

Rising Melanoma Incidence Rates of the Trunk among Younger Women in the United States

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Abstract

Background: Melanoma rates are rising among young women, possibly due to increasing UV radiation to previously protected body sites. Therefore, we examined melanoma incidence trends by age, gender, and body site. Descriptive methods were complemented with the age-period-cohort parameters net drift and longitudinal age trend.

Methods: Case and population data were obtained from the Surveillance, Epidemiology, and End Results (SEER) 9 Registries Database (1975-2006). Net drift summarized the average annual percentage change in log-linear rates per year of calendar-time (or year of diagnosis). Longitudinal age trend summarized the average annual percentage change by attained age at diagnosis. Early- and late-onset melanomas have low and high longitudinal age trends, respectively.

Results: There were 105,829 melanomas diagnosed in the SEER 9 Registries. The overall age-adjusted incidence rate (IR) for melanoma was 17.7/100,000 person-years. Age-specific IRs were greater among women than men prior to age 40 years. Among women, IRs decreased for all anatomic sites relative to the trunk. The highest net drift occurred in truncal lesions among women (net drift, 3.8%/year of calendar time; 95% confidence interval, 3.5-4.0%). The lowest longitudinal age trends also were observed for truncal lesions among women (longitudinal age trend, 5.4%/year of attained age; 95% confidence interval, 5.1-5.7).

Conclusions: Although melanoma IRs overall have risen for decades, the combination of high net drift and low longitudinal age trend show that melanomas are rising preferentially on the trunk among young women.

Impact: Future surveillance and analytic studies should consider melanoma effect modification by age, gender, and body site. *Cancer Epidemiol Biomarkers Prev*; 19(9); 2401-6. ©2010 AACR.

Introduction

A continuous increase of cutaneous malignant melanoma incidence rates has been observed in the United States over the last four decades (1). The underlying causes of these rising melanoma trends are widely debated, although most authors attribute them to environmental risk factors and changes in sun exposure behavior (2). If the long-standing increases are caused by changes in sun-related behavior between generations, site-specific surveillance may be the most effective way of following these changes (3). It also has been recognized that anatomic sites of melanomas vary by gender, with the majority of melanomas occurring on the trunk and the lower extremity among men and women, respectively (4). Given that an increase in tan-seeking UV radiation exposure

might place anatomic sites usually covered by clothing at greater relative risk for melanoma, i.e., the trunk among women (5), we further assessed melanoma incidence trends by age, gender, and anatomic body site.

Materials and Methods

Case and population data among white women and men were obtained from the National Cancer Institute's Surveillance, Epidemiology, and End Results (SEER) 9 Registries Database (6). SEER's 9 registries include 5 states (Connecticut, Hawaii, Iowa, New Mexico, and Utah) and 4 metropolitan areas (Atlanta, Detroit, San Francisco-Oakland, and Seattle-Puget Sound), covering approximately 10% of the U.S. population (6). Demographic and tumor characteristics included gender, age at diagnosis, and anatomic body site. We created 16 4-year age groups (ages 15-18, 19-22, ..., 75-78 years) and 8 4-year time periods (1975-1978, 1979-1982, ..., 2003-2006). Anatomic sites were defined using the International Classification of Diseases for Oncology-3rd edition (ICD-O-3; ref. 7) as previously described (8). Anatomic body sites included skin of the face, head, and neck (C44.0-44.4), trunk (C44.5, including back, abdomen, and chest), upper extremity (C44.6), lower extremity

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Table 1. Cutaneous malignant melanoma from SEER 9 Registries Database, 1975-2006

