
WHAT’S KNOWN ON THIS SUBJECT: The incidence of childhood and adolescent melanoma has been significantly increasing up to 2004. Risk factors (fair skin, light-colored hair/eyes, female gender, presence of nevi, family history, increased number of sunburns, and exposure to UV radiation) are associated with melanoma.

WHAT THIS STUDY ADDS: This study describes incidence trends of melanoma diagnosed between the ages of 0 and 19 years and from 1973 through 2009 by gender, stage and age at diagnosis, primary site, and exposure to UV radiation.

abstract

OBJECTIVE: Childhood and adolescent melanoma is rare but has been increasing. To gain insight into possible reasons underlying this observation, we analyzed trends in melanoma incidence diagnosed between the ages of 0 and 19 years among US whites by gender, stage, age at diagnosis, and primary site. We also investigated incidence trends by UV-B exposure levels.

METHODS: By using Surveillance, Epidemiology, and End Results (SEER) program data (1973–2009), we calculated age-adjusted incidence rates (IRs), annual percent changes, and 95% confidence intervals for each category of interest. Incidence trends were also evaluated by using jointpoint and local regression models. SEER registries were categorized with respect to low or high UV-B radiation exposure.

RESULTS: From 1973 through 2009, 1230 children of white race were diagnosed with malignant melanoma. Overall, pediatric melanoma increased by an average of 2% per year (95% confidence interval, 1.4%–2.7%). Girls, 15- to 19-year-olds, and individuals with low UV-B exposure had significantly higher IRs than boys, younger children, and those living in SEER registries categorized as high UV-B. Over the study period, boys experienced increased IRs for melanoma on the face and trunk, and females on the lower limbs and hip. The only decreased incidence trend we observed was among 15- to 19-year-olds in the high UV-B exposure group from 1985 through 2009. Local regression curves indicated similar patterns.

CONCLUSIONS: These results may help elucidate possible risk factors for adolescent melanoma, but additional individual-level studies will be necessary to determine the reasons for increasing incidence trends. Pediatrics 2013;131:846–854

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ABBREVIATIONS

APC—annual percent change
CI—confidence interval
IR—incidence rate
loess—local regression
SEER—Surveillance, Epidemiology, and End Results

Ms Wong carried out the analyses, drafted and revised the manuscript, and approved the final manuscript as submitted; Dr Harris supervised analytical methods, reviewed the manuscript, and approved the final manuscript as submitted; Dr Rodriguez-Galindo reviewed the manuscript and approved the final manuscript as submitted; and Dr Johnson conceptualized and designed the study, critically reviewed the manuscript, and approved the final manuscript as submitted.

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Malignant melanoma is the most common skin cancer in children and adolescents <20 years, representing 1% of all new cases diagnosed annually in the United States. Two previous studies reported significant incidence increases of 2.3% per year between 1973 and 2001 and 1992 and 2004. Melanoma incidence among young Caucasian women in the United States is also increasing at an annual rate of 2.7%.

Risk factors for adult melanoma include fair skin, white race, light-colored hair/eyes, female gender, increased numbers of benign/dysplastic nevi or childhood sunburns, melanoma family history, the genetic disease xeroderma pigmentosum, and UV radiation exposure. There is also an increased risk for melanoma in adulthood among survivors of hereditary retinoblastoma, Hodgkin lymphoma, and gonadal tumors, and soft tissue sarcoma. Recent studies indicate indoor tanning is a risk factor, whereas use of sun protection methods is associated with a decreased melanoma risk.

Childhood and adolescent melanoma risk factors are less well understood. Whereas melanomas in older children and adolescents (≥10 years) behave similarly to adult melanomas, those in younger individuals are thought to have a different etiology. Unlike adults, more girls are affected than boys, and whites are at higher risk than other racial groups. Other reported associations include number of melanocytic nevi, tanning ability, and freckling. Melanomas are also associated with sites of medium/large congenital nevi and xeroderma pigmentosum. Other factors include placental metastases from the mother and immunosuppression.

Although studies have highlighted increasing adult melanoma incidence and illuminated likely contributing factors to population trends, no recent studies have specifically focused on childhood and adolescent melanoma incidence. Therefore, our objective was to describe trends in childhood and adolescent melanoma incidence diagnosed between the ages of 0 and 19 years in the United States by gender, stage, age at diagnosis, and primary site for the period 1973 through 2009 by using data from the Surveillance, Epidemiology, and End Results (SEER) database. In addition, we investigated associations with UV exposure levels.

