

## Recent Trends in Cutaneous Melanoma Incidence Among Whites in the United States

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**Background:** It is not yet clear whether increasing melanoma incidence is real or whether recent incidence trends mainly reflect improved diagnosis. To address this question, we examined the most recent melanoma incidence patterns among the white population stratified by sex, age, tumor stage, and tumor thickness by use of data from the Surveillance, Epidemiology, and End Results Program. **Methods:** We examined log-transformed age-specific rates for melanoma by 5-year age groups and time periods by year of diagnosis and birth cohort. Melanoma trends were further examined among broader age groups (<40 years, 40–59 years, and ≥60 years) by tumor stage and tumor thickness. Rates were age-adjusted to the 1970 U.S. standard population, and trends were tested by use of a two-sided Student's *t* test. **Results:** Melanoma incidence increased in females born since the 1960s. From 1974–1975 through 1988–1989, upward trends for the incidence of localized tumors and downward trends for the incidence of distant-stage tumors occurred in the age group under 40 years. In the more recent time period, 1990–1991 through 1996–1997, age-specific rates among females compared with males generally remained stable or declined more for distant-stage tumors and increased less for local-stage tumors. Thin tumors (<1 mm) increased statistically significantly in all age groups ( $P < .05$  for all), except in men under age 40 years. In contrast, rates for thick tumors (≥4 mm) increased statistically significantly ( $P = .0003$ ) only in males aged 60 years and older. **Conclusion:** Melanoma incidence may well continue to rise in the United States, at least until the majority of the current population in the middle-age groups becomes the oldest population. The recent trends may reflect increased sunlight exposure. [J Natl Cancer Inst 2001;93:678–83]

Skin melanoma is among the most rapidly increasing cancers among the white population in the United States (1), although the rate of increase in the incidence rate appears to be declining. The lifetime risk of being diagnosed with melanoma is 1.91% in white men and 1.37% in white women (2). Sun exposure in childhood (3) and intense intermittent sun exposures (4–7) are suggested to be the major environmental risk factors. We recently reported the changing geographic patterns of mortality from melanoma on the basis of data from 1950 through 1994 (8). In the investigation presented in this article, we analyze the incidence patterns of melanoma stratified by sex, age, tumor stage, and tumor thickness to determine whether the increasing melanoma incidence is real or whether the increasing recent trends mainly reflect improved diagnosis.

### METHODS

Incidence data for invasive melanoma were obtained from the Surveillance, Epidemiology, and End Results (SEER)<sup>1</sup> Program; data for *in situ* melanoma were excluded from analyses. Annual sex-specific and age-adjusted rates using the 1970 U.S. standard population were calculated and then plotted by year of diagnosis. Their trends were assessed by a joinpoint regression model (9), which characterizes changing trends over successive segments of time and the amount of increase or decrease within each segment. To describe age-specific trends by year of diagnosis and year of birth, we computed rates by 5-year age groups (15–19 years, 20–24 years, . . . , 80–84 years, and 85 years or older) and by 5-year time periods (from 1973–1977 through 1993–1997); 5-year (grouped and averaged) rates provide more stable rates. Then we plotted the rates by calendar year of diagnosis (middle year of the 5-year group) or calendar year of birth by use of a logarithmic scale for the ordinate (10).

We also fitted a formal age–period–cohort model (11) to these data to evaluate changes in the slope of incidence trends by birth cohort. The change in the slope (*C*) was quantified by use of the identifiable parameter (12,13) centered on birth-cohort *j* as defined by

$$C = (3\gamma_{j+3} + \gamma_{j+2} - \gamma_{j+1} - 3\gamma_j) - (3\gamma_j + \gamma_{j-1} - \gamma_{j-2} - 3\gamma_{j-3}),$$

where  $\gamma_j$  denotes the birth-cohort effect identified by birth-cohort *j*. This parameter compares two linear contrasts, the first contrast characterizing the slope of the birth-cohort curve for the later birth cohorts (*j* to *j* + 3) and the second characterizing the slope for the earlier birth cohorts (*j* – 3 to *j*). A negative value for this parameter indicates a decrease in the birth-cohort slope around cohort *j*.