	All cases		Females		Males		
Total <i>n</i>	105,829		48,183		57,646		
% of total cases	100		45.5		54.5		
Rate	17.7		15.2		21.4		
Mean age, years	55.7		53.0		57.9		
Variable	All cases		Females		Males		IRRFemale:Male (95% CI)
	<i>n</i>	Rate	<i>n</i>	Rate	<i>n</i>	Rate	
Age at diagnosis							
<20 years	1,036	0.6	628	0.7	408	0.5	1.6 (1.4-1.8)
20-29 years	6,598	6.8	4,212	8.9	2,386	4.8	1.8 (1.7-1.9)
30-39 years	13,987	14.6	8,069	17.0	5,918	12.3	1.3 (1.3-1.4)
40-49 years	18,635	22.5	9,225	22.3	9,410	22.8	1.0 (0.9-1.0)
50-59 years	19,941	30.4	8,395	25.3	11,546	35.8	0.7 (0.6-0.7)
60-69 years	19,040	39.5	7,016	27.4	12,024	53.2	0.5 (0.5-0.6)
70-79 years	16,614	49.6	6,177	31.7	10,437	74.7	0.4 (0.4-0.5)
≥80 years	9,978	53.3	4,461	35.4	5,517	90.1	0.3 (0.3-0.4)
Anatomic site							
Face/head/neck	20,643	3.5	6,701	2.0	13,942	5.5	0.3 (0.3-0.4)
Trunk	35,155	5.9	12,003	3.9	23,152	8.3	0.4 (0.4-0.5)
Upper extremity	24,584	4.1	12,328	3.9	12,256	4.5	0.9 (0.8-0.9)
Lower extremity	20,589	3.4	15,391	4.9	5,198	1.9	2.6 (2.6-2.7)
Other*	4,858	0.8	1,760	0.6	3,098	1.2	0.5 (0.4, 0.5)

NOTE: Rates are per 100,000 and age-adjusted to the 2000 U.S. Standard Population (Census P25-1130). Incidence rates and confidence intervals were derived from SEER*Stat software program 6.52. Relative risks were expressed as IRRs, where a given characteristic was compared with a referent characteristic with an assigned IRR of 1.0. Confidence intervals (δ method) are 95% for IRR. **"Other" includes tumors coded as skin, not otherwise specified in SEER.

(C44.7), and all "other or unknown" body sites combined into a single category. Combining of the "other or unknown" category had no statistically significant effects on the results (data not shown).

We used SEER*Stat 6.5.2 (6) to obtain age-standardized (2000 U.S. population) invasive melanoma incidence rates (IR) and to assess statistical significance at the 95% confidence level. Relative risks for anatomic body sites were expressed as incidence rate ratios (IRR) in which face/head/neck, upper extremity, and/or lower extremity were compared with the trunk as the referent site with an assigned IRR of 1.0. For example, $IRR_{\text{face/head/neck:trunk}} < 1.0$ showed that IRs were greater for the trunk than for face/head/neck. $IRR_{\text{face/head/neck:trunk:trunk}} > 1.0$ showed that IRs were greater for the face/head/neck than for trunk. Secular trends in the IRRs were expressed as percentage change (%CH) from the earliest to the most recent 4-year time period (1975-1982 to 1999-2006). All statistical tests were two-sided.

We used MATLAB 2009b (9) to calculate median age at diagnosis, as well as age-period-cohort parameters to simultaneously assess age-specific incidence rates that

were adjusted for calendar period and birth cohort effects. Two very useful and estimable age-period-cohort parameters for descriptive studies are the net drift (10) and the longitudinal age trend (11). Net drift is the sum of the linear trends in the period and cohort effects for all age groups combined. It estimates the average annual percentage change in the logarithm of the incidence rates over time. Net drift is conceptually similar to the estimated annual percentage change of the age-standardized incidence rate. Longitudinal age trend is another type of drift parameter that is defined as the sum of the linear trends in the age and period effects. It estimates the average annual percentage change in the logarithm of the incidence rates per year of attained age. Early-onset and late-onset cancers have low and high longitudinal age trends, respectively (12).

Results

There were 105,829 microscopically confirmed invasive cutaneous melanomas diagnosed in SEER's 9 Registries Databases from 1975 through 2006. The overall

age-adjusted IR was 17.7/100,000 person-years (p-y). The mean age at diagnosis was lower in women than men (53.0 versus 57.9, respectively; $P < 0.001$; Table 1). Age-specific IRs were greater among women than men prior to age 40 years [IR, 6.9 versus 4.6/100,000 p-y respectively; IRR, 1.5; 95% confidence interval (95% CI), 1.4-1.6; $P < 0.001$].

