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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 2004-2007 at ages 25-59, were ascertained from a statewide cancer registry; age-, 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, device types 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 1167 cases and 1101 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). Odds ratios 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 International Agency for Research on Cancer that tanning devices are carcinogenic in humans.

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Keywords

melanoma; indoor tanning; case-control study

Introduction

Melanoma incidence increased 2.2% and 2.1% annually between 1997 and 2006 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 ten most common cancers in Caucasians, even as most common cancers are declining or stable. Intense, intermittent solar ultraviolet radiation has long been thought to account for the rise in melanoma (2). Indoor tanning is an artificial source of intermittent ultraviolet 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 U.S. cities found that the average number of tanning salons exceeded the average number of Starbucks or McDonald's (4).

In 2009, the International Agency for Research on Cancer (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 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), history of indoor tanning has been only weakly associated with melanoma (IARC (5) reported a summary odds ratio based on 19 studies of 1.15, 95% CI 1.00, 1.31), and limitations of these studies include the lack of information on sun exposure (a known correlate of indoor tanning use (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 reported on age of initiation in the same manner (11,17,21-23,²⁵,27,28,30-32). Consequently, the evidence is limited that melanoma occurrence increases with frequent indoor tanning use. In addition, only three studies have examined melanoma in relation to indoor tanning use during adolescence (30-32), when indoor tanning is most likely to be initiated (37). While 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 1980's emitted much higher levels of UVB compared to normal solar ultraviolet radiation. These were followed by the introduction in the 1980's of devices emitting primarily UVA to address the public's concern about burning (42-45). In the 1990's, 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 that 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 law, 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 websites, 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 vary 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 who 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 utilized 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 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 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 eleven outdoor activities in which the participant had engaged for at least four days per year in the decade years. The outdoor activities included time spent at the beach or pool, sunbathing, boating or waterskiing, 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 recruiting controls, we implemented procedures in July 2007 to assess potential for selection bias. Among persons who refused participation at the first recruitment call (excluding persons explicit about no further contact or who 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

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 non-participants. 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 and 95% confidence intervals for the 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 to 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/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, odds ratios and 95% confidence intervals were also adjusted for income (\leq \$60,000, >\$60,000, missing), education (completed college, did not complete college), eye color (grey/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 one 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 non-users (never tanners, plus non-users of a specific device) of conventional, highspeed/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 subytpe) 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.

Results

Eligibility was determined for 72.5% of cases and 56.3% of controls (Table 1). Among known eligible cases and controls, 1167 cases (84.6%) and 1101 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). Since ageand gender-adjusted odds ratios varied only slightly from multivariate-adjusted odds ratios, the latter are described throughout. The multivariate-adjusted odds ratio 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 odds ratios ranged between approximately 2.5 and 3.0 for the highest category of use--50+ hours, more than 100 sessions, ten 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 odds ratios 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, odds ratios 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 ten or more years compared to users for only one year (adjusted odds ratio 1.77, 95% CI 1.19, 2.63).

Controls reported use of different types of devices that generally coincided with their availability over time (Figure 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 non-users 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 who 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 odds ratios for the likelihood of melanoma among past compared to never users of indoor tanning were similar for participants and non-participants (Table 5). Among cases and controls who did and did not report speaking with a physician, crude odds ratios were each around 1.2, weaker than what was observed among all study participants. However, multivariate adjustment resulted in an odds ratio of 1.72 among cases and controls who 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 who reported speaking to their physician precluded calculation of an adjusted odds ratio in this group.

