNA damage and *TP53* mutations. Follow-up investigations of immune responses induced by UVA and UVB and their relationship to NHL may thus be warranted, particularly as recent efforts to link the protective association between sun exposure and NHL to vitamin D pathways have largely resulted in null associations.

Although epidemiological and laboratory research has definitively linked indoor tanning to skin cancer aetiology, investigations into other cancers remain sparse. Our results suggest that further investigations of indoor tanning on other cutaneous malignancies, such as NHL, should be pursued.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Table I

Risk estimates (odds ratios and 95% confidence intervals) for measures of sun sensitivity and UV radiation (tanning booth, UV treatment) and B-cell NHL among non-Hispanic Caucasian women in the Los Angeles County NHL case control study (2004–2008).

Characteristic	Cases n=625	Controls n=625	OR (95% CI)*
Sunburn			
Never	372	313	1
Ever	239	299	0.62 (0.49–0.80)
Sunburned, but not hospitalized/medicated	197	260	0.59 (0.45–0.77)
Sunburned, requiring hospitalization/medication for blistering	40	33	0.94 (0.57–1.56)
Unknown	16	19	0.65 (0.33–1.31)
Total number of sunburns			
Never	372	313	1
1–2	118	144	0.63 (0.46–0.86)
3–5	60	75	0.66 (0.45–0.98)
6+	58	78	0.56 (0.37–0.84)
Unknown	17	15	0.83 (0.40–1.72)
p-trend**			0.001
Indoor tanning (ever used)			
Never	566	573	
Tanning or Sun lamp	57	51	1.27 (0.82–1.97)
Tanning booth	52	48	1.25 (0.79–1.96)
Sun lamp only	5	3	1.64 (0.38–7.14)
Tanning booth (years of use)			
Never	566	573	
< 1	13	15	1.10 (0.51–2.38)
1–<2	10	6	1.66 (0.60–4.62)
2–<5	14	14	1.18 (0.54–2.58)
5+	15	12	1.39 (0.61–3.18)
p-trend**			0.59
Tanning booth (number of times used, quartile)			
Never	566	573	
< 25	12	10	1.45 (0.61–3.44)
25–<50	13	14	1.18 (0.54–2.57)
50–<150	13	13	1.04 (0.46–2.35)
150+	14	11	1.47 (0.65–3.35)
p-trend**			0.64
Tanning booth (age at start, tertile; years)			
Never	566	573	
< 22	17	15	1.34 (0.56–3.17)
22–<32	16	12	1.71 (0.76–3.85)

Characteristic	Cases n=625	Controls n=625	OR (95% CI)*
32+	19	21	1.02 (0.54–1.92)
p-trend**			0.73
UV treatment			
Never	578	574	
Ever	39	38	0.99 (0.62–1.57)
UV treatment (weeks of use)			
Never	578	574	
<13 (Median)	14	18	0.76 (0.37–1.55)
13–<52	11	14	0.70 (0.31–1.57)
52+	9	6	1.45 (0.51–4.12)
p-trend**			0.81
UV treatment (age at start, years)			
Never	578	574	
17 (Median)	20	23	0.80 (0.42–1.49)
18+	19	15	1.28 (0.64–2.56)

* further adjusted for SES and family history of haematological malignancy.

** Trend test excludes unknown group

UV, ultra violet; OR, odds ration; 95% CI, 95% confidence interval

Risk estimates for tanning and sun sensitivity, stratified by cutaneous and systemic B-cell NHL among non-Hispanic women in the Los Angeles County NHL case control study (2004–2008).

Table II

Characteristic	Controls (n=625)	Cutaneous NHL (n=13)	Systemic NHL (n=612)	Cutaneous NHL OR (95% CI)**	Systemic NHL OR (95% CI)**
Indoor tanning					
Never	573	9	557	1	1
Tanning booth or Sun lamp	51	4	53	7.76 (1.70–35.47)	1.13 (0.74–1.73)
Tanning booth	48	3	49	5.91 (1.15–30.32)	1.11 (0.72–1.73)
Sun lamp only	3	1	4	28.27 (2.34–340.75)	1.35 (0.30–6.15)
Sunburn					
Never	313	8	364	1	1
Ever	299	5	234	0.67 (0.22–2.07)	0.66 (0.53–0.84)
Indoor tanning and sunburns					
Neither	276	7	330	1	1
Sunburn only	285	2	214	0.28 (0.06–1.36)	0.62 (0.49–0.79)
Tanning booth use only	36	1	32	1.77 (0.17–18.24)	0.79 (0.47–1.34)
Both	14	3	20	15.75 (2.56–96.87)	1.23 (0.60–2.53)
UV treatment					
Never	574	12	566	1	1
Ever	38	1	38	1.32 (0.17–10.47)	1.02 (0.64–1.63)

* Adjusted for SES (high, mid high, mid, mid low and low), age group (<50, 50–64, 65), and 1st degree relative with haematological malignancy (yes, no, unknown).

OR, odds ratio; 95% CI, 95% confidence interval; NHL, Non-Hodgkin lymphoma; UV, ultraviolet; SES, standard error of skewness.