METHODS

Study Population

We used SEER*Stat software (version 7.0.9) to access SEER 9 incidence data, which included cases from 1973 through 2009. The SEER 9 cancer registries include Atlanta (1975+), Connecticut, Detroit, Hawaii, Iowa, New Mexico, San Francisco-Oakland, Seattle-Puget Sound (1974+), and Utah. We included first malignancies only of melanoma diagnosed <20 years as defined according to the International Classification of Childhood Cancer categories.

Variable Classification

Stage at diagnosis was classified by using SEER historic stage A, with localized, regional, distant, and unstaged categories. Primary site of melanoma was coded according to the International Classification of Diseases for Oncology, Third Edition. Age categorization (0–9, 10–14, and 15–19 years) was based on standard age groups available from SEER 9 (<1, 1–4, 5–9, 10–14, and 15–19 years), the small number of cases from 0 to 9 years (n = 104), and the general thought that melanoma etiology is different in children <10 years than adolescents (10–19 years). The methodology for stratifying SEER registries according to UV-B radiation flux has been previously described. Average annual UV-B flux was collected from various geographic locations and varied by latitude, altitude, and sky cover. Originally, the SEER registries were categorized as north (Seattle, Connecticut, Detroit, Iowa), central (San Francisco-Oakland, San Jose-Monterey, Utah), or south (Atlanta, Los Angeles, New Mexico). However, because of the small number of cases, we categorized the registries into 2 groups with those locations previously designated “north” classified as low UV-B and all others classified as high UV-B exposure.

Statistical Analysis

Age-standardized (2000 US standard population) incidence rates (IRs) were calculated by SEER*Stat and expressed as melanoma cases per 100,000 people. Incidence by gender, stage and age at diagnosis, primary site, and UV-B exposure were examined. Annual percentage change (APCs), and 95% confidence intervals (CIs) were assessed by using Joinpoint Regression Software (version 3.5.0) to calculate weighted least-squares regressions. Because of the small number of cases, we allowed ≤1 inflection point, or joinpoint, to be fit when determining any magnitude or directional changes in incidence. The independent variable was calendar year in 5-year intervals except for the interval 2003 through 2009 that included 7 years. Because cancer rates arise from a Poisson distribution and are skewed for rare cancers, the dependent variable was the natural logarithm of the age-adjusted IR for melanoma by gender, stage and age at diagnosis, site, and UV-B exposure. Because of unstable 1-year trend estimates resulting from few cases in some subcategories, IRs and APCs were based on number of cases over each 5-year time interval. Local regression (loess) was used to examine incidence patterns over time by using the same interval endpoints. Loess is a nonparametric, fitting method used in the presence of outliers in the data. Loess analyses were conducted in
RESULTS

Of the 1317 childhood and adolescent melanoma cases diagnosed from 1973 through 2009, 7 occurred among blacks; 33 among American Indians, Alaska Natives, or Asian/Pacific Islanders; 1 of unspecified race; 46 of unknown race/ethnicity; and 1230 among whites. Because of the small number of nonwhite melanoma cases, we included only whites in our analyses. Frequencies, IRs, and best-fit joinpoint regression models by gender, age and stage at diagnosis, primary site, and UV-B exposure are presented in Table 1. The melanoma IR was 1.6 times higher in girls (7.4) than in boys (4.6). Within each age group, melanoma incidence was also higher among girls than boys (data not shown). Melanoma IRs increased substantially since the 1970s by an average of 2% per year for both boys (APC, 1.9%; 95% CI, 1.1%–2.6%) and girls (APC, 2.2%; 95% CI, 1.4%–3.1%) with no significant joinpoints.

Melanoma incidence increased with age with IRs of 1.1, 3.6, and 18.0 among 0- to 9-, 10- to 14-, and 15- to 19-year olds, respectively. However, APCs were only significant among 10- to 14-year olds (APC, 2.9%; 95% CI, 1.0%–4.7%) and 15- to 19-year olds (APC, 1.9%; 95% CI, 1.2%–2.5%).

By stage, the incidence was higher in localized (IR = 4.6) than regional melanomas (IR = 0.8). Among localized melanomas (limited to organ in which it began, without evidence of spread), the rate increased significantly from 1973 to 1990 with an APC of 4.3% (95% CI, 0.5%–8.2%), followed by a non-significant APC of 0.9% from 1990 to 2009 (95% CI, −1.8% to 3.5%). For regional melanomas (beyond primary site to nearby lymph nodes, organs, or tissues), a significant increase was observed over the entire period (APC, 5.9%; 95% CI, 2.7%–9.2%).