Discussion

Our study has several important findings. First, we found that melanoma occurred more frequently among indoor tanners compared to persons who 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, who would not ordinarily expose this site to ultraviolet 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 can be considered "safe". In addition, burns from indoor tanning appeared to be fairly common and conferred a similar risk of melanoma to sunburns. These associations remained significant even after 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 who 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 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 ultraviolet radiation. Although no other study has analyzed data in the same manner as we did, three reports provide further support for our observation. One recent report found total hours of sun bed exposure to be much higher (34 vs 9 hours) among persons who first tanned indoors before compared to 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 to elicit use of specific devices that emit differing amounts of UVB and UVA, we observed considerably stronger odds ratios for melanoma among users of high speed or high pressure devices than among users of conventional devices. We still cannot be certain, however, 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 percent 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). And recently, inspections of tanning devices in European tanning salons have revealed

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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 ultraviolet 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). While disentangling which wavelength is responsible for melanoma development may 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 (58) and a pooled analysis (59), of 57 and 15 studies, respectively, 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 under-reporting 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. While 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 to most case-control studies of melanoma, we cannot exclude the possibility that non-differential misclassification obscured a relationship between sun exposure and melanoma.

Although the prevalence of indoor tanning among participating controls (51.1%) is high compared to 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 odds ratios for the association between indoor tanning use and melanoma were identical for participants and non-participants. We were also concerned that cases who had discussed the study with their physician may have reported higher frequency of indoor tanning use than cases who 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 over-reporting was similar for both cases and controls in this group, and the adjusted odds ratio among cases and controls who 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, while 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.

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Legend

| Device | e Types |
|--------|----------------------|
| | Conventional |
| | High Speed/Intensity |
| | High Pressure |
| | Sun Lamp |

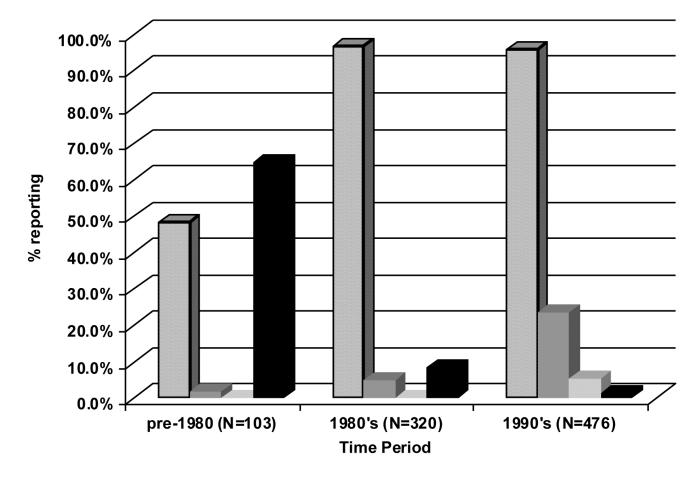


Figure 1. Tanning Device Use by Time Period Among 563 Controls, Skin Health Study

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| | Ca | Cases | Cor | Controls |
|--|------|---------|------|----------|
| | Z | (%) | Z | (%) |
| Total from cancer registry (cases) or from drivers license list (controls) | 2026 | (100.0) | 3095 | (100.0) |
| Unable to determine eligibility | | | | |
| Total | 557 | (27.5) | 1354 | (43.7) |
| No phone available | 16 | 164 | 5 | 598 |
| Not reached by phone | L | 71 | 5 | 273 |
| Subject Refused | L | 79 | 4 | 468 |
| Physician refusal | 12 | 124 | | |
| Died | 2 | 23 | | 15 |
| Non-participating institution | 6 | 93 | | |
| Other | (1) | 3 | | |
| Respondent not eligible | | | | |
| Total | 89 | (4.4) | 151 | (4.9) |
| Prior melanoma | | 76 | | 4 |
| Non-cutaneous melanoma | (1 | 2 | | |
| Not melanoma | - | _ | | |
| Not residing in Minnesota | 0 | 0 | C | 63 |
| Language/other | Ē | 10 | | 74 |
| Respondents screened and eligible | | | | |
| Total | 1380 | (68.1) | 1590 | (51.4) |
| Did not return self-administered questionnaire | 186 | (13.5) | 447 | (28.1) |
| Did not return | 1 | 128 | 6 | 269 |
| Refused | 5 | 55 | 1 | 174 |
| Died | (1 | 5 | | - |
| Other | - | _ | | 3 |
| Did not complete telephone interview | 27 | (1.9) | 42 | (2.7) |

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|--------------------------|--|
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| Cases Controls | N (%) N (%) | 17 26 | 9 14 | 1 2 |
|----------------|-------------|-------|------|-----|
| | | | | |