The most common anatomic sites were the lower extremity in women (IR, 4.9 per 100,000 p-y; 95% CI, 4.8-5.0) and the trunk in men (IR, 8.3 per 100,000 p-y; 95% CI, 8.2-8.4; Table 1). Notwithstanding these overall rates, the frequency distributions of melanomas shifted over time by gender and anatomic site (Table 2). Among women, incidence rates decreased for all anatomic sites relative to the trunk with negative percentage changes in the $IRR_{\text{site:trunk}}$ ranging from -11.8% for $IRR_{\text{upper extremity:trunk}}$ to -24.0% for $IRR_{\text{face/head/neck:trunk}}$. Conversely, among men, incidence rates generally increased for anatomic sites relative to the trunk with the exception of the lower extremity (i.e., $IRR_{\text{lower extremity:trunk}}$ -6.8%).

The age-period-cohort net drift and longitudinal age trend for melanoma by gender and anatomic site are shown in Fig. 1A and B, respectively. The greatest secular trends occurred for truncal lesions among women with the highest net drifts (Fig. 1A), i.e., net drift at 3.8% per year of calendar time (95% CI, 3.5-4.0%). In a sensitivity analysis that was stratified by age groups <40 and ≥ 40 years, we observed similar increases for trunk melanomas among women ages <40 years but not among women ages ≥ 40 years. Longitudinal age trends were generally

lower for women than for men (Fig. 1B), consistent with the well-acknowledged predominance of early-onset melanomas among women (8). Indeed, the lowest longitudinal age trends were observed for truncal lesions among women, i.e., the longitudinal age trend was 5.4% per year of attained age (95% CI, 5.1-5.7).

Discussion

Despite the long-term increases in melanoma incidence rates, there has been only one recent trend analysis by anatomic site at a single large academic center in the United States (13). Although it is well established that the majority of melanomas occur on the trunk and the lower extremities for men and for women, respectively (4), our results further showed that melanoma of the trunk in women increased between the time periods 1975-1982 and 1999-2006 over 9 SEER Registries in the United States at a greater rate than for other sites in women, whereas the opposite was observed for men. The increase in trunk melanoma in women could be secondary to changes in sun exposure from various cultural, environmental, or behavioral factors. As described earlier, changes in the net drift suggest differential secular trends, whereas differences in longitudinal age trends suggest differential age-related biological or natural history effects. Hence, the combination of high net drift and low longitudinal age trend of female trunk melanoma in Fig. 1A and B shows that melanomas are rising preferentially on the trunk among young women.

Table 2. Temporal trends for cutaneous malignant melanoma by sex and anatomic site, using SEER 9 Registries Database (1975-2006)

	1975-1982			1999-2006			1975-1982 to 1999-2006 Percentage change in $IRR_{\text{site:trunk}}$ (95% CI)
	<i>n</i>	Rate	$IRR_{\text{site:trunk}}$ (95% CI)	<i>n</i>	Rate	$IRR_{\text{site:trunk}}$ (95% CI)	
Females							
Trunk	1,582	2.3	1.0	4,667	5.3	1.0	NA
Face/head/neck	1,038	1.5	0.7 (0.1-0.7)	2,475	2.6	0.5 (0.5-0.5)	-24.0% (-20.1 to -28.7)
Upper extremity	1,737	2.6	1.1 (1.0-1.2)	4,741	5.3	1.0 (0.8-1.0)	-11.8% (-11.4 to -12.3)
Lower extremity	2,286	3.3	1.4 (1.4-1.5)	5,747	6.5	1.2 (1.2-1.3)	-16.1% (-15.6 to -16.7)
Males							
Trunk	2,914	4.8	1.0	8,988	11.1	1.0	NA
Face/head/neck	1,479	2.7	0.6 (0.5-0.6)	5,936	7.9	0.7 (0.7-0.7)	24.6% (23.6-25.2)
Upper extremity	1,338	2.2	0.5 (0.4-0.5)	5,213	6.6	0.6 (0.6, 0.6)	27.3% (26.1-28.5)
Lower extremity	699	1.2	0.3 (0.2-0.3)	2,087	2.5	0.2 (0.2, 0.2)	-6.8% (-6.6 to -7.2)

NOTE: Rates are per 100,000 and age-adjusted to the 2000 U.S. Standard Population (Census P25-1130). Incidence rates and confidence intervals were derived from SEER*Stat software program 6.52. Relative risks were expressed as IRRs, where a given characteristic was compared with a referent characteristic with an assigned IRR of 1.0. Confidence intervals (δ method) are 95% for IRR and percentage change. Percentage changes were calculated using 1 year for each end point. Abbreviation: NA, not applicable.