Among primary sites, significantly increased trends were observed from 1973 through 2009 for the skin on unspecified parts of the face (APC, 4.5%; 95% CI, 0.7%–8.4%), trunk (APC, 2.8%; 95% CI, 1.2%–4.5%), and lower limbs and hip (APC, 2.6%; 95% CI, 1.7%–3.5%). With respect to UV-B exposure, overall IRs were slightly higher in high (IR = 6.7, 95% CI 6.2%–7.3%) than low (IR = 5.4, 95% CI 5.1%–6.0%) UV-B registries. Melanoma incidence increased from 1973 through 2009 in low UV-B areas with an APC of 3.7% (95% CI, 2.6%–4.7%), whereas the IRs in high UV-B registries remained fairly stable (Table 1).

The loess curves varied by age at diagnosis, but the trends by gender within each group were similar (Fig 1). Overall, girls had higher IRs than boys, and 15- to 19-year-olds had the highest incidence at each time point examined. For boys and girls, there was a slightly negative slope between 1990 and 1995 for 15- to 19-year-olds and 10- to 14-year-olds. Overall, the trends were almost parallel for all age groups. The trend remained nonsignificant among 0- to 9-year-olds and also for 10-
14-year-olds until 1995, where a slight increase in incidence begins. We further analyzed IRs by site and UV-B exposure by gender (Table 2). For site, we focused on only those with overall significant trends from Table 1, because many sites had too few numbers to continue stratifying by gender or age at diagnosis. Although the overall melanoma IR was similar for boys and girls, there were significant differences by site. Among boys, there was an increasing IR on the skin of other/unspecified parts of the face from 1973 through 2009 (APC, 5.2%; 95% CI, 1.3%—9.2%). In addition, the skin of the trunk had a less steep linear increase from 1973 through 2009 (APC, 2.6%; 95% CI, 0.9%—4.4%). Females had a significantly increasing IR in the lower limbs and hip (APC, 3.2%; 95% CI, 1.8%—4.7%). Only low UV-B exposure demonstrated an increasing trend in melanoma incidence with the rates being similar for both genders.

Finally, we examined IRs for site and UV-B exposure by age at diagnosis (Table 3). There were no significant trends among 0- to 9-year-olds. Among 10- to 14-year-olds, only IRs in the lower limbs and hip increased (APC, 3.3%; 95% CI, 0.7%—6.0%). In 15- to 19-year-olds, incidence increased significantly on the trunk (APC, 3.0%; 95% CI, 1.6%—4.4%) and lower limbs and hip (APC, 2.5%; 95% CI, 1.2%—3.8%). Among low UV-B exposure cases, there were significant incidence increases, with the greater increased rate among 10- to 14-year-olds (APC, 4.6%; 95% CI, 1.9%—7.3%) than 15- to 19-year-olds (APC, 3.3%; 95% CI 2.2%—2.4%). In addition, cases among 15- to 19-year-olds categorized as high UV-B exposure experienced a decreased IR starting in 1985 (APC, —1.5%; 95% CI, —2.9% to 0.1%). This is the only significant negative trend among all of our analyses. The loess curve for 15- to 19-year-olds by UV-B exposure shows incidence in the low UV-B group exceeding the high UV-B group in 2000 and
continuing to increase through the end of the study period (Fig 2).

We conducted additional analyses that included individuals with unknown race ($n = 48$; data not shown). Comparison of loess curves and incidence trends demonstrated similar findings, with few differences in APC trends. There was an additional significant trend among female cases on the skin of the trunk (APC, 6.3%; 95% CI, 1.4%–11.5%). Although larger numbers made this trend apparent, they could not be confirmed when using white race cases only. In addition, the best-fit model for cases among 15- to 19-year-olds on the skin of the trunk contained 1 joinpoint when including unknown race (1975–1990: APC, 5.6%; 95% CI, 4.5%–6.7%; 1990–2009: APC: 1.2%; 95% CI, 0.6%–1.9%). There was 1 significant trend among whites only that was not observed when individuals with unknown race were included (15- to 19-year-olds in high UV-B regions). We note, however, that the race restriction allowed us to find significant trends, even though the numbers are slightly smaller. Overall, using only whites in the analysis provided similar results to when we included cases of unknown race.