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(69.2)

(84.6) 1101

1167

Completed self-administered questionnaire and Telephone interview

Refused/incomplete Died/Incapable

Not reached

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Table 2

Comparison of cases and controls in the Skin Health Study

| | Ű | Cases | Co | Controls | Crude | Crude Odds Ratio |
|-------------------------------|-----|--------|-----|----------|-------|------------------|
| Characteristic | Z | (%) | Z | (%) | 5) | (95% CI) |
| Age (years) | | | | | | |
| 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 | 669 | (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) | 7 | (0.2) | | |
| Eye color | | | | | | |
| Grey/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) |
| Blond | 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) |

| | С | Cases | Col | Controls | Crude | Crude Odds Ratio |
|--|-----|--------|-----|----------|-------|------------------|
| Characteristic | N | (%) | Z | (%) | 6) | (95% CI) |
| Fair | 827 | (70.9) | 746 | (67.8) | 3.63 | (1.83, 7.18) |
| Light olive | 114 | (8.8) | 191 | (17.4) | 1.95 | (0.96, 3.99) |
| Dark olive, brown, black | 11 | (0.0) | 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 | (0.0) | 9 | (0.5) | | |
| Freckles | | | | | | |
| Many | 18 | (1.6) | 11 | (1.0) | 1.90 | (0.89, 4.06) |
| Some | 75 | (6.4) | 4 | (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) | 9 | (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) | | |
| Lifetime routine sun exposure, hours | | | | | | |
| 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 | 9 | (0.5) | 4 | (0.4) | | |
| Lifetime sun exposure from outdoor activities, hours | | | | | | |
| High | 388 | (33.2) | 367 | (33.3) | 0.95 | (0.78, 1.16) |
| Medium | 378 | (32.4) | 377 | (34.2) | 06.0 | (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, hours | | | | | | |

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| | C | Cases | Col | Controls | Crude | Crude Odds Ratio |
|---|-----|--------|-----|----------|-------|------------------|
| Characteristic | Z | (%) | Z | (%) | 6) | (95% CI) |
| 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 | 9 | (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 one day) | | | | | | |
| >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 | ю | (0.3) | 7 | (0.2) | | |

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The association between indoor tanning history with melanoma risk, Skin Health Study

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| | | Cases | 3 | Controls | Age- and Gender- Adjusted Odds Ratio | usted Odds Katio | Multivariate Adjusted Odds Ratio T | isted Odds Ratio/ |
|----------------------------|-----|--------|-----|----------|--------------------------------------|------------------|---------------------------------------|-------------------|
| Indoor Tanning | Z | (%) | z | (%) | (95% CI) | (II | (95% | (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, hours | | | | | | | | |
| 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) | 99 | (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, years | | | | | | | | |
| <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, years | | | | | | | | |
| 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 | | | | | | | | |

| Multivariate Adjusted Odds Ratio \dot{t} | Cases Controls Age- and Gender- Adjusted Odds Ratio Multivariate Adjusted Odds Ratio † | Controls | Cases |
|--|---|----------|-------|
| | | | |
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| Indoor Tanning | Z | (%) N | Z | (%) | (95% CI) | (I) | (95% CI) | CI) |
|--|-----|-----------------------|-----|------------|----------|--------------|----------|--------------|
| No | 476 | 476 (40.8) 410 (37.2) | 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 | 50 | | | | | | | |
| 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 | 536 (45.9) | 435 | 435 (39.5) | 1.71 | (1.41, 2.08) | 1.67 | (1.35, 2.07) |
| Yes | 195 | 195 (16.7) 127 (11.5) | 127 | (11.5) | 2.19 | (1.67, 2.88) | 2.00 | (1.48, 2.70) |

⁷Adjusted for age, gender, eye color, natural hair color, freckles, moles, income, education, family history of melanoma, routine sun exposure, outdoor activity sun exposure, outdoor job exposure, mean sunscreen use, number of lifetime painful sunburns; additional 16 cases and 12 controls excluded because the number of missing was too small to be included as its own category. Table 4

