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Research Article

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Indoor Tanning and Risk of Melanoma: A Case-Control Study in a Highly Exposed Population

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Abstract

Background: Indoor tanning has been only weakly associated with melanoma risk; most reports were unable to adjust for sun exposure, confirm a dose-response, or examine specific tanning devices. A population-based case-control study was conducted to address these limitations.

Methods: Cases of invasive cutaneous melanoma, diagnosed in Minnesota between 2004 and 2007 at ages 25 to 59, were ascertained from a statewide cancer registry; age-matched and gender-matched controls were randomly selected from state driver's license lists. Self-administered questionnaires and telephone interviews included information on ever use of indoor tanning, types of device used, initiation age, period of use, dose, duration, and indoor tanning–related burns. Odds ratios (OR) and 95% confidence intervals (CI) were adjusted for known melanoma risk factors.

Results: Among 1,167 cases and 1,101 controls, 62.9% of cases and 51.1% of controls had tanned indoors (adjusted OR 1.74; 95% CI, 1.42-2.14). Melanoma risk was pronounced among users of UVB-enhanced (adjusted OR, 2.86; 95% CI, 2.03-4.03) and primarily UVA-emitting devices (adjusted OR, 4.44; 95% CI, 2.45-8.02). Risk increased with use: years ($P < 0.006$), hours ($P < 0.0001$), or sessions ($P = 0.0002$). ORs were elevated within each initiation age category; among indoor tanners, years used was more relevant for melanoma development.

Conclusions: In a highly exposed population, frequent indoor tanning increased melanoma risk, regardless of age when indoor tanning began. Elevated risks were observed across devices.

Impact: This study overcomes some of the limitations of earlier reports and provides strong support for the recent declaration by the IARC that tanning devices are carcinogenic in humans. *Cancer Epidemiol Biomarkers Prev; 19(6); 1557–68. ©2010 AACR.*

Introduction

Between 1997 and 2006, melanoma incidence increased 2.2% and 2.1% annually in the United States among Caucasian males and females, respectively (1). These trends have resulted in melanoma ranking first among men and second among women as the fastest increasing cancer for the 10 most common cancers in Caucasians, even as most common cancers are declining or stable. Intense, intermittent solar UV radiation has long been thought to account for the rise in melanoma (2). Indoor tanning is an artificial source of intermittent UV radiation exposure that has gained in popularity since the early 1980s. The indoor tanning industry estimates that approximately 30 million Americans visit indoor tanning salons each year (3). A recent report based on data from 116 cities in the United States found that the average number of tanning salons exceeded the average number of Starbucks or McDonald's (4).

In 2009, the IARC classified tanning devices as carcinogenic to humans (5). The IARC report may have little effect on indoor tanning use in the United States, in part, because the industry has used limitations of the studies reviewed by the IARC and hypotheses regarding potential health benefits, such as vitamin D, to counter possible health concerns (6). With at least 29 reports to date (7-35), past history of indoor tanning has been only weakly associated with melanoma (ref. 5; the IARC reported a summary odds ratio of 1.15; 95% CI, 1.00-1.31 based on 19 studies), and limitations of these studies include the lack of information on sun exposure (a known correlate of indoor tanning use; ref. 36) in the majority of studies, and a low or presumed low prevalence of exposure to indoor tanning. Only 11 studies have provided some detail about the exposure, but none measured dose-response or

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reported on age of initiation in the same manner (11, 17, 21-23, 25, 27, 28, 30-32). Consequently, the evidence that melanoma occurrence increases with frequent indoor tanning use is limited. In addition, only three studies have examined melanomas in relation to indoor tanning use during adolescence (30-32), when indoor tanning is most likely to be initiated (37). Although moderately strong associations have been reported, point estimates were imprecise, perhaps due to the low frequency of exposure (30, 32) or number of events (31).

Information on the risk of melanoma associated with specific devices is also lacking. Tanning devices emit both UVB and UVA. The UVB component has been considered to be the putative factor for skin carcinogenesis, but cutaneous melanocytes absorb both UVB and UVA (38), and mechanisms have been proposed by which UVA might lead to skin cancer, including indirect damage to DNA via reactive oxygen species (39-41). A complicating factor is that devices have changed over time. For example, devices available prior to the 1980s emitted much higher levels of UVB compared with normal solar UV radiation. These were followed by the introduction in the 1980s of devices emitting primarily UVA to address the public's concern about burning (42-45). In the 1990s, UVB was reintroduced in high-speed or high-intensity devices to produce deeper tans, and high-pressure devices emitting almost exclusively UVA also became available. Year of use or device type could serve as proxies for UVB versus UVA exposure in epidemiologic studies. However, in most studies, cases were diagnosed prior to 1990, and only a few studies have measured device- or period-specific exposure (21, 23, 27, 30-32). Although the IARC report designated UVA as "carcinogenic" in humans, device- and period-specific results from epidemiologic studies have been inconclusive with respect to melanoma.