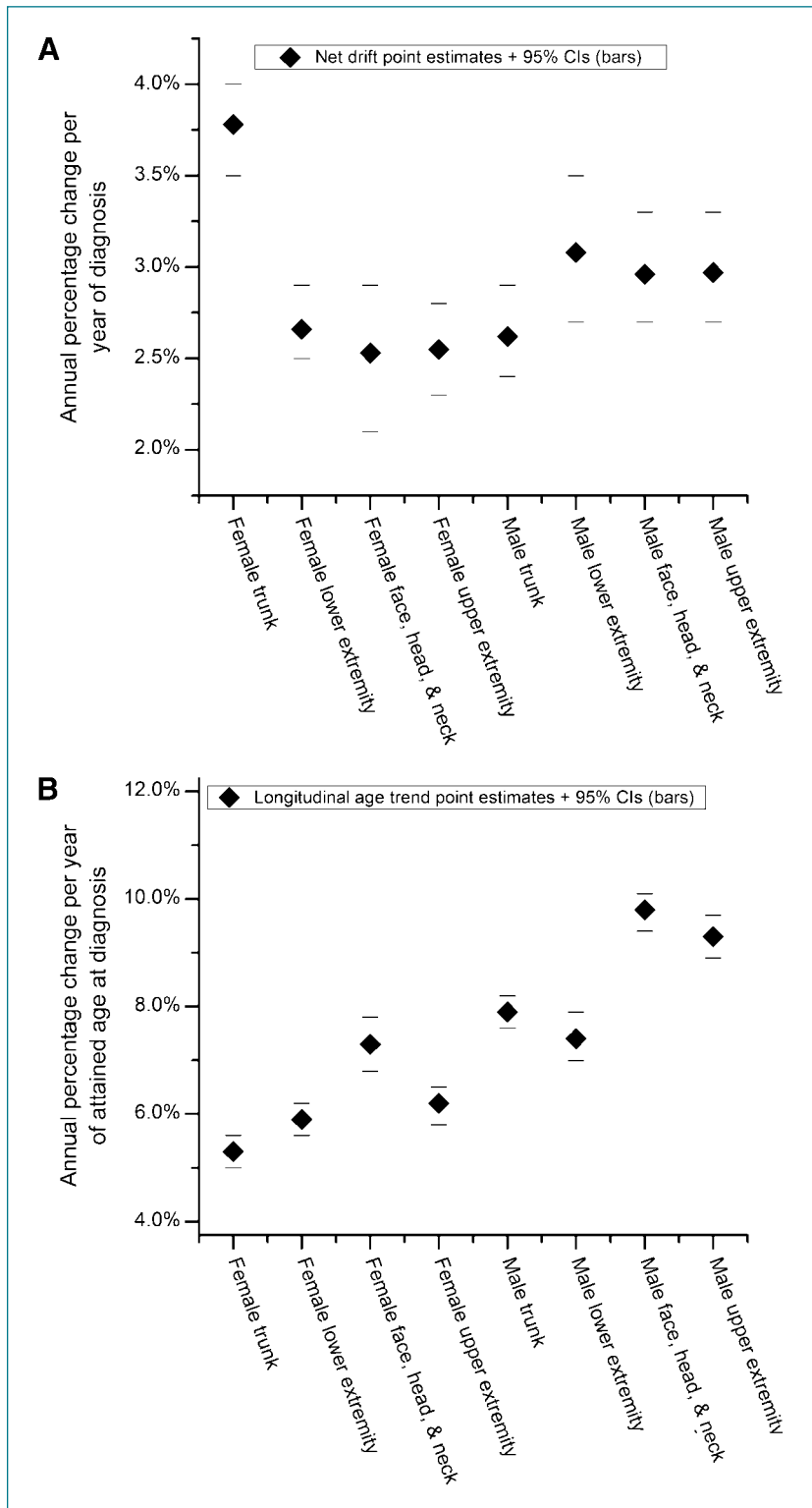


Figure 1. Age-period-cohort parameters for invasive cutaneous melanoma by gender and anatomic body site (SEER 9; 1975-2006). A, net drift point estimates and 95% CI (bars). Net drift is a summary measure of the overall linear trend in the period plus cohort effects. It is closely related to the estimated annual percentage change in the age-standardized incidence rate (see text for details). B, longitudinal age trend point estimates and 95% CI (bars). Longitudinal age trend is a summary measure for the overall linear trend in the age plus period effects. Low longitudinal age trends represent tumors that develop early in life; high longitudinal age trends reflect tumors that develop late in life.

Past studies in the United States (13) and other countries have also shown the increasing prevalence of trunk melanoma in women (14) and younger patients (15, 16). Melanomas developing at different body sites

are thought to be associated with distinct patterns of sun exposure, and the different anatomic distribution of lesions in men and women has been attributed to gender-specific patterns of sun exposure (15). Melanomas of the

head and neck are associated with chronic sun exposure, whereas trunk melanomas are thought to be associated with intermittent patterns of sun exposure, supporting the hypothesis that melanomas may arise through divergent causal pathways (8, 17). Some authors have suggested that susceptibility of melanocytes to malignant transformation might be site dependent, which could help explain why the relevance of known risk factors is not uniform by body site (18). The variable age distribution of risk by gender and anatomic site, particularly for trunk melanoma, might also support the hypothesis of a possible modulator role of sex hormones in female trunk melanoma (16). Estrogens are known to increase the number of melanocytes and modify their melanin content (19). However, one would need to hypothesize that sex hormones are changing over time; hence, the relationship between sex hormones and trunk melanoma should be analyzed further.

The rising melanoma incidence rates of the trunk in young women could also be partially caused by changes in clothing patterns. Young females are frequently wearing bikinis on the beach, and summer female casual clothes often leave part of the back and front of the trunk exposed to the sun (16). Finally, the increase in melanomas of the trunk in women could also be secondary to changes in sun exposure or a result of increased tanning behavior. It is worth noting that usage of tanning beds, recently classified by the International Agency of Research on Cancer as a cause of melanoma (20), is most prevalent among young women (21, 22).