Melanoma cases were categorized into three defined tumor stages: local, regional, and distant (2). Local stage indicates that the cancer is confined to the skin as the primary site, regional stage indicates that the cancer involves regional lymph nodes, and distant stage indicates that the cancer has spread to other organs of the body from its primary site. To examine historic and more recent trends of melanoma by these tumor stages, rates age-adjusted to the 1970 U.S. standard population were computed for age groups: under 40 years, 40–59 years, 60 years and older, and all ages combined for grouped (and averaged) calendar years from 1974–1975 through 1988–1989 and from 1990–1991 through 1996–1997. Estimated annual percent changes (EAPCs) were calculated by fitting a regression line to the natural logarithm of the age-adjusted rates, weighted by the inverse of the estimated variance of the logarithm of age-adjusted rates, using the calendar year as the predictor variable, i.e.,  $y = bx + a$ , where  $y = \ln(\text{rate})$ ,  $x = \text{calendar year}$ , and  $a = \text{constant}$ ; then the EAPC =  $(e^b - 1) \times 100$ . The coefficients, *b*, were tested for being different from zero by use of the two-sided Student's *t* test at  $P < .05$  significance level (14).

Information on tumor thickness in the SEER database is available for cases diagnosed since 1988 (15). We categorized invasive melanoma cases according to their thickness into less than 1 mm, 1 to less than 4 mm, and greater than or equal to 4 mm. Then we computed the annual age-adjusted rates from 1988 through 1997 by thickness for all primary lesions for age groups less than 40 years, 40–59 years, 60 years and older, and all ages. We also computed the

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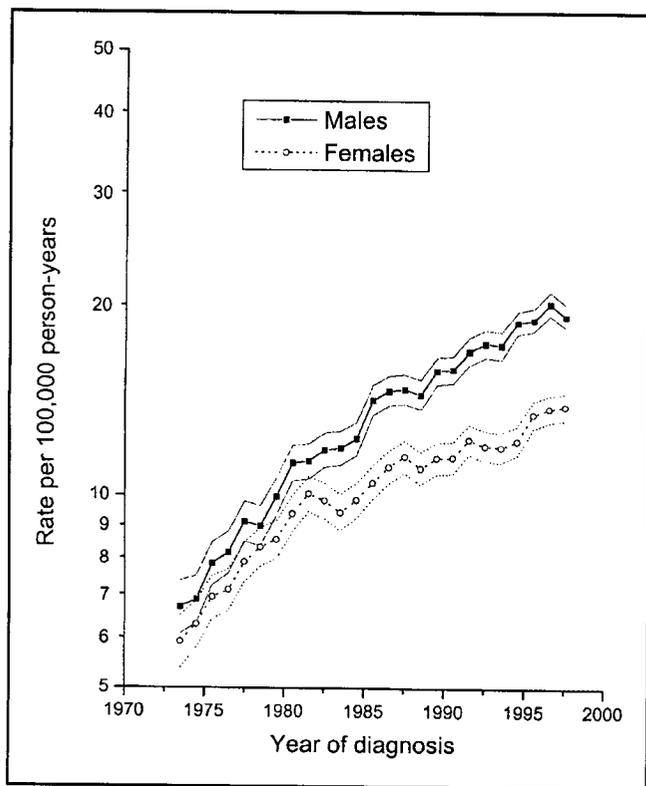
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age-adjusted rates by thickness for only the first primary melanoma. The EAPCs for all primaries were calculated by following the method described above.