In 2004, we initiated the Skin Health Study, a population-based case-control study of indoor tanning in relation to risk of melanoma, that was specifically designed to address the limitations of prior research. The study was conducted in Minnesota, a state with documented high prevalence of the behavior (37). We collected more detailed information than most studies to assess not only melanoma risk associated with frequent use, years of use, and age at which use began, but also with specific devices and period of use to distinguish exposure to UVB or UVA. We also obtained information on known confounders and enrolled a sufficiently large sample size to allow for subgroup analyses which have rarely been possible. Our results are presented here.

Materials and Methods

Ascertainment and recruitment of cases and controls

The Skin Health Study was approved by the Institutional Review Board at the University of Minnesota. Cases were ascertained by the Minnesota Cancer Surveillance System, a population-based, statewide cancer registry. Individuals with invasive cutaneous melanoma, any histologic type, diagnosed between July 2004 and December 2007, between the ages of 25 and 59, with a state driver's license or state identification card, were eligible to participate. The lower age limit allowed for a latency period for melanoma development among indoor tanning users exposed during adolescence; age was truncated at 59 years because indoor tanning decreases with age. In accordance with state laws, the cancer registry first obtained physician permission for research staff to contact his or her patient before releasing case information to research staff; consent was assumed after allowing sufficient time for physician response. Controls were randomly selected from the Minnesota state driver's license list (which includes persons with state identification cards) and frequency-matched to cases in a 1:1 ratio on age (in 5-year age groups) and gender.

Eligible cases and controls were required to be English-speaking and to have a telephone number. We used several methods for obtaining telephone numbers including hiring companies specializing in locating individuals, manually searching publicly available databases, telephone books, and web sites, or sending a letter requesting a telephone number if these other methods were unsuccessful. Once we located a telephone number, we then sent a letter introducing the research study, followed by a telephone call to invite participation. Data collection began in December 2004 and was completed in March 2009.

Data collection and participation

After receiving a self-administered questionnaire, selected information was entered into a computer-assisted telephone interview system to facilitate a subsequent, detailed 1-hour telephone interview. A reference date was assigned to each participant. For cases, this date was the date of diagnosis, and for controls, this date was the date the invitation letter was sent less the mean time between cases' diagnosis and when cases were released to the study.

Exposure measurement

Because devices varied widely and no standardized instruments to measure exposure to tanning devices were available, we developed and pilot-tested a new tanning device instrument by first conducting in-depth interviews with seven individuals that had tanned indoors to identify device types, determine their common names, and find the best approach for collecting lifetime history of indoor tanning use. From this process, we developed a mixed mode instrument for collecting information about tanning devices used at various ages, which we tested with another 32 individuals. The final instrument, consisting of a self-administered questionnaire and telephone interview, was implemented in this study.

The self-administered portion of the tanning device instrument contained six columns with photographs for

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each device: regular tanning beds/booths without facial lamps (variable ratios of UVB to UVA), regular tanning beds/booths with facial lamps (similar to devices without facial lamps; facial lamps are primarily UVA emitting), high-speed or high-intensity tanning beds/booths (UVB enhanced), high-pressure tanning beds/booths (primarily UVA emitting), sun lamps, or partial body tanners. Under each column, participants checked the age at which the device had been used, in 5-year age blocks from age 11 to age 59 (the oldest age at reference date). This information was then entered into the computer-assisted telephone interview system to guide device-specific questions during the telephone interview about use in each 5-year age period. These telephone-based questions included the number of years used within each 5-year age period, location of use (home, business, or other), and whether use was "occasional" or "fairly regular." If the participant was an occasional user, we asked about times per year of use, and if a fairly regular user, we asked about the number of months in which use occurred, and then times used per month. We also asked about the number of minutes of a typical session. We derived the specific years in which use occurred from birth year, year at reference age, age at tanning initiation, and age at tanning cessation. We calculated measures of ever use (based on reported age of initiation), dose (hours, sessions), and duration (years) across all devices, for specific devices, and for specific time periods. We classified regular beds/booths with and without facial lamps as conventional devices, and dropped partial tanners due to infrequent use. We also asked about frequency of burns attributed to an indoor tanning session or to sun after indoor tanning.

Other risk factors

We collected skin, hair and eye color, and presence and pattern of freckles and moles via the self-administered questionnaire. Education, income, family history of melanoma (diagnosed in parents, siblings, children, grandparents, grandchildren), all sun exposure measures, history and number of painful sunburns before and after age 18, and sunscreen use were collected during the telephone interview. Lifetime routine sun exposure was

Table 1. Outcome of recruitment of cases and controls (Skin Health Study)

	Cases	Controls
	n (%)	*n* (%)
Total from cancer registry (cases) or from drivers license list (controls)	2,026 (100.0)	3,095 (100.0)
Unable to determine eligibility		
Total	557 (27.5)	1,354 (43.7)
No phone available	164	598
Not reached by phone	71	273
Subject refused	79	468
Physician refusal	124	—
Died	23	15
Nonparticipating institution	93	—
Other	3	—
Respondent not eligible		
Total	89 (4.4)	151 (4.9)
Prior melanoma	76	14
Noncutaneous melanoma	2	—
Not melanoma	1	—
Not residing in Minnesota	0	63
Language/other	10	74
Respondents screened and eligible		
Total	1,380 (68.1)	1,590 (51.4)
Did not return self-administered questionnaire	186 (13.5)	447 (28.1)
Did not return	128	269
Refused	55	174
Died	2	1
Other	1	3
Did not complete telephone interview	27 (1.9)	42 (2.7)
Not reached	17	26
Refused/incomplete	9	14
Died/incapable	1	2
Completed self-administered questionnaire and telephone interview	1,167 (84.6)	1,101 (69.2)