This analysis has important limitations. Like most population-based registry studies, our analyses lacked information on individual risk factors, particularly a history of UV radiation exposure and characterization of nevus pattern, and had the potential of incomplete data collection. It is also widely recognized that trends in melanoma incidence are affected by underreporting (23) and surveillance issues. Melanoma has a longer reporting delay (up to 7 to 10 years) than other cancer sites because of the difficulties associated with reporting a cancer that is increasingly diagnosed in a nonhospital

setting (24). Because there is a delay, the melanoma estimates for recent years are minimal levels of risk and may rise as data collection for recent years is completed. Case finding is, therefore, an important aspect of data quality control for the SEER program, and SEER has adjusted data collection activities for melanoma to try to minimize errors. Age-period-cohort models share in all of the intrinsic limitations of standard descriptive studies. Additionally, because age, period, and cohort are collinear (cohort = period – age), it is impossible to determine the independent effects for age, period, and cohort, giving rise to the so-called nonidentifiability issue. Nonetheless, the parameters net drift and longitudinal age trend can be identified in the restricted age-period-cohort model, following the method of Holford (25). Thus, using these two estimable parameters, we have shown statistically significant evidence for rising trunk melanomas in young women in the United States.

In conclusion, we present evidence for changing melanoma anatomic trends in the United States. Trunk melanomas among younger women in the United States are increasing relative to all other anatomic body sites, suggesting different trends in carcinogenic exposures or etiologic differences by melanoma anatomic site. Future surveillance and analytic studies on melanoma should include gender and anatomic site.

Disclosure of Potential Conflicts of Interest

The authors state no conflict of interest.

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