## RESULTS

Between 1973 and 1997, 60 541 invasive skin melanoma cases were diagnosed among whites residing in the SEER areas. The incidence rates are expressed as the number of cases per 100 000 person-years of observation. Age-adjusted incidence rates almost tripled among males, from 6.7 in 1973 to 19.3 in 1997, and more than doubled among females, from 5.9 to 13.8 (Fig. 1). Joinpoint analyses showed that the rates rose less steeply in the recent period compared with the earlier period for both males and females. In men, the EAPCs declined from 7.2 between 1973 and 1980 to 3.6 between 1980 and 1997; in women, the EAPCs declined from 6.7 between 1973 and 1980 to 2.2 between 1980 and 1997.

Fig. 2 shows the temporal trends of melanoma by 5-year age groups at diagnosis. In the early years, incidence among white males increased rapidly in most age groups. Rates continued to rise in the middle-aged and older-aged groups, while they tended to stabilize in the younger-aged groups in the more recent years. The patterns among females were generally similar to those among males, although rates increased less rapidly in females in the early years; more recently, rates flattened in the middle-aged groups and appeared to increase in the younger-aged groups. A notable difference in the age-specific incidence patterns between males and females was that the rates among females, compared with males, were numerically higher for the age



**Fig. 1.** Age-adjusted (to 1970 U.S. standard population) skin melanoma incidence and 95% confidence intervals (outer lines) among the white population stratified by sex in the Surveillance, Epidemiology, and End Results Program areas from 1973 through 1997.

groups under 40 years but lower for the age groups 40 years or older.