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Table 2. Comparison of cases and controls in the Skin Health Study

Characteristic	Cases *n* (%)	Controls *n* (%)	Crude OR (95% CI)
Age (y)			
25-29	76 (6.5)	68 (6.2)	1.03 (0.72-1.46)
30-39	198 (17.0)	193 (17.5)	0.94 (0.75-1.20)
40-49	407 (34.9)	393 (35.7)	0.95 (0.79-1.15)
50-59	486 (41.6)	447 (40.6)	1.00
Gender			
Male	468 (40.1)	445 (40.4)	0.99 (0.83-1.17)
Female	699 (59.9)	656 (59.6)	1.00
Income			
<$60,000	348 (29.8)	373 (33.9)	0.82 (0.69-0.98)
$60,000+	798 (68.4)	703 (63.9)	1.00
Missing	21 (1.8)	25 (2.2)	
Completed college			
No	612 (52.4)	610 (55.4)	0.88 (0.75-1.04)
Yes	555 (47.6)	489 (44.4)	1.00
Missing	0 (0.0)	2 (0.2)	
Eye color			
Gray/blue	529 (45.3)	445 (40.4)	1.46 (1.18-1.82)
Green	175 (15.0)	142 (12.9)	1.52 (1.14-2.01)
Hazel	237 (20.3)	236 (21.4)	1.24 (0.96-1.59)
Brown	226 (19.4)	278 (25.3)	1.00
Natural hair color			
Red	120 (10.3)	46 (4.2)	3.53 (2.43-5.12)
Blonde	362 (31.0)	226 (20.5)	2.17 (1.73-2.72)
Light brown	396 (33.9)	438 (39.8)	1.22 (1.00-1.50)
Dark brown/black	289 (24.8)	391 (35.5)	1.00
Skin color			
(inside upper arm)			
Very fair	215 (18.4)	128 (11.6)	5.50 (2.70-11.18)
Fair	827 (70.9)	746 (67.8)	3.63 (1.83-7.18)
Light olive	114 (9.8)	191 (17.4)	1.95 (0.96-3.99)
Dark olive, brown, black	11 (0.9)	36 (3.2)	1.00
Moles			
Many	71 (6.1)	12 (1.1)	13.81 (7.32-26.05)
Some	250 (21.4)	92 (8.4)	6.35 (4.73-8.51)
Few	644 (55.2)	545 (49.5)	2.76 (2.25-3.39)
None	191 (16.4)	446 (40.5)	1.00
Missing	11 (0.9)	6 (0.5)	
Freckles			
Many	18 (1.6)	11 (1.0)	1.90 (0.89-4.06)
Some	75 (6.4)	44 (4.0)	1.98 (1.34-2.92)
Few	196 (16.8)	127 (11.5)	1.79 (1.39-2.30)
Very few	326 (27.9)	278 (25.3)	1.36 (1.12-1.66)
None	547 (46.9)	635 (57.7)	1.0
Missing	5 (0.4)	6 (0.5)	
Family history of melanoma			
Yes	216 (18.5)	224 (20.3)	0.87 (0.71-1.08)
No	939 (80.5)	850 (77.2)	1.00
Missing	12 (1.0)	27 (2.5)	

(*Continued on the following page*)

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Table 2. Comparison of cases and controls in the Skin Health Study (Cont'd)

Characteristic	Cases *n* (%)	Controls *n* (%)	Crude OR (95% CI)
Lifetime routine sun exposure (h)			
High	372 (31.9)	382 (34.7)	0.85 (0.70-1.05)
Medium	390 (33.4)	365 (33.1)	0.94 (0.77-1.15)
Low	399 (34.2)	350 (31.8)	1.00
Missing	6 (0.5)	4 (0.4)	
Lifetime sun exposure from outdoor activities (h)			
High	388 (33.2)	367 (33.3)	0.95 (0.78-1.16)
Medium	378 (32.4)	377 (34.2)	0.90 (0.74-1.10)
Low	397 (34.0)	357 (32.5)	1.00
Missing	4 (0.4)	0 (0.0)	
Lifetime sun exposure from outdoor jobs (h)			
High	210 (18.0)	232 (21.1)	0.84 (0.68-1.04)
Low	262 (22.5)	225 (20.4)	1.08 (0.88-1.33)
None	689 (59.0)	640 (58.1)	1.00
Missing	6 (0.5)	4 (0.4)	
Mean lifetime sunscreen use			
High	405 (34.7)	351 (31.9)	1.31 (1.07-1.61)
Medium	409 (35.0)	349 (31.7)	1.34 (1.09-1.63)
Low	352 (30.2)	401 (36.4)	1.00
Missing	1 (0.1)	0 (0.0)	
Lifetime number of burns from sun (lasting more than 1 d)			
>5	739 (63.3)	595 (54.0)	2.56 (1.67-3.93)
3-5	224 (19.2)	215 (19.5)	2.15 (1.36-3.39)
1-2	168 (14.4)	221 (20.0)	1.57 (0.99-2.49)
None	33 (2.8)	68 (6.3)	1.00
Missing	3 (0.3)	2 (0.2)	