Association between indoor tanning device types and period of indoor tanning use and the likelihood of melanoma, Skin Health Study

| Multivariate Adjusted Odds Ratio † | |
|---|--|
| s Age- and Gender-Adjusted Odds Ratio | |
| Controls | |
| Cases | |

| Indoor Tanning | Z | (%) | Z | (%) | | (95% CI) | | | (95% CI) |
|---------------------------|-----|--------|-----|--------|------|----------|-------------------|------|--------------|
| 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. | (1.51, 2.21) | 1.76 | (1.43, 2.17) |
| High speed/High intensity | 200 | (17.1) | 118 | (10.7) | 2.72 | (1: | (1.99, 3.70) | 2.86 | (2.03, 4.03) |
| High pressure | 55 | (4.7) | 25 | (2.3) | 3.79 | (2.: | (2.22, 6.49) | 4.44 | (2.45, 8.02) |
| Sun Lamp | 108 | (9.3) | 79 | (7.2) | 1.88 | (1: | (1.34, 2.63) | 1.85 | (1.27, 2.70) |
| Periods of use | | | | | | | | | |
| Before 1990 | 135 | (11.6) | 96 | (8.7) | 1.85 | (1: | (1.37, 2.49) | 1.63 | (1.18, 2.27) |
| After 1990 | 269 | (23.1) | 223 | (20.3) | 1.72 | (1: | (1.36, 2.19) | 1.78 | (1.37, 2.32) |
| Both Periods | 327 | (28.0) | 235 | (21.3) | 1.94 | (1. | (1.55, 2.44) | 1.83 | (1.42, 2.36) |
| Adjusted for # years used | | | | | | | | | |
| Before 1990 | | | | | 1.76 | (1: | (1.30, 2.38) | 1.53 | (1.09, 2.13) |
| After 1990 | | | | | 1.51 | (1) | (1.61, 1.95) | 1.51 | (1.14, 2.01) |
| Both Periods | | | | | 1.33 | (0) | (0.96, 1.84) 1.15 | 1.15 | (0.81, 1.64) |

⁷ Adjusted for age, gender, eye color, natural hair color, freckles, moles, income, education, family history of melanoma, routine sun exposure, outdoor activity sun exposure, outdoor job exposure, mean sunscreen use, number of lifetime painful sunburns; additional 16 cases and 12 controls excluded because the number of missing was too small to be included as its own category. Association between indoor tanning and risk of melanoma by possible recall and selection bias among cases and controls, Skin Health Study

| | Cases | | | amenta and a second and a second and a second and a second a secon | and a second second | 1 ano. 22 /0 CT |
|--|-------|------|-----------|--|---------------------|-----------------|
| Observed | | | | | | |
| All Participants | | | | | | |
| Z | 1167 | 1101 | | | | |
| % ever tanned indoors | 62.9 | 51.1 | 51.1 1.62 | (1.37, 1.92) | 1.74 | (1.42, 2.14) |
| Evaluation of recall bias | | | | | | |
| Participants who talked with their physician I | | | | | | |
| Z | 21 | ю | | | | |
| % ever tanned indoors | 71.4 | 66.7 | 1.25 | (0.10, 16.50) | 2 | |
| Participants who did not talk with their physician | | | | | | |
| Z | 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 | | | | | | |
| Non-participants who answered brief questionnaire | | | | | | |
| Z | 107 | 180 | | | | |
| % ever tanned indoors | 60.8 | 48.3 | 1.62 | (1.00, 3.61) | ارى | |

Not possible to estimate due to small numbers.

 $\mathcal{F}_{Confounders not collected on non-participants.}$

⁷ Adjusted for age, gender, eye color, natural hair color, freckles, moles, income, education, family history of melanoma, routine sun exposure, outdoor activity sun exposure, outdoor job exposure, mean sunscreen use, number of lifetime painful sunburns; analysis among all participants excludes additional 16 cases and 12 controls because the number of missing was too small to be included as its own category; analysis of recall bias excludes additional 2 cases and 3 controls only for the same reason.