Original Investigation

Association Between Indoor Tanning and Melanoma in Younger Men and Women

DeAnn Lazovich, PhD; Rachel Isaksson Vogel, MS; Martin A. Weinstock, MD, PhD; Heather H. Nelson, PhD; Rehana L. Ahmed, MD, PhD; Marianne Berwick, PhD

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IMPORTANCE In the United States and Minnesota, melanoma incidence is rising more steeply among women than men younger than 50 years. To our knowledge, no study has examined age- and sex-specific associations between indoor tanning and melanoma to determine if these trends could be due to greater indoor tanning use among younger women.

OBJECTIVE To examine associations between indoor tanning and melanoma among men and women younger than 50 years.

DESIGN, SETTING, AND PARTICIPANTS Population-based case-control study conducted in Minnesota of 681 patients (465 [68.3%] women) diagnosed as having melanoma between 2004 and 2007, and 654 controls (446 [68.2%] women), ages 25 to 49 years.

EXPOSURE Indoor tanning, defined as any use, first age of use, and total sessions.

MAIN OUTCOMES AND MEASURES Crude and adjusted odds ratios (ORs) and 95% CIs were calculated for melanoma in relation to indoor tanning exposure for men and women by diagnosis or reference age (<30, 30-39, 40-49 years). Sex-specific associations for indoor tanning and melanoma by anatomic site were examined.

RESULTS Compared with women aged 40 to 49 years, women younger than 40 years initiated indoor tanning at a younger age (16 vs 25 years, $P < .001$) and reported more frequent indoor tanning (median number of sessions, 100 vs 40, $P < .001$). Women younger than 30 years were 6 times more likely to be in the case than the control group if they tanned indoors (crude OR, 6.0; 95% CI, 1.3-28.5). Odds ratios were also significantly elevated among women, ages 30 to 49 years (adjusted OR, 3.5; 95% CI, 1.2-9.7 for women 30-39 years; adjusted OR, 2.3; 95% CI, 1.4-3.6 for women 40-49 years); a dose response was observed among women regardless of age. Among men, results by age were inconsistent. The strongest OR for indoor tanning by anatomic site was for melanomas arising on the trunk of women (adjusted OR, 3.7; 95% CI, 1.9-7.2).

CONCLUSIONS AND RELEVANCE Indoor tanning is a likely factor for the steeper increase in melanoma rates in the United States among younger women compared with men, given the timing of when women initiated indoor tanning relative to diagnosis. The melanoma epidemic can be expected to continue unless indoor tanning is restricted and reduced.

Author Affiliations: Author affiliations are listed at the end of this article.

Corresponding Author: DeAnn Lazovich, PhD, Division of Epidemiology & Community Health, University of Minnesota, 1300 S Second St, Ste 300, Minneapolis, MN 55454 (lazov001@umn.edu).

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Melanoma incidence rates are higher in women than men until about age 50 years, with rates increasing over time in both younger men and women consistent with the well-recognized melanoma epidemic.[1,2] In about 1995, however, the rising rates of melanoma in the United States seemed to diverge by sex. By 2006, the incidence of melanoma was not only higher, but had increased more steeply among younger women than men.[3] Also during the same period, a change in anatomic site of melanoma occurred; the most common site for melanoma diagnosed in the United States shifted away from the trunk to other sites among men and from the head and neck and extremities to the trunk among younger but not older women.[1] These disease patterns among younger women are attributed, in part, to their greater use of indoor tanning, classified as a human carcinogen by the World Health Organization in 2009.[4]

Young non-Hispanic white females in the United States report the highest prevalence of indoor tanning use of any group. About 31% of high school girls (vs 6% of boys) and 25% of women, ages 18 to 34 years (vs <5% among similar-aged men) engage in the practice annually; most of these female users report tanning indoors at least 10 times in the past year.[5-8] However, to our knowledge, no study has reported separately for men and women on the association between indoor tanning practices and melanoma diagnosed at younger ages.

We previously found that melanoma risk was increased by 74% among indoor tanners compared with nontanners, ages 25 to 59 years.[9] We also observed a strong dose response: frequent indoor tanning (defined as ≥50 hours, >100 sessions, or ≥10 years of lifetime use) vs none increased the likelihood of melanoma by 2.5 to 3.0 times. To empirically inform prior suppositions about the changes in the disease patterns described herein, we reanalyzed the Skin Health Study data to examine the likelihood of melanoma in relation to ever use of indoor tanning, age at indoor tanning initiation, and indoor tanning frequency separately for men and women according to age at diagnosis of the cases or reference age for controls: younger than 30 years, 30 to 39 years, and 40 to 49 years.

Methods

Study Sample

Study methods have been published elsewhere[9]; the institutional review board at the University of Minnesota approved the Skin Health Study and all participants provided written informed consent. Briefly, men and women diagnosed as having invasive melanoma (cases) between 2004 and 2007 at ages 25 to 59 years, were identified from the state cancer registry; controls were randomly selected from the Minnesota State Driver's License lists and frequency matched to cases on age and sex. A letter inviting participation was mailed to cases and controls, followed by a telephone call. If willing to participate, we mailed a self-administered questionnaire and then completed a telephone interview with those returning the questionnaire. Participants reported their demographics, phenotypic characteristics, family history of melanoma, sun exposure, sunburns, sunscreen use, and indoor tanning. A total of 1167 cases (57.6% response overall, 84.6% among cases screened and eligible) and 1101 controls (35.6% response overall, 69.2% among controls screened and eligible) participated. For this analysis, we restricted the study sample to men (216 in case group, 208 in control group) and women (465 in case group, 446 in control group) who were younger than 50 years at diagnosis (case group) or reference age (control group), because this is the age group where melanoma rates in women exceed those in men.[2]

Measures

In the self-administered questionnaire, we queried about any use of 4 common types of tanning devices in 5-year age groups from ages 11 to 49 years (the upper age limit restriction for this analysis). Previously, we found the different device types reported by controls aligned well with device availability over time.[9] Participants reporting use of any device within a 5-year age period were then asked in the telephone interview about the total number of sessions and years that each device was used. We calculated the total number of indoor tanning sessions by summing sessions across all 5-year age blocks in which use was reported. We then classified users according to either 1 to 10 or more than 10 lifetime sessions. We also asked for the exact age when participants first tanned indoors and divided participants according to those who initiated the behavior before age 25 years. These categories are consistent with a recent meta-analysis of melanoma in relation to indoor tanning dose and age at initiation.[10] The state cancer registry provided data on anatomic site of the tumor, which we classified as head and neck region, trunk, upper limbs, and lower limbs.

Statistical Analysis

We stratified Skin Health Study participants by age at diagnosis for cases or reference age for controls (<30, 30-39, 40-49 years) and sex. Comparisons of phenotypic and UV radiation behaviors between cases and controls within age- and sex-specific strata were conducted using X^2 tests for categorical data and Wilcoxon Rank Sum tests for continuous data. We used logistic regression to calculate ORs and 95% CIs for the association between ever use of indoor tanning, age at indoor tanning initiation, number of sessions, and risk of melanoma within each age- and sex-specific stratum. Among the youngest individuals, we only present sex-specific crude ORs and 95% CIs for the association between indoor tanning measures and melanoma risk due to small sample size and/or high prevalence of indoor tanning exposure that precluded multivariable adjustment. For the other age × sex groups, we used the same strategy for adjustment as our original report, choosing confounders if they resulted in a meaningful change of the crude OR or to be consistent with previous reports. These confounders included eye color (gray or blue, green, hazel, brown); hair color (red, blond, light brown, dark brown or black); skin color (very fair, fair, all other); freckles (none, few, some, or many); moles (none, few, some, or many); income (<$60 000, ≥$60 000); college education (did or did not complete college); family history of melanoma (yes or no); total lifetime sunburns (continuous); sun exposure from routine, recreational,

Table 1. Phenotypic and UV Radiation Behavior Among Cases (by Age Range at Diagnosis) and Controls (Reference Age Range)

Characteristic	Age at Diagnosis or Reference Age Range					
	< 30 y (n = 144)		30-39 y (n = 391)		40-49 y (n = 800)	
	Cases (n = 76)	Controls (n = 68)	Cases (n = 198)	Controls (n = 193)	Cases (n = 407)	Controls (n = 393)
Women						
No.	63	61	140	135	262	250
Blue eyes, %	46.0	41.0	42.9	33.3[a]	41.2	36.0
Phenotype risk score, mean	3.0	2.9	3.1	2.7[b]	3.1	2.8[c]
Fair or very fair skin, %	85.7	77.1	83.6	81.5	87.4	80.0
Freckles pattern (mean, score 1-4)	1.9	1.8	1.6	1.7	2.0	1.8[a]
Mole pattern (mean, score 1-4)	2.4	1.9[c]	2.3	1.8[c]	2.1	1.7[c]
Melanoma family history, %	24.6	28.8	20.1	15.4	18.5	19.6
Routine sun, median, ×100 h	11.0	11.6	15.3	14.9	20.4	21.0
Outdoor activity sun, median, ×100 h	7.7	8.2	11.3	11.1	15.1	15.4
Sunburns, median, No.	9.0	6.5	7.0	6.0	10.0	6.0[c]
Ever tanned indoors, %	96.8	83.6[a]	94.3	79.3[c]	78.6	62.0[c]
Age of initiation, median, y	16.0	16.0	16.0	17.0	24.5	25.0
Sessions, median, No.	110.0	95.0	130.0	73.0[a]	49.5	28.0[b]
Tumors located on trunk, %	33.3	NA	35.0	NA	24.4	NA
Men						
No.	13	7	58	58	145	143
Blue eyes, %	30.8	42.9	39.7	31.0	46.9	41.3
Phenotype risk score, mean	3.4	2.4	2.8	2.4[a]	2.9	2.7[a]
Fair or very fair skin, %	92.3	57.2	89.7	70.7[a]	90.3	83.9
Freckles pattern (mean, score 1-4)	2.2	1.4	1.8	1.5[a]	1.9	1.6[b]
Mole pattern (mean, score 1-4)	2.1	2.0	2.2	1.8[c]	2.1	1.7[c]
Melanoma family history, %	7.7	16.7	17.2	29.3	17.6	19.6
Routine sun, median, ×100 h	13.0	13.3	21.8	22.8	26.8	30.0
Outdoor activity sun, median, ×100 h	10.1	9.4	13.1	14.0	15.6	19.8
Sunburns, median, No.	40.0	6.0[a]	12.0	9.5	12.0	9.0
Ever tanned indoors, %	46.2	57.1	51.7	44.8	47.5	37.1
Age of initiation, median, y	16.5	16.0	19.5	20.5	25.0	30.0
Sessions, median, No.	7.0	70.5	22.0	12.5	20.0	24.5
Tumors located on trunk, %	46.2	NA	41.4	NA	49.0	NA

Abbreviation: NA, not applicable.

[a] Statistical significance for difference between cases and controls: $P < .05$.

[b] Statistical significance for difference between cases and controls: $P < .01$.

[c] Statistical significance for difference between cases and controls: $P < .001$.

or occupational activities (continuous); and mean lifetime sunscreen use (continuous). We also calculated multivariable-adjusted ORs and 95% CIs for the association between ever use of indoor tanning and melanoma by anatomic site separately for men and women, all ages combined.

Results

Among the 681 patients in this analysis, 465 (68.3%) were women, and 446 (68.2%) of the 654 in the control group were women. Although few differences were statistically significant, women with blue eyes, fair skin, more moles, and greater number of painful sunburns were more likely to fall into the case group than the control group, regardless of age (**Table 1**). The median hours of routine and recreational sun exposure were fairly similar among females in both groups, but indoor tanning was most common among women in the case group who were younger than 40 years (95.1% versus 80.6% for controls younger than 40 years, $P < .001$). For women younger than 40 years at diagnosis or reference age, the median age at indoor tanning initiation was 16 years versus 25 years among women 40 years or older ($P < .001$) . The total median number of indoor tanning sessions was also considerably higher among women younger than 40 years (100 versus 40, $P < .001$), especially within the case group (120 versus 76 for controls younger than 40 years, $P = .04$). Thirty-three percent (21 participants) of females in the case group diagnosed before age 30 years had melanomas arising on their trunk compared with 24% (64 participants) of those who were 40 to 49 years old at diagnosis.

With just 13 males in the case group and 7 in the control group younger than 30 years at diagnosis or reference age, we were unable to compare their various characteristics or behaviors to other men (Table 1). Among older males in the case group compared with the control group, the patterns for eye and skin color, presence of moles, sun exposure, and sun-

burns were similar to what we observed among women. Regardless of case or control status, men were less likely to report indoor tanning use compared with women (44.3% versus 78.2%, $P < .001$), but among men between ages 30 to 49 years, a higher proportion of those in the case group reported indoor tanning use than those in the control group (48.3% versus 42.4%, $P = 0.28$). Among men ages 30 to 39 years, 41% were diagnosed as having melanoma of the trunk compared with 49% of men ages 40 to 49 years.

Indoor tanning use was strongly associated with melanoma risk among women, especially if younger than 30 years at diagnosis or reference age (**Table 2**). All but 2 of the 63 youngest women in the case group reported tanning indoors; the crude OR for indoor tanning and melanoma was 6.0 (95% CI, 1.3-28.5). Because these same women had all begun tanning indoors before age 25 years, the crude OR and 95% CI for age at initiation and melanoma diagnosis were identical to the estimate for having ever tanned indoors. Nearly all females in the case group younger than 30 years at diagnosis also reported tanning indoors more than 10 times (crude OR; 6.1, 95% CI, 1.3- 29.0). Although associations between indoor tanning and melanoma were attenuated in the other age groups, they remained quite strong. For women who were 30 to 39 years at their diagnosis of melanoma or reference age, an adjusted OR of 3.5 (95% CI, 1.2- 9.7), and for women who were 40 to 49 years at diagnosis or reference age, an adjusted OR of 2.3 (95% CI, 1.4- 3.6), were observed for having ever tanned indoors compared with women who had no exposure to indoor tanning. In these older age groups, women were nearly 3 to 4 times more likely to develop melanoma if they had been exposed to more than 10 sessions. They were at increased risk of melanoma whether or not they started tanning indoors before age 25 years.

Among men, the strength of the association between ever use of indoor tanning and melanoma was variable, likely owing to the small sample size for some age groups (**Table 3**). Odds ratios ranged from a crude OR of 0.6 (95% CI, 0.1- 4.1) if diagnosed before the age of 30 years to an adjusted OR of 2.0 (95% CI, 1.1-3.6) if diagnosed between 40 and 49 years. No clear pattern between age at indoor tanning initiation, nor for a dose-response in relation to melanoma, was observed when men were stratified on age at diagnosis (or reference age).

By tumor location, the strongest association between indoor tanning and melanoma was observed among women for melanomas arising on the trunk (**Table 4**), with an adjusted OR of 3.7 (95% CI, 1.9-7.2). For other anatomic sites among women, ORs for indoor tanning and melanoma were 1.4 for upper limb, 2.3 for lower limb, and 2.5 for head or neck tumors. However, the 95% CIs for these ORs included the null value except for melanomas found on the lower limbs in women (95% CI, 1.3-4.0). Among men, indoor tanning was most strongly associated with melanomas occurring on the head or neck (adjusted OR, 3.0; 95% CI, 1.1-8.3). Although somewhat attenuated, associations were, nevertheless, also strongly and statistically significantly associated with melanomas on the trunk (adjusted OR, 2.0; 95% CI, 1.1-3.6) and upper limbs (adjusted OR, 2.3; 95% CI, 1.0-5.1). No association was observed between indoor tanning and melanomas arising on the lower limbs in men.

Discussion

Younger women who tanned indoors experienced a 2.3- to 6-fold increase in the likelihood of developing melanoma; this relationship was particularly evident among women in their 20s. We were not able to observe similar associations among younger men, likely because of poor statistical power to detect them given that fewer men are diagnosed as having melanoma at younger ages, and men are less frequent users of indoor tanning compared with women. Women in their 20s seemed to be at highest risk of developing melanoma from indoor tanning compared with any other age group of women or any age group of men because they initiated the behavior at the youngest age and reported a high median number of tanning sessions relative to their age. Given the substantial proportion of young women today who began indoor tanning as adolescents, this result is particularly concerning because their risk of developing melanoma in the future may be very high.

We posit that these results for younger women and men from Minnesota explain, in part, the diverging trends in melanoma incidence between similar-aged men and women in the United States. Female participants in our study were diagnosed in a period coinciding with rising melanoma rates in Minnesota, especially among women younger than 50 years. From 1995 to 2011 in Minnesota, the rate of melanoma among younger men increased 2% per year, but increased 5% per year among younger women,[11] closely mirroring published reports from US data between 1995 and 2006.[3] In addition, the timing of indoor tanning exposure in relation to the years of diagnosis among female participants is consistent with our claim that indoor tanning is likely driving incidence rates in younger women. In our study, women diagnosed as having melanoma in their 20s initiated indoor tanning in the early to mid 1990s, while those in their 40s did so in the mid 1980s, providing evidence for a plausible median latency period for melanoma of 9.5 to 21.0 years on average. The evidence is strongly consistent with expectations regarding exposure timing and melanoma development during a period when melanoma incidence rates were rapidly increasing in younger women, but much less so in younger men.

Our study is the sole study to examine the association between indoor tanning and melanoma according to age at diagnosis *and* sex, so direct comparisons to other reports are not possible. Nevertheless, our findings for women younger than 30 years at diagnosis or reference age are in agreement with all other studies that examined this association stratified by age at diagnosis.[12-14] In those reports, statistically significant ORs from 6.6 to 8.0 were reported for individuals diagnosed or interviewed before ages 30 years[12,14] or 36 years,[13] *and* who reported tanning indoors on a regular basis, more than 10 times per year or more than 10 lifetime sessions. A few case-control studies[15-17] reported results for indoor tanning and melanoma stratified by sex. Walter et al[16] found an association for

Table 2. Indoor Tanning Use and Melanoma Risk Among Women by Age Range at Diagnosis or Reference Age Range[a]

Indoor Tanning Characteristic	< 30 y (n = 124)				30 - 39 y (n = 275)				40 - 49 y (n = 512)			
	No. (%)		OR (95% CI)		No. (%)		OR (95% CI)		No. (%)		OR (95% CI)	
	Cases (n = 63)	Controls (n = 61)	Crude	Adjusted	Cases (n = 140)	Controls (n = 135)	Crude	Adjusted	Cases (n = 262)	Controls (n = 250)	Crude	Adjusted
Ever tanned indoors												
No	2 (3.2)	10 (16.4)	1 [Ref]	1 [Ref]	8 (5.7)	28 (20.7)	1 [Ref]	1 [Ref]	56 (21.4)	95 (38.0)	1 [Ref]	1
Yes	61 (96.8)	51 (83.6)	6.0 (1.3-28.5)	NE	132 (94.3)	107 (79.3)	4.3 (1.9-9.9)	3.5 (1.2-9.7)	206 (78.6)	155 (62.0)	2.3 (1.5-3.3)	2.3 (1.4-3.6)
Age at initiation, y												
< 25	61 (96.8)	51 (83.6)	6.0 (1.3-28.5)	NE	123 (87.9)	92 (68.2)	4.7 (2.0-10.7)	3.5 (1.2-9.8)	103 (39.3)	76 (30.4)	2.3 (1.5-3.6)	2.2 (1.3-3.7)
≥ 25	0	0	-	-	9 (6.4)	15 (11.1)	2.1 (0.7-6.6)	3.3 (0.8-13.3)	103 (39.3)	79 (31.6)	2.2 (1.4-3.4)	2.3 (1.4-3.9)
Sessions, No.												
1 - 10	4 (6.3)	4 (6.6)	5.0 (0.6-39.1)	NE	13 (9.3)	17 (12.6)	2.7 (0.9-7.8)	1.8 (0.5-6.7)	42 (16.0)	45 (18.0)	1.6 (0.9-2.7)	1.5 (0.8-2.8)
> 10	57 (90.5)	47 (77.0)	6.1 (1.3-29.0)	NE	119 (85.0)	89 (65.9)	4.7 (2.0-10.8)	3.9 (1.4-11.0)	162 (61.8)	104 (41.6)	2.6 (1.8-4.0)	2.7 (1.7-4.4)
Missing	*0*	*0*			*0*	*1*			*2*	*6*		

Abbreviations: NE, not estimable; OR, odds ratio; Ref, reference.

[a]The ORs and 95% CIs were adjusted for eye color (gray or blue, green, hazel, brown), hair color (red, blond, light brown, dark brown or black), skin color (very fair, fair, all other), freckles (none, few, some, many), moles (none, few, some or many), income (<$60 000, ≥$60 000), college education (did or did not complete college), family history of melanoma (yes or no), total number of lifetime sunburns (continuous), outdoor routine sun exposure (continuous), outdoor activity sun exposure (continuous), outdoor job sun exposure (continuous), and mean lifetime sunscreen use (continuous).

Table 3. Indoor Tanning Use and Melanoma Risk Among Men by Age Range at Diagnosis or Reference Age Range[a]

Indoor Tanning Characteristic	< 30 y (n = 20)				30 - 39 y (n = 116)				40 - 49 y (n = 288)			
	No. (%)		OR (95% CI)		No. (%)		OR (95% CI)		No. (%)		OR (95% CI)	
	Cases (n = 13)	Controls (n = 7)	Crude	Adjusted	Cases (n = 58)	Controls (n = 58)	Crude	Adjusted	Cases (n = 145)	Controls (n = 143)	Crude	Adjusted
Ever tanned indoors												
No	7 (53.8)	3 (42.9)	1 [Ref]	1 [Ref]	28 (48.3)	32 (55.2)	1 [Ref]	1 [Ref]	76 (52.4)	90 (62.9)	1 [Ref]	1 [Ref]
Yes	6 (46.2)	4 (57.1)	0.6 (0.1-4.1)	NE	30 (51.7)	26 (44.8)	1.3 (0.6-2.7)	1.4 (0.5-4.0)	69 (47.6)	53 (37.1)	1.5 (1.0-2.5)	2.0 (1.1-3.6)
Age at initiation, y												
< 25	6 (46.2)	4 (57.1)	0.6 (0.1-4.1)	NE	21 (36.2)	20 (34.5)	1.2 (0.5-2.7)	1.0 (0.3-3.1)	29 (20.0)	16 (11.2)	2.1 (1.1-4.2)	2.7 (1.2-5.9)
≥ 25	0	0	-	-	9 (15.5)	6 (10.3)	1.7 (0.5-5.4)	4.1 (0.8-22.5)	40 (27.6)	37 (25.9)	1.3 (0.7-2.2)	1.7 (0.9-3.3)
Sessions, No.												
1 - 10	4 (30.8)	1 (14.2)	1.7 (0.1-22.5)	NE	6 (10.3)	12 (20.7)	0.6 (0.2-1.7)	0.3 (0.1-1.5)	27 (18.6)	12 (8.4)	2.7 (1.3-5.6)	3.4 (1.4-8.2)
> 10	2 (15.4)	3 (42.9)	0.3 (0.0-2.7)	NE	23 (39.7)	14 (24.1)	1.9 (0.8-4.3)	2.8 (0.8-9.4)	42 (29.0)	38 (26.6)	1.3 (0.8-2.2)	1.7 (0.9-3.3)
Missing	*0*	*0*			*1*	*0*			*0*	*3*		

Abbreviations: NE, not estimable; OR, odds ratio; Ref, reference.

[a]The ORs and 95% CIs were adjusted for eye color (gray or blue, green, hazel, brown), hair color (red, blond, light brown, dark brown or black), skin color (very fair, fair, all other), freckles (none, few, some, many), moles (none, few, some or many), income (<$60 000, ≥$60 000), college education (did or did not complete college), family history of melanoma (yes or no), total number of lifetime sunburns (continuous), outdoor routine sun exposure (continuous), outdoor activity sun exposure (continuous), outdoor job sun exposure (continuous), and mean lifetime sunscreen use (continuous).

Table 4. Indoor Tanning and Melanoma Risk at Specific Body Locations Among Men and Women, All Ages Combined[a]

	Controls (n = 654)	Cases (n = 681)			
		Head and/or Neck (n = 68)		Trunk (n=235)	
Ever Used	No. (%)	No. (%)	AOR (95% CI)[b]	No. (%)	AOR (95% CI)[b]
Men					
No	125 (60.1)	18 (52.9)	1 [Reference]	48 (47.5)	1 [Reference]
Yes	83 (39.9)	16 (47.1)	3.0 (1.1-8.3)	53 (52.5)	2.0 (1.1-3.6)
Women					
No	133 (29.8)	6 (17.6)	1 [Reference]	13 (9.7)	1 [Reference]
Yes	313 (70.2)	28 (82.4)	2.5 (0.8-7.3)	121 (90.3)	3.7 (1.9-7.2)
		Upper Limbs (n = 154)		Lower Limbs (n = 209)	
Men					
No	125 (60.1)	26 (54.2)	1 [Reference]	16 (55.2)	1 [Reference]
Yes	83 (39.9)	22 (45.8)	2.3 (1.0-5.1)	13 (44.8)	1.3 (0.5-3.1)
Women					
No	133 (29.8)	24 (22.6)	1 [Reference]	22 (12.2)	1 [Reference]
Yes	313 (70.2)	82 (77.4)	1.4 (0.8-2.5)	158 (87.8)	2.3 (1.3-4.0)

Abbreviation: AOR, adjusted odds ratio.

[a] Four males and 11 female cases had unknown tumor site.

[b] The AORs and 95% CIs were adjusted for eye color (gray or blue, green, hazel, brown), hair color (red, blond, light brown, dark brown or black), skin color (very fair, fair, all other), freckles (none, few, some, many), moles (none, few, some or many), income (< $60 000, ≥ $60 000), college education (did or did not complete college), family history of melanoma (yes or no), total number of lifetime sunburns (continuous), outdoor routine sun exposure (continuous), outdoor activity sun exposure (continuous), outdoor job sun exposure (continuous), and mean lifetime sunscreen use (continuous).

indoor tanning and melanoma in men but not women; the other studies were inconsistent or inconclusive, likely because the cases were mostly diagnosed in the 1980s, before indoor tanning became widely available.

Two recent meta-analyses[10,18,19] found a summary OR of 1.4 (95% CI, 1.0-1.8) or 1.6 (1.4-1.9) if indoor tanning was started before age 25 years or age 35 years, respectively. These results likely reflect the effect of cumulative exposure, given that the earlier age a person begins tanning indoors, the greater dose that person acquires over time. In our previous report,[9] and also the report by Cust et al,[14] the amount (eg, duration or dose) of indoor tanning was more important than the age at which indoor tanning was initiated for melanoma development. But an examination of exposure to indoor tanning by age at melanoma diagnosis asks a different question—whether early-onset melanoma could be due to increased genetic susceptibility, such that indoor tanning accelerates its onset among persons predisposed to develop the condition. Because women diagnosed as having melanoma at the youngest ages in our study reported a high number of tanning sessions, despite having less time to reach that dose than women diagnosed at older ages, we suspect that indoor tanning frequency is likely the more important factor that accounts for our results. Tanning devices also could have changed over time to be more carcinogenic than older devices, as studies[20-23] of UV radiation emissions from tanning beds in Europe and Australia have shown. Thus, younger indoor tanners exposed to newer devices may be at greater risk of melanoma than older tanners.

We observed the strongest association between indoor tanning and melanoma by anatomic site for melanomas arising on the trunk in women. Although not as strong as for women, men who tanned indoors also experienced a 2-fold increased risk for developing melanomas of the trunk. These findings are consistent with the divergent pathway hypothesis for melanoma, which posits that intermittent solar UV radiation exposure in persons with many nevi, in contrast to chronic solar UV radiation exposure in persons with fewer nevi, initiates melanoma development at a younger age, with tumors occurring on anatomic sites typically protected from the sun.[24-26] Our results suggest that indoor tanning, an artificial source of UV radiation delivered intermittently, may substitute for sun exposure to similar effect. Although others have shown that persons diagnosed as having melanoma of the trunk or in sites less likely to be sun exposed were more likely to use indoor tanning compared with those with melanoma arising elsewhere on the body,[27,28] considerable variation exists for the association of indoor tanning and melanoma by anatomic site, in part, owing to relatively small numbers of melanoma cases for each anatomic site.[12-14,16,17,28,29]

Study Limitations

Stratification by age at diagnosis or reference age resulted in smaller sample sizes and wide CIs for several associations. In addition, we only report the crude OR for men and women in the youngest age group. Adjustment for known confounders resulted in too many missing values and, among women, concern that the exceedingly high, much stronger estimate after adjustment was unstable. Notably, adjustment for confounding did not alter the interpretation of any other results among other age groups of women where sample sizes were larger and variation in indoor tanning use was greater. Our case-control study design and low response rates could raise concerns about selection and recall bias. We performed 2 ancillary studies during the conduct of the Skin Health Study to assess these biases.[9] In the first study, we randomly selected nonresponders and inquired about their indoor tanning use by telephone. We found the association between indoor tanning and melanoma to be similar in responders and nonresponders. In the second study, we assessed recall bias in patients who did and did not speak with their physician about the study prior to their participation. Too few individuals had

spoken with their physician to allow for adjusted estimates of risk in that group, but the association for indoor tanning and melanoma for patients who did not talk to their physician relative to controls was nearly identical after adjustment for confounding to our overall finding. While these ancillary studies have their own limitations, they offer no evidence for bias as the basis for our results. We have no reason to think the results reported herein would be more prone to bias than what we previously reported.

Conclusions

Our analysis reinforces findings from a recent report[14] from Australia on indoor tanning and melanoma diagnosed at a young age and provides evidence that indoor tanning is a likely driver of diverging trends in men and women younger than 50 years in the United States. At the time of this report, 13 states had banned access to commercial indoor tanning services for individuals younger than 18 years.[30] In 2014, the US Food and Drug Administration required indoor tanning devices to include warning labels against use by minors.[31] And in the same year, the Surgeon General released its Call to Action on Skin Cancer,[32] which proposed ongoing surveillance, tailored messages for indoor tanning avoidance, organizational policies, and legislative actions to limit indoor tanning use by minors and young adults. Our results indicate that these efforts need to be accelerated and expanded beyond bans on minor access to indoor tanning to curb the melanoma epidemic, which seems likely to continue unabated, especially among young women, unless exposure to indoor tanning is further restricted and reduced.

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Author Affiliations: Masonic Cancer Center, University of Minnesota, Minneapolis (Lazovich, Isaksson Vogel, Nelson, Ahmed); Division of Epidemiology and Community Health, University of Minnesota, Minneapolis (Lazovich, Nelson); Center for Dermatoepidemiology, VA Medical Center, Providence, Rhode Island (Weinstock); Department of Dermatology, Rhode Island Hospital, Providence (Weinstock); Department of Dermatology and Epidemiology, Brown University, Providence, Rhode Island (Weinstock); Department of Dermatology, University of Minnesota, Minneapolis (Ahmed); Department of Internal Medicine, University of New Mexico Cancer Center, Albuquerque (Berwick); Division of Epidemiology and Biostatistics, University of New Mexico, Albuquerque (Berwick).

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NOTABLE NOTES

Healing the Bee's Knees—On Honey and Wound Healing

Tetyana Rogalska, MD(C)

Since antiquity, honey has been revered for its natural healing properties. It has been used for treatment of gastrointestinal tract illnesses, treatment of pain, and defense from infection. However, it is its historical use in the treatment of skin wounds, burns, and ulcers that has sparked a renewed interest in recent years. Emerging scientific study of honey's therapeutic mechanisms has provided evidence for the antimicrobial and wound healing benefits behind this enduring tradition.

The ancient Egyptians were almost certainly the first to use honey for the treatment of wounds and infections, with the earliest record in the Smith papyrus dating from the 17th century BC. In this oldest-known treatise on trauma surgery, honey is combined with grease and lint as a prescription for a standard wound salve. The grease is derived from animal fat and mixed with honey in a 2:1 ratio, serving as an antiseptic barrier to protect the wound from infection.[1]

The ancient Greeks, who viewed honey as the "nectar of the Gods," also adopted it in their medical practices. Honey was not only used with vegetable or animal fat, but it was also mixed with white vinegar, alum, sodium carbonate, and bile. This cocktail formed an ointment known as *enheme*, which was used to desiccate the wound and prevent suppuration. The astringent properties of the alum, the osmotic pressure of the honey, and the alkali pH of the sodium carbonate and bile contributed to the antiseptic activity of the dressing.[1] Dioscorides (circa AD 50), a surgeon in the Roman army, later wrote of honey as the treatment of choice "for all rotten and hollow ulcers."[2(p13)] Indeed, its application in wound healing has continued to modern times; it is used as a traditional therapy in Ghana for infected leg ulcers,[2] in the Arabian Peninsula for fungal infections of the skin,[3] and in Chinese medicine to prevent scarring and discoloration.[3]

While novel dressings, biologic treatments, and negative pressure therapy have revolutionized wound care, honey may be finding a renewed role in the wound healing paradigm. In addition to its antibacterial and antifungal effects, honey has been observed to promote tissue regeneration through angiogenesis, granulation, and reepithelialization.[2] Animal models have shown that honey reduces inflammation in superficial burns, and clinical trials comparing honey to silver sulfadiazine have found it to accelerate healing with better relief of pain, less exudate, and lower incidence of hypertrophic scarring or postburn contracture.[2] Stemming from this growing body of evidence, there has been resurgence in the use of medical-grade honey in clinical practice. With honey's wound-healing history spanning both continents and millennia, this "divine nectar" is certainly poised to find a renaissance in modern medicine.

Author Affiliation: School of Medicine, Queen's University, Kingston, Ontario, Canada.

Corresponding Author: Tetyana Rogalska, MD(C), School of Medicine, Queen's University, 80 Barrie St, Kingston, ON K7L 3N6, Canada (trogalska@qmed.ca).

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