obtained by multiplying the number of days by the number of hours typically spent outside on weekdays and weekends during winter and summer months in the decade years (at age 10, 20, 30, 40, and 50, depending on a person's age), and summing across decades. This instrument was developed by Kricker et al. and found to be reliable and well correlated with skin damage (46-49). Sun exposure during outdoor activities was based on a list of 11 outdoor activities in which the participant had engaged for at least 4 days per year in the decade years. The outdoor activities included time spent at the beach or pool, sunbathing, boating or water-skiing, fishing, playing or coaching outdoor team sports, walking, hiking or jogging, biking, roller skating or rollerblading, golfing, playing tennis, playing outside, and gardening. The total number of days spent in each activity was multiplied by the number of hours for each activity, and summed across activities and decades. We also asked about total hours of sun exposure associated with all outdoor jobs during warmer and cooler months and calculated total hours in a manner similar to total hours for routine and outdoor activity sun exposure. Lifetime sunscreen use was measured by averaging the frequency of sunscreen use (almost always, more than half the time, about half the time, less than half the time, rarely, never) associated with each outdoor activity reported in each decade year.

Assessment of bias

Due to challenges in recruiting controls, we implemented procedures in July 2007 to assess potential for selection bias. Among persons that refused participation at the first recruitment call (excluding persons explicit about no further contact or that we had been unsuccessful in reaching), we randomly selected cases and controls to re-contact and ask six questions. The questions included past use of indoor tanning ("have you ever tanned indoors?"), total number of sessions if used, number of lifetime sunburns, skin sensitivity to sun, sunscreen use, and income. We also attempted to re-contact and query all cases and controls that had not returned the self-administered questionnaire by this point. Going forward, we then asked these questions of all persons during routine reminder calls to return the self-administered questionnaire. Altogether, we obtained this information from 32% of cases and 15% of controls among all nonparticipants.

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Table 3. The association between indoor tanning history with melanoma risk (Skin Health Study)

Indoor tanning	Cases *n* (%)	Controls *n* (%)	Age- and gender-adjusted OR (95% CI)	Multivariate adjusted OR* (95% CI)
Never used	433 (37.1)	538 (48.9)	1.00	1.00
Ever used	734 (62.9)	563 (51.1)	1.81 (1.51-2.21)	1.74 (1.42-2.14)
Frequency of use (h)				
1-9	322 (27.6)	289 (26.2)	1.58 (1.28-1.96)	1.46 (1.15-1.85)
10-19	74 (6.3)	66 (6.0)	1.62 (1.12-2.34)	1.81 (1.21-2.70)
20-49	129 (11.1)	90 (8.2)	2.10 (1.53-2.88)	2.18 (1.54-3.08)
50+	200 (17.1)	95 (8.6)	3.27 (2.42-4.41)	3.18 (2.28-4.43)
P trend			<0.0001	<0.0001
Frequency of use, sessions				
≤10	149 (12.8)	141 (12.8)	1.47 (1.12-1.93)	1.34 (1.00-1.81)
11-24	130 (11.1)	100 (9.1)	1.84 (1.36-2.48)	1.80 (1.30-2.49)
25-100	173 (14.8)	147 (13.4)	1.71 (1.30-2.23)	1.68 (1.25-2.26)
>100	275 (23.6)	154 (14.0)	2.71 (2.08-3.51)	2.72 (2.04-3.63)
P trend			0.0005	0.0002
Age at initiation (y)				
<18	209 (17.9)	161 (14.6)	2.18 (1.62-2.94)	1.85 (1.33-2.57)
18-24	175 (15.0)	125 (11.4)	2.14 (1.60-2.85)	1.91 (1.39-2.62)
25-34	150 (12.9)	143 (13.0)	1.43 (1.09-1,87)	1.46 (1.09-1.97)
35+	199 (17.1)	134 (12.1)	1.79 (1.38-2.33)	1.83 (1.37-2.43)
P trend			0.37	0.68
Duration of use (y)				
1	123 (10.5)	110 (10.0)	1.52 (1.13-2.03)	1.47 (1.06-2.02)
2-5	236 (20.2)	194 (17.6)	1.74 (1.36-2.21)	1.64 (1.26-2.15)
6-9	124 (10.6)	95 (8.6)	1.93 (1.41-2.64)	1.85 (1.31-2.61)
10+	245 (21.0)	146 (13.3)	2.47 (1.90-3.21)	2.45 (1.83-3.28)
P trend			0.0036	0.006
Burns from indoor tanning				
No	476 (40.8)	410 (37.2)	1.60 (1.32-1.95)	1.59 (1.28-1.97)
Yes	258 (22.1)	153 (13.9)	2.60 (2.00-3.39)	2.28 (1.71-3.04)
Number of times burned, indoor tanning				
1	62 (5.3)	37 (3.4)	2.46 (1.59-3.82)	2.40 (1.49-3.87)
2	53 (4.5)	41 (3.7)	1.99 (1.28-3.10)	1.83 (1.13-2.99)
3-5	70 (6.0)	46 (4.2)	2.42 (1.60-3.66)	2.05 (1.31-3.20)
>5	72 (6.2)	29 (2.6)	4.04 (2.52-6.49)	3.12 (1.86-5.23)
P trend			0.0001	0.01
Burns from sun after indoor tanning				
No	536 (45.9)	435 (39.5)	1.71 (1.41-2.08)	1.67 (1.35-2.07)
Yes	195 (16.7)	127 (11.5)	2.19 (1.67-2.88)	2.00 (1.48-2.70)

NOTE: Frequency totals for indoor tanning measures might not add up to 100% due to missing values.
*Adjusted for age, gender, eye color, natural hair color, skin color, freckles, moles, income, education, family history of melanoma, routine sun exposure, outdoor activity sun exposure, outdoor job exposure, mean sunscreen use, and number of lifetime painful sunburns; an additional 16 cases and 12 controls were excluded because the number of missing values was too small to be included as its own category.

We also assessed recall bias possibly introduced by physicians revealing the study hypothesis to their patients prior to permitting the release of names. So, beginning in May 2008, we asked each participant at the end of the telephone interview (12.9% and 17.3% of all interviewed cases and controls, respectively) if they had talked to a physician about the study before we first made contact with them.

Statistical analysis

Using multiple logistic regression, we calculated odds ratios (OR) and 95% confidence intervals (CI) for the

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likelihood of melanoma associated with having ever tanned indoors, frequency of use (total hours, sessions, or years), age of initiation, and burns from indoor tanning or sun after indoor tanning. Total hours, sessions, or years were divided into categories comparable with other reports. For these measures, a *P* value for trend was calculated by treating the categories as ordinal. We compared cases to controls according to the types of indoor tanning devices used and period of use, i.e., before 1990, 1990 or later, or in both periods. The year 1990 was chosen to identify the time period when high-speed/high-intensity and high-pressure devices became more widely available. We also examined use according to tumor location (head and neck, trunk, upper or lower limbs) and gender. All analyses were first adjusted for age at reference date (in years) and gender (if not stratified on this characteristic). In multivariate analyses, ORs and 95% CIs were also adjusted for income (≤$60,000, >$60,000, missing), education (completed college, did not complete college), eye color (gray/blue, green, hazel, or brown), hair color (red, blond, light brown, or dark brown/black), skin color (very fair, fair, light olive versus dark olive, brown, very dark brown, or black), freckles (none, very few, few, some, many, missing), moles (none, few, some, many, missing), family history of melanoma (yes or no, missing), total lifetime painful sunburns lasting more than 1 day (continuous), routine sun exposure (continuous), sun exposure from outdoor activities (continuous), sun exposure from outdoor jobs (continuous), and lifetime sunscreen use (continuous). A total of 16 cases and 12 controls were excluded because of missing data for one or more confounders.

To examine whether indoor tanning exposure initiated at a young age reflected higher cumulative exposure or biological susceptibility among younger persons, we examined age of initiation and duration of use simultaneously (among indoor tanners only), while adjusting for previously mentioned confounders. Similarly, we examined the period of use while controlling for total number of years used to determine whether or not exposure to earlier devices conferred greater risk than later devices, independent of total years of exposure. We compared users relative to nonusers (never tanners, plus nonusers of a specific device) of conventional, high-speed/high-intensity, and high-pressure devices in the same model to assess whether each device contributed independently to melanoma risk. We allowed for latency by estimating the likelihood of melanoma associated with indoor tanning use by stratifying according to use initiated more than or less than 15 years from the reference date. Associations between indoor tanning use and melanoma were examined by tumor characteristics (tumor site, Breslow's depth, presence of ulceration, or histologic subtype) and tested for statistically significant differences by age at diagnosis, gender, and phenotypic characteristics. Finding no evidence that results were modified by these characteristics (e.g., *P* for interaction by phenotypic characteristics ranged from 0.37 to 0.76), we present results for all cases and controls.

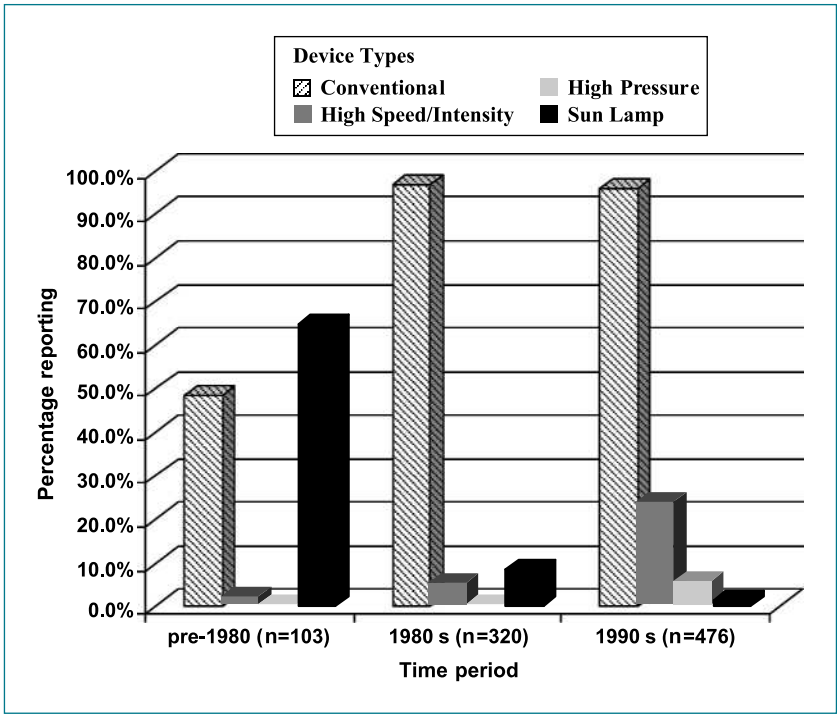

Figure 1. Tanning device use by time period among 563 controls (Skin Health Study).

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Results

Eligibility was determined for 72.5% of cases and 56.3% of controls (Table 1). Among known eligible cases and controls, 1,167 cases (84.6%) and 1,101 controls (69.2%) completed the self-administered questionnaire and telephone interview between December 2004 and March 2009. Due to frequency matching, cases and controls had similar age and gender distributions (Table 2); 98% of cases and 96% of controls were Caucasian. Phenotypic characteristics known to increase melanoma risk and greater number of sunburns were more common among cases than controls. For sun exposure, we observed no association with case-control status whether we assessed sun exposure from routine, outdoor recreational activities or occupational lifetime exposure. History of sunscreen use was reported more frequently by cases than controls in the crude analysis.

Indoor tanning use was reported by 62.9% of cases and 51.1% of controls (Table 3). Because age- and gender-adjusted ORs varied only slightly from multivariate-adjusted ORs, the latter are described throughout. The multivariate-adjusted OR for the likelihood of melanoma in relation to having ever tanned indoors was 1.74 (95% CI, 1.42-2.14) and confidence intervals excluded the null value. Melanoma risk increased markedly with frequency of use. Adjusted ORs ranged between approximately 2.5 and 3.0 for the highest category of use—50+ hours, more than 100 sessions, 10 or more years—and the P for trend was 0.006 to <0.0001, depending on the measure. A significant trend in the likelihood of melanoma with increasing number of sessions was also observed for melanomas arising on each tumor site (data not shown). When examined by gender, this dose-response pattern held for both men ($P < 0.0001$) and women ($P < 0.0001$) with melanoma arising on the trunk, among men with melanoma on the head and neck ($P = 0.05$), and among women diagnosed with melanoma on the upper ($P = 0.006$) or lower limbs ($P < 0.0001$). Cases were also more likely than controls to report having experienced painful burns from indoor tanning (adjusted OR, 2.28; 95% CI, 1.71-3.04), a greater number of indoor tanning-related burns (P trend = 0.01), or painful sunburns at a time when they thought they were protected from the sun by indoor tanning (adjusted OR, 2.00; 95% CI, 1.48-2.70).

Adjusted ORs for the likelihood of melanoma among users of indoor tanning relative to never users were similarly elevated regardless of the age when indoor tanning began (Table 3; P trend = 0.68). When we restricted the analysis to indoor tanners and simultaneously modeled age of initiation and total years used, ORs were attenuated for each category of age at which use began or according to number of years, but the significant trend associated with duration remained (data not shown). After accounting for age at initiation among indoor tanners, the risk of melanoma was concentrated among users for 10 or more years compared with users for only 1 year (adjusted OR, 1.77; 95% CI, 1.19-2.63).

Table 4. Association between indoor tanning device types and period of indoor tanning use and the likelihood of melanoma (Skin Health Study)

Indoor tanning	Cases	Controls	Age- and gender-adjusted OR (95% CI)	Multivariate adjusted OR* (95% CI)
	n (%)	*n* (%)		
Never used	433 (37.1)	538 (48.9)	1.00	1.00
Ever used device				
Conventional	697 (59.7)	535 (48.6)	1.83 (1.51-2.21)	1.76 (1.43-2.17)
High speed/high intensity	200 (17.1)	118 (10.7)	2.72 (1.99-3.70)	2.86 (2.03-4.03)
High pressure	55 (4.7)	25 (2.3)	3.79 (2.22-6.49)	4.44 (2.45-8.02)
Sun lamp	108 (9.3)	79 (7.2)	1.88 (1.34-2.63)	1.85 (1.27-2.70)
Periods of use				
Before 1990	135 (11.6)	96 (8.7)	1.85 (1.37-2.49)	1.63 (1.18-2.27)
After 1990	269 (23.1)	223 (20.3)	1.72 (1.36-2.19)	1.78 (1.37-2.32)
Both periods	327 (28.0)	235 (21.3)	1.94 (1.55-2.44)	1.83 (1.42-2.36)
Adjusted for no. of years used				
Before 1990			1.76 (1.30-2.38)	1.53 (1.09-2.13)
After 1990			1.51 (1.61-1.95)	1.51 (1.14-2.01)
Both periods			1.33 (0.96-1.84)	1.15 (0.81-1.64)

NOTE: Frequency totals for indoor tanning measures might not add up to 100% due to missing values.
*Adjusted for age, gender, eye color, natural hair color, skin color, freckles, moles, income, education, family history of melanoma, routine sun exposure, outdoor activity sun exposure, outdoor job exposure, mean sunscreen use, and number of lifetime painful sunburns; an additional 16 cases and 12 controls were excluded because the number of missing values was too small to be included as its own category.

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Table 5. Association between indoor tanning and risk of melanoma by possible recall and selection bias among cases and controls (Skin Health Study)

Observed	Cases	Controls	Crude OR (95% CI)	Adjusted OR (95% CI)*
All participants				
n	1,167	1,101		
% ever tanned indoors	62.9	51.1	1.62 (1.37-1.92)	1.74 (1.42-2.14)
Evaluation of recall bias				
Participants who talked with their physician[†]				
n	21	3		
% ever tanned indoors	71.4	66.7	1.25 (0.10-16.50)	—[‡]
Participants who did not talk with their physician				
n	130	188		
% ever tanned indoors	57.7	52.7	1.23 (0.78-1.92)	1.72 (0.92-3.22)
Evaluation of selection bias				
Nonparticipants who answered brief questionnaire				
n	107	180		
% ever tanned indoors	60.8	48.3	1.62 (1.00-3.61)	—[§]

*Adjusted for age, gender, eye color, natural hair color, skin color, freckles, moles, income, education, family history of melanoma, routine sun exposure, outdoor activity sun exposure, outdoor job exposure, mean sunscreen use, and number of lifetime painful sunburns; analysis among all participants excludes an additional 16 cases and 12 controls because the number of missing values was too small to be included as its own category. Analysis of recall bias excludes only two additional cases and three controls for the same reason.

[†]Excludes nine cases and three controls who responded "don't know" or whose response was missing.

[‡]Not possible to estimate due to small numbers.

[§]Confounders not collected on nonparticipants.

Controls reported use of different types of devices that generally coincided with their availability over time (Fig. 1); cases were more likely than controls to report use of each type of device shown. The likelihood of melanoma was significantly increased 2.86 and 4.44 times for users of high-speed/high-intensity devices and high-pressure devices, respectively; and 1.76 and 1.85 times for users of conventional devices and sunlamps, respectively, relative to never users (Table 4). When the reference group was changed to be nonusers of a specific device (as opposed to never users), the associations were attenuated, ranging from 1.6 to 1.9 depending on the device, yet confidence intervals for each estimate still excluded 1.0 (data not shown). The risk of melanoma was elevated for use occurring before or after 1990, or in both periods (Table 4). After accounting for the number of years of indoor tanning use in each period, these associations persisted except among cases and controls that reported use in both periods. The associations by device type, dose and duration were similar whether use was initiated at least 15 years prior to or within 15 years of the reference date (data not shown).

Crude ORs for the likelihood of melanoma among past compared with never users of indoor tanning were similar for participants and nonparticipants (Table 5). Among cases and controls that did and did not report speaking with a physician, crude ORs were each ~1.2, weaker than what was observed among all study participants. However, multivariate adjustment resulted in an OR of 1.72 among cases and controls that said they did not speak to their physician before enrolling in the study, similar to the overall point estimate of 1.74. The small number of cases and controls that reported speaking to their physician precluded calculation of an adjusted OR in this group.

Discussion

Our study has several important findings. First, we found that melanoma occurred more frequently among indoor tanners compared with persons that never engaged in this activity. Second, we found a strong dose-response relationship between melanoma risk measured by total hours, sessions, or years. Furthermore, this dose-response was also seen for melanomas arising on the trunk, not only in men but also in women, that would not ordinarily expose this site to UV radiation except when tanning or sunbathing. Third, we found an increased risk of melanoma with use of each type of tanning device as well as with each period of tanning use, suggesting that no device could be considered "safe." In addition, burns from indoor tanning seemed to be fairly common and conferred a similar risk of melanoma to sunburns. These associations remained significant even after

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adjusting for the potential confounding effects of known risk factors for melanoma.

We did not confirm the IARC report's emphasis on an increased risk of melanoma with first exposure to indoor tanning "in youth", defined as use before the age of 36 (5). Except for one cohort and two case-control studies that examined indoor tanning during adolescence in relation to melanoma (30-32), all other reports considered use prior to ages 25 to 30 (11, 17, 21), or restricted the analysis to cases diagnosed before the age of 36 (22, 28). This restriction, however, could have resulted in the exclusion of older cases and controls that may have been exposed at a younger age. An elevated risk of melanoma associated with first use at younger ages has been consistently observed across these studies, but this is also the case for indoor tanning used at older ages in some reports reviewed by the IARC (11, 17, 22, 28, 31). Our study was designed to specifically evaluate indoor tanning use initiated at any age. And by simultaneously accounting for duration of use among indoor tanners, our analysis indicates that early age exposure is most likely a marker for cumulative exposure, the reason for an excess risk of melanoma, not that younger individuals are at increased susceptibility to the effects of UV radiation. Although no other study has analyzed these data in the same manner as we did, three reports provide further support for our observation. One recent report found total hours of sunbed exposure to be much higher (34 versus 9 hours) among persons that first tanned indoors before compared with after age 15 years (32). And in two studies that stratified frequency of indoor tanning use by age of cases, elevated risks for melanoma were observed for those with 10 or more sessions, regardless of age (22), or for those with regular use up to the age of 60 (28).

With our carefully designed questionnaire eliciting the use of specific devices that emit differing amounts of UVB and UVA, we observed considerably stronger ORs for melanoma among users of high-speed or high-pressure devices than among users of conventional devices. We still cannot be certain, however, that these results reflect higher exposure to UVB from high-speed devices or higher exposure to UVA from high-pressure devices. First, the proportion of subjects reporting use of these devices was quite low. Second, studies have shown that the percentage of UVB and UVA emitted depends on the type of lamp, the quality of maintenance, and the level of degradation—information that cannot be collected through retrospective recall (50-53). Recently, inspections of tanning devices in European tanning salons have revealed poor compliance with regulations for the allowable distribution of UVB versus UVA, with a concomitant increase in the proportion of UVB beyond permissible limits over time (54-56). If UVA is carcinogenic in humans, as stated in the IARC report, our findings are biologically plausible. However, it is also possible that the devices we assessed, regardless of our classification scheme, emitted sufficient UVB for that component of UV radiation to be the reason for the observed associations. Similar to our experience, other studies that collected information about device types have not been able to single out any one type as being higher risk than another (21, 27, 30, 32). Nor have most studies, ours included, found higher risks of melanoma associated with indoor tanning exposure in a specific period, despite changes in emission of UV components over time (21, 23, 30, 57). Although disentangling which wavelength is responsible for melanoma development might not be possible in epidemiologic studies, the evidence also indicates that all indoor tanning devices are harmful.

We did not find lifetime routine sun exposure or sun exposure via recreational outdoor activities or occupations to be associated with melanoma risk, nor were these results changed by a detailed examination of sun exposure according to season, decade age, type of outdoor activity, indoor tanning status, or tumor site. Indeed, published studies reveal that the relationship between sun exposure and melanoma is complex, and depends on whether the exposure is intermittent or chronic; inconsistencies in its measurement further complicates an understanding of these relationships. A meta-analysis of 57 studies (58) and a pooled analysis of 15 studies (59) each reported fairly weak associations between total sun exposure and melanoma, no relationship to chronic exposure (based on outdoor occupations), moderately strong associations with intermittent exposure (usually defined as sunbathing, time spent during sunny vacations, or outdoor recreational activities), and strong associations with sunburn. Thus, our results are in agreement with these reports for chronic exposure and sunburns. To the extent that sunburns are a marker of intermittent sun exposure, then our results adequately represent the independent effect of indoor tanning use on the risk of melanoma. Differential underreporting of sun exposure by cases seems to be a less likely explanation of these trends in our study; had it been operative, we might have expected the same to occur for cases' report of artificial solar exposure. Although our findings could reflect less variation in sun exposure among a relatively homogenous population residing in Minnesota, or the younger age of our study sample in contrast with most case-control studies of melanoma, we cannot exclude the possibility that nondifferential misclassification obscured a relationship between sun exposure and melanoma.

Although the prevalence of indoor tanning among participating controls (51.1%) is high compared with most other reports, we do not think this is due to differential selection of indoor tanners into the study. In a 2002 Minnesota statewide survey of adults, age 18 and older (37), we found that overall, 36.3% of respondents reported indoor tanning use; prevalence was higher (42%) in the sample with the same age range as the current study. More importantly, the frequency of indoor tanning use was very similar when we compared participating and nonparticipating cases and controls and crude ORs for the association between indoor tanning use and melanoma were identical for participants and

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nonparticipants. We were also concerned that cases that had discussed the study with their physician might have reported higher frequency of indoor tanning use than cases that did not. We attempted to address this potential bias by querying both cases and controls in the latter part of the study. The fact that several controls (whose physicians were not contacted) reported discussions with their physician about the study prior to participating is also interesting. As the prevalence of overreporting was similar for both cases and controls in this group, and the adjusted OR among cases and controls that did not speak with a physician was similar to what we reported for the entire sample, recall bias seems less likely to explain our results. This conclusion is further supported by a recent nested case-control study, which reported no consistent pattern of recall bias for indoor tanning or other melanoma risk factors (60).

In summary, our study provides strong evidence that indoor tanning is a risk factor for melanoma. Due to the strength of the association, the dose-response, the results by tumor site (especially the trunk), and the ability to account for known confounders, our results address several limitations of previous studies. Our results also indicate that the number of times an individual is exposed to indoor tanning is more important than exposure to indoor tanning at an early age. Our ancillary studies on bias, although limited in scope, suggest that our results are not explained by selection or recall bias. In conclusion, our results add considerable weight to the IARC report that indoor tanning is carcinogenic in humans and should be avoided to reduce the risk of melanoma.

Disclosure of Potential Conflicts of Interest

No potential conflicts of interest were disclosed.

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Indoor Tanning and Risk of Melanoma: A Case-Control Study in a Highly Exposed Population

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