**DISCUSSION**

Similar to recent adult patterns, our analyses indicate melanoma incidence is increasing among adolescents. While overall trends were similar for both genders, melanoma incidence in boys is specifically increasing on the skin of the face and trunk, but only on the lower limbs and hip for girls. As expected, trends by stage at diagnosis correspond to the development of sentinel lymph node biopsies, which is associated with regional upstaging of melanomas starting in the early 1990s. However, this shift in incidence cannot explain the overall increase from 1973 through 2009. Finally, there was an unexpected increased trend in low UV-B exposure registries, with a negative trend in high UV-B registries for 15- to 19-year-olds starting in 1985.

Increasing incidence of childhood and adolescent melanoma have also been reported in other countries. An Australian study reported a significantly increased trend from 1983 through 1996 for children ≤14 years of age followed by a significantly decreased incidence trend that corresponds to the launch of Australian sun protection education campaigns in

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**TABLE 2** APC for Anatomic Site of Melanoma and UV-B Exposure by Gender, From 1973 Through 2009

<table>
<thead>
<tr>
<th>Category</th>
<th>Male APC (95% CI)</th>
<th>Female APC (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>All sites</td>
<td></td>
<td></td>
</tr>
<tr>
<td>C44.3: Skin of other/unspecified</td>
<td></td>
<td></td>
</tr>
<tr>
<td>parts of face</td>
<td></td>
<td></td>
</tr>
<tr>
<td>C44.5: Skin of trunk</td>
<td></td>
<td></td>
</tr>
<tr>
<td>C44.7: Skin of lower limb and hip</td>
<td></td>
<td></td>
</tr>
<tr>
<td>UV-B exposure</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Low</td>
<td></td>
<td></td>
</tr>
<tr>
<td>High</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

All data are 1973–2009 except as noted.
* APC was calculated via weighted least-squares regression.
* Best fit model contained 1 joinpoint. APC (0 joinpoint), 0.03%; 95% CI, −1.2 to 1.0.
* Years 1990–2009.
* Indicates statistical significance at the .05 level.

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**TABLE 3** APC for Anatomic Site of Melanoma and UV-B Exposure by Age at Diagnosis

<table>
<thead>
<tr>
<th>Age Group</th>
<th>Male APC (95% CI)</th>
<th>Female APC (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>0–9 y</td>
<td></td>
<td></td>
</tr>
<tr>
<td>10–14 y</td>
<td></td>
<td></td>
</tr>
<tr>
<td>15–19 y</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

All data are 1973–2009 except as noted.
* APC was calculated via weighted least-squares regression.
* Best fit model contained 1 joinpoint. APC (0 joinpoint), 0.03%; 95% CI, −1.8 to 1.7.
* Years 1990–2009.
* Indicates statistical significance at the .05 level.
the late 1980s. Decreasing melanoma incidence from 1993 through 2002 has also been reported in Swedish individuals <20 years old, which has also been suggested to result from education campaigns aimed at reducing sun exposure starting in the mid-1980s. A study in England reported an increased melanoma incidence trend for female 15- to 24-year-olds from 1968 through 2005. The increasing melanoma incidence, especially in 15- to 19-year-olds, is consistent with our analyses. For 0- to 9-year-olds, melanoma incidence was fairly stable from 1973 through 2009. No other study has reported, to our knowledge, on trends in this age group. Our incidence trends for primary site of melanoma by gender are also similar to other studies among 15- to 39-year-olds and across all age groups.

Possible reasons underlying the overall increase in adolescent melanoma incidence in the United States over 1973 through 2009 fall into 3 major categories: (1) temporal changes in the prevalence of melanoma risk factors, such as increased UV exposure from natural (sunlight) and artificial (tanning beds) sources; (2) increased melanoma case ascertainment; and (3) melanoma overdiagnosis. A major melanoma risk factor is UV exposure. Early-life sun exposure may be critical with respect to melanoma risk because most of an individual’s total lifetime UV exposure occurs during childhood. Solar UV-B rays are primarily responsible for sunburns. Children and adolescents spend more time outdoors, especially in the summer, and may receive 3 times more UV-B rays annually than adults. However, studies reported no change in sunburn prevalence among adolescents or association between melanoma and UV exposure in children <15 years old. Studies also suggest UV exposure had been increasing over the past 30 years in higher latitudes. Recent data has indicated stable UV measurements since the
1990s. This is consistent with our results suggesting UV-B exposure is not the primary factor in increased melanoma incidence. However, all significantly increasing trends for melanoma over our study period occurred in sun-exposed areas of the body. Although solar UV-B exposure is a confirmed melanoma risk factor, increasing evidence suggests UV-A exposure from tanning beds also increases risk. The growth of the indoor tanning industry began in the 1970s. Indoor tanning prevalence is highest among US adolescents with 24% of 13- to 19-year-olds reporting any use, and 11.7% reporting frequent use of ≥10 times. A cross-sectional US study also described similar findings with 24.6% of 15- to 19-year-old girls reporting having ever used tanning beds. In addition to girls being more likely to tan indoors than boys, cities with higher percentages of whites and lower UV index scores have significantly higher densities of indoor tanning facility densities. Increased availability of such facilities in lower versus higher UV areas could explain why adolescent melanoma incidence is only increasing in the low UV-B exposure group. In addition, the differences in indoor tanning practices and availability of such facilities could explain why melanoma incidence is greater in girls than in boys.

Increased maternal age has been associated with an increased risk for childhood/adolescent melanoma, which could partially explain the increasing incidence as the average parental age has increased over time. Additional research is needed to confirm whether maternal age and other familial factors can explain the observed trends. It is also possible that childhood and adolescent melanoma incidence trends are due to increased capture of melanoma cases by cancer registries. Recent evidence suggests the current increased adult melanoma incidence is predominantly explained by an increasing incidence of thinner melanomas. Increased ascertainment of thinner melanomas could explain the observed trends. Although thickness data were available starting in 1988, only 54% of melanomas in our analyses had known thickness. Because sentinel lymph node biopsies are recommended for patients with tumors >1 mm, it is possible that cases diagnosed in the localized stage reflect temporal trends in thin melanomas. With this caveat in mind, trends still did not suggest that increases in melanoma after 1990 were driven by thin melanomas. Finally, although increased melanoma incidence has been attributed to overreporting in other cancer registries, SEER is considered the gold standard for case ascertainment. Increases in local/regional melanomas could also be attributed to more unstaged cases being classified with respect to stage, but this would not explain the overall increased incidence. Additional investigation into the completeness of SEER is warranted to resolve whether capture of melanomas by registry has increased over time.

Improved completeness in capturing melanomas could be attributed to heightened awareness. Early detection and treatment was encouraged through the ABCD (asymmetry, border irregularity, color variegation, or diameter >0.6 cm) rule starting in 1985. In the same year, the American Academy of Dermatology began sponsoring free skin cancer screening clinics. Increased melanoma capture, coupled with increased UV exposure and use of tanning beds, could all contribute to the incidence increases. A third factor that could contribute to the observed increase in adolescent melanoma is overdiagnosis. Increased incidence trends in adults have been characterized as the result of overdiagnosis after changes in diagnostic criteria in the 1970s and subjective interpretation when distinguishing melanoma from benign nevi. It is currently unclear whether misclassification of benign nevi as malignant melanoma in SEER has increased over time or contributes to the rising incidence of adolescent melanoma. We also acknowledge the complexity of differential diagnosing melanocytic lesions in young children, especially on the face. Lesions of benign or indeterminate malignant potential are possibly responsible for changes in incidence or site predominance. However, the age trends suggest increased incidence in malignant melanoma is responsible for our findings.

Our study includes over 30 years of melanoma incidence data from 9 US cancer registries. Our results are consistent in older children with trends observed in adult melanoma populations and provide new insights into the current trends in childhood and adolescent melanoma. The strengths of using SEER include the high rate of case ascertainment and data quality. However, with an ecologic study design, we did not have individual-level information on outdoor UV exposure, indoor tanning behavior, familial factors, or thickness of lesions that would allow causal inferences with respect to trends. In addition, changes in diagnosis patterns over time may have affected incidence data in a manner that we could not account for in our analysis.

CONCLUSIONS

Melanoma incidence continues to increase from previous studies, especially in adolescents and sun-exposed areas of the body with some evidence for geographic variation. These data did not indicate that UV-B exposure was a driving factor for increased incidence. Future individual-level studies are
needed to elucidate the underlying reasons for the increasing incidence of adolescent melanoma. Despite increasing rates, we note that malignant melanoma survival rates have increased since the 1970s. Five-year survival is currently nearly 100% for cases diagnosed in localized stages versus 82% for cases diagnosed in regional or distant stages. These data emphasize the importance of early detection.

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