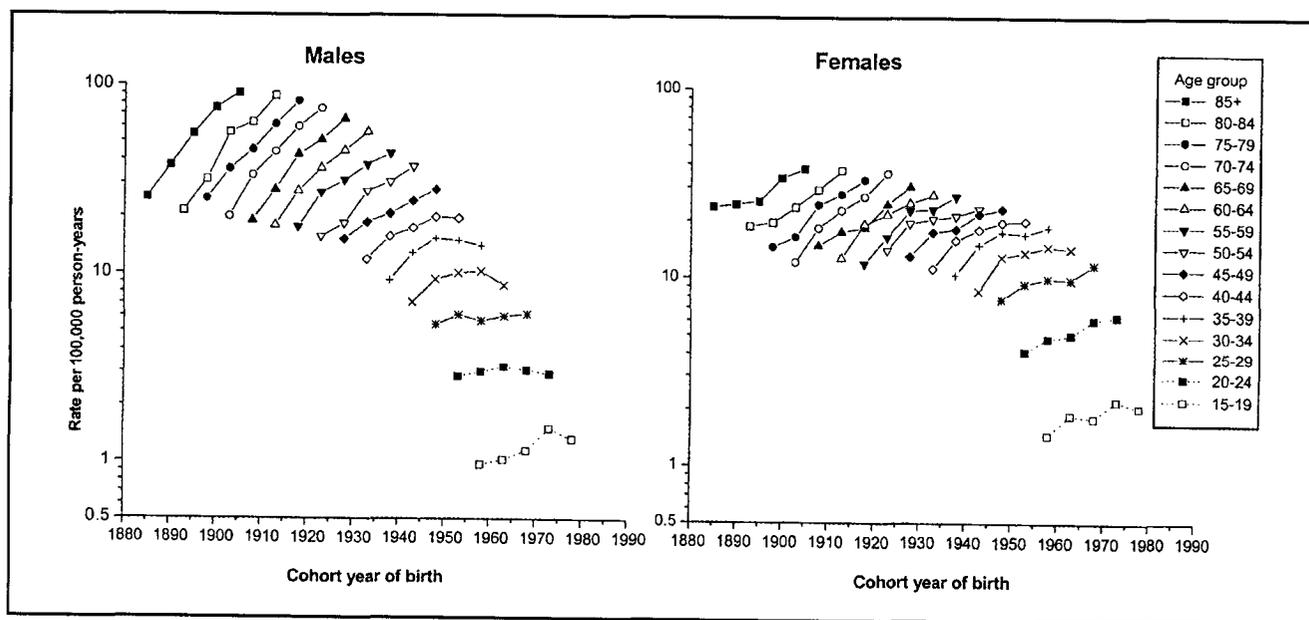
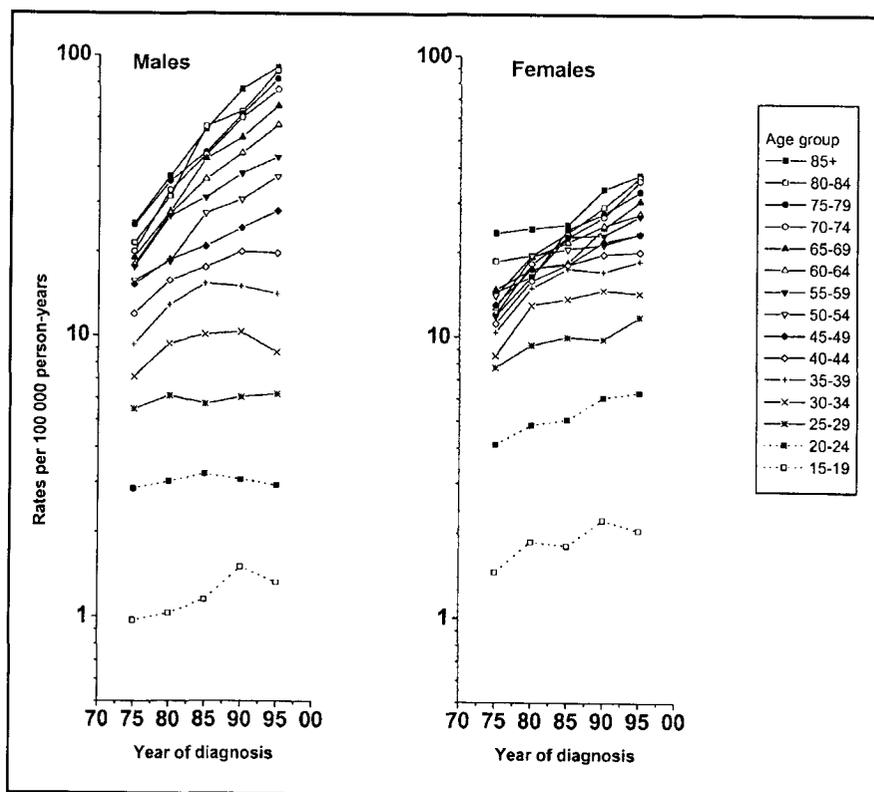
Fig. 3 presents age-specific incidence patterns by year of birth. The points vertically above each cohort year portray the cohort's age-specific incidence experience. Among males, all age-specific rates continued to increase until the 1950 birth cohort and tended to stabilize or decline among the more recent birth cohorts. Among females, age-specific rates also continued to rise although less rapidly in cohorts born before 1950. Female rates flattened in those born between 1950 and 1960 and then increased in those born since the 1960s. The formal age-period-cohort analysis of these data showed that the birth-cohort effects began to recede in men and women born in the pivotal period from 1945 through 1950, with estimates for change in slope  $C$  for melanoma incidence trend =  $-1.5781$  (95% confidence interval [CI] =  $-2.3974$  to  $-0.7588$ ) ( $P = .0002$ ) for white males and  $C = -0.768$  (95% CI =  $-1.1831$  to  $-0.3528$ ) ( $P = .0003$ ) for white females.

Fig. 4 shows the sex-specific, age-adjusted melanoma incidence trends by tumor stage, while Table 1 summarizes the trends by tumor thickness for all ages and broad age groups in two time periods, from 1974–1975 through 1988–1989 and from 1990–1991 through 1996–1997. For all ages combined, rates for each stage appeared to be higher in males than in females (Fig. 4), as were the annual percent changes in each tumor stage and in both time periods (Table 1). In the 1974–1975 through 1988–1989 period, rates for all ages combined statistically significantly (all  $P < .05$ ; see Table 1 for individual  $P$  values) increased for each tumor stage in males but only for local-stage disease in females. For the sex-specific age groups, rates increased statistically significantly for local-stage disease for each age groups of males and females and for distant-stage diseases for 40–59 years of females and for 60 years and older of males. The proportion of cases with unknown stage between 1974–1975 and 1988–1997 decreased from 11.6% to 7.0% among males and from 12.4% to 5.2% among females. However, the rates for all ages combined increased among males, while they decreased among females (data not shown).

In the 1990–1991 through 1996–1997 period (Table 1), rates for all ages combined increased for every tumor stage but were statistically significant increased ( $P < .05$ ; see Table 1 for individual  $P$  values) only for localized and for regional tumors among males. For ages under 40 years, rates decreased for each tumor stage in males and for distant-stage disease in females, while rates statistically significantly increased ( $P = .027$ ) for regional-stage disease in females. For ages 40–59 years, rates stabilized or declined for each tumor stage, except for statistically significantly increased ( $P = .0462$ ) local-stage disease in males. For ages 60 years and older, all stages showed upward trends but were statistically significantly increased ( $P < .05$ ; see Table 1 for individual  $P$  values) for local- and regional-stage tumors among males and for local-stage tumors among females.

Table 2 shows the sex-specific melanoma trends by age groups and by tumor thickness from 1988, the first year that this information was available, through 1997. For all ages combined, rates increased statistically significantly ( $P < .05$ ; see Table 2 for individual  $P$  values) for every thickness category except for thick tumors ( $\geq 4$  mm) among females. Rates increased more rapidly in males than in females and more so for thick tumors. For ages under 40 years, the only upward trend among males

**Fig. 2.** Age-specific skin melanoma incidence among the white population stratified by sex and calendar year of diagnosis (middle year of the 5-year group plotted on the x-axis) in the Surveillance, Epidemiology, and End Results Program areas from 1973–1977 through 1993–1997.

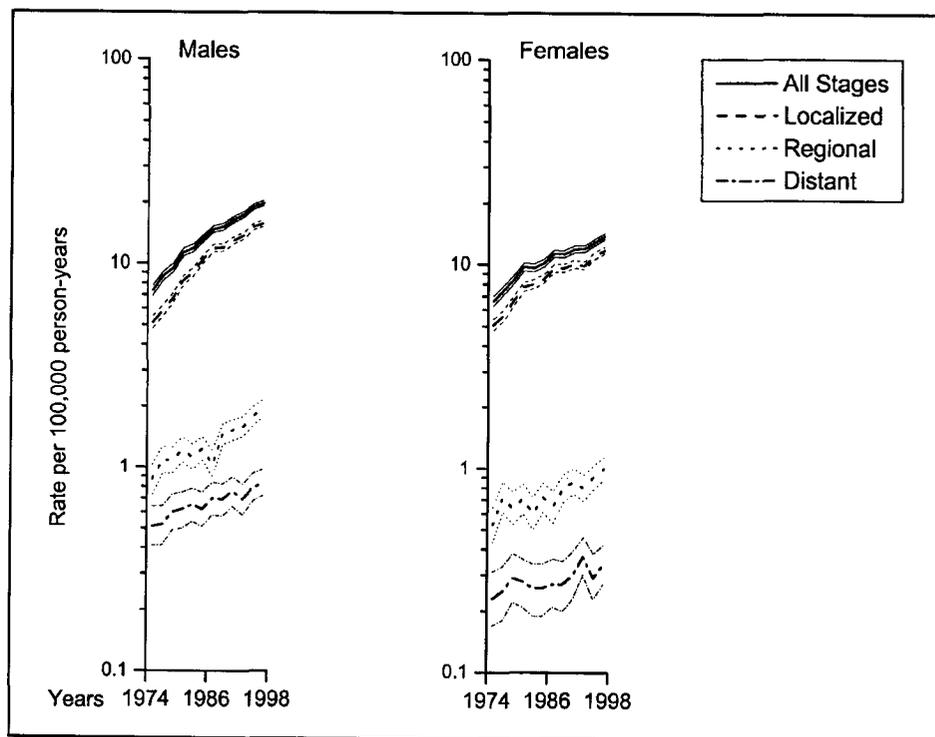


**Fig. 3.** Age-specific skin melanoma incidence among the white population stratified by sex and birth-cohort year in the Surveillance, Epidemiology, and End Results Program areas from 1973–1977 through 1993–1997. The points vertically above each cohort year portray the cohort's age-specific incidence experience.

was in thin tumors; intermediate and thick tumors showed downward trends. However, none of these trends were statistically significant ( $P > .05$ ). Among females under 40 years old, in contrast, all trends were upward but were statistically significant increased only for thin melanoma (<1 mm). For ages 40–59 years, rates among males increased statistically significantly for all thickness categories except thick tumors. Among females, in

comparison, rates increased statistically significantly for thin tumors, while they decreased nonsignificantly for thick tumors. In ages 60 years and older, rates rose for all thickness categories, except thick tumors among females. Analyses of these data for all tumors and for first primary tumors showed that rates for only first-counted primary tumors and for all primary tumors counted were nearly equal within each tumor-thickness category (data

**Fig. 4.** Age-adjusted (to 1970 U.S. standard population) skin melanoma incidence and 95% confidence intervals (outer lines) among the white population stratified by sex and tumor stage in the Surveillance, Epidemiology, and End Results Program areas from 1974–1975 to 1996–1997.



**Table 1.** Melanoma incidence trends by age groups and tumor stages, SEER\* Program (from 1974–1975 through 1988–1989 and 1990–1991 through 1996–1997)

Age, y	Stage	1974–1975 through 1988–1989				1990–1991 through 1996–1997			
		Males		Females		Males		Females	
		EAPC†	P‡	EAPC†	P‡	EAPC†	P‡	EAPC†	P‡
All	Local	6.4	.0001	4.6	.0001	3.5	.0184	3.0	.0773
	Regional	2.3	.0358	1.6	.1220	4.4	.0148	3.0	.1711
	Distant	2.2	.0010	0.4	.4295	2.0	.3092	0.1	.9739
	All	5.1	.0001	3.7	.0002	3.3	.0082	2.7	.0399
<40	Local	3.3	.0078	4.0	.0004	-1.6	.5578	1.6	.2552
	Regional	0.5	.2157	-1.4	.4510	-3.9	.3665	9.6	.0270
	Distant	-0.1	.9753	-4.2	.0599	-3.3	.7064	-1.9	.6590
	All	2.4	.0225	3.0	.0013	-2.1	.4236	1.6	.2024
40–59	Local	5.5	.0001	4.4	.0003	2.2	.0462	2.3	.2183
	Regional	1.1	.2754	2.1	.1886	5.4	.1049	-1.1	.7986
	Distant	2.3	.0549	4.1	.0353	2.8	.2945	-4.0	.0989
	All	4.4	.0001	3.7	.0005	2.5	.0059	2.0	.2073
≥60	Local	8.7	.0001	5.7	.0001	5.8	.0150	5.1	.0014
	Regional	3.7	.0571	2.0	.1513	5.4	.0210	3.7	.3099
	Distant	3.2	.0009	0.2	.8347	2.7	.2597	3.8	.5101
	All	7.0	.0001	4.1	.0001	5.2	.0141	4.3	.0149

\*SEER = Surveillance, Epidemiology, and End Results.

†EAPC = estimated annual percent change.

‡All P values were two-sided.

not shown). Second primary tumors accounted for 4% of the total counts in the thin (<1 mm) and unknown tumor thickness categories and for 2% in the thick tumor category (≥4 mm). The proportion of unknown thickness categories for all ages combined decreased from 27.2% in 1988–1989 to 18.3% in 1996–1997 among males and from 22.0% to 16.2% among females for comparable time periods. Rates declined for each sex- and age group-specific unknown-thickness category (data not shown).

## DISCUSSION

The melanoma incidence has not abated, and melanoma is still among the most rapidly rising cancers in the United States. Older men carry the highest melanoma risk in the United States. Not only did the large proportion of melanoma occur in individuals aged 60 years and older, but also rates of melanoma in the more recent period increased faster in those aged 60 years

**Table 2.** Melanoma incidence trends by age groups and tumor thickness, SEER\* Program (from 1988 through 1997)

Age, y	Thickness†	Males		Females	
		EAPC‡	P§	EAPC‡	P§
All	Thin	5.0	.0001	4.1	.0001
	Intermediate	4.4	.0009	2.5	.0341
	Thick	6.1	.0076	1.0	.6242
	All	3.4	.0001	2.5	.0001
<40	Thin	1.6	.2651	2.2	.0057
	Intermediate	-1.4	.4256	1.7	.3250
	Thick	-1.8	.7225	3.7	.5867
	All	-1.0	.4023	1.2	.0701
40-59	Thin	4.4	.0005	3.7	.0008
	Intermediate	2.3	.0422	1.0	.3835
	Thick	5.3	.0925	-1.1	.7349
	All	2.7	.0001	2.0	.0069
≥60	Thin	6.6	.0001	6.7	.0001
	Intermediate	7.4	.0001	4.4	.0041
	Thick	7.7	.0003	1.2	.6635
	All	5.1	.0001	4.3	.0001

\*SEER = Surveillance, Epidemiology, and End Results.

†Tumor thickness categories: thin = less than 1 mm; intermediate = 1-4 mm; thick = greater than or equal to 4 mm.

‡EAPC = estimated annual percent change.

§All P values were two-sided.

and above, especially in men. Hence, overall melanoma incidence rates in the United States may well continue to rise for some time into the future.

The elevated birth-cohort risks before 1950 were consistent with previous findings (16), while the increased birth-cohort risks after 1960 among females were unexpected, since prior reports (16,17) suggested stabilized or declined rates for cohorts born after 1950. Although long-term data on sun-exposure behaviors and attitudes in the United States are unavailable to relate them with birth-cohort risks, it has been suggested that the birth-cohort risks of melanoma are the results of sun-exposure behaviors and attitudes of each generation of males and females during childhood and adulthood (8,17). Robinson et al. (18) reported on trends in sun-exposure knowledge, behaviors, and attitudes in the United States on the basis of analysis of survey data from two time periods, 1986 and 1996. The proportion of people who experienced at least one sunburn, the most consistently associated sun-exposure variable with melanoma (19), statistically significantly increased from 30% in 1986 to 39% in 1996. However, data were inadequate to evaluate differences by birth cohort.

The birth-cohort incidence patterns for females born after 1960 were different from the mortality patterns; mortality consistently declined in cohorts born after 1950 (8,17). The birth-cohort mortality patterns in the SEER areas were generally similar to the national birth-cohort mortality patterns (data not shown), with declines among recent cohorts. Increasing melanoma incidence in the face of declining mortality was reported in New Zealand (20), in England (21), and in a number of other European countries (22). Possible factors contributing to the divergence of incidence and mortality rates include changes in diagnostic criteria and improvement in survival. However, there appeared to be little change over time in histopathologic criteria in the diagnosis of melanoma (23,24).

Survival rates for patients with melanoma increased over time in all age groups in the SEER areas (2). For cases diagnosed

between 1974-1975 and 1992-1993, the 5-year relative survival increased from 84.5% to 91.5% for ages under 40 years, from 79.4% to 87.51% for ages 40-59 years, from 73% to 88% for ages 60 years and older, and from 79.2% to 88.2% for all ages combined. Furthermore, survival for all ages and sexes combined has changed from 89.1% to 95.6% after localized disease, from 56.5% to 59.5% after regional disease, and from 14.0% to 10% after metastatic disease. The general improvement in survival may be related to greater awareness of melanoma by health professionals and the general public, leading to the detection of the disease at an earlier stage. From 1974-1975 through 1988-1989, upward trends for rates of local-stage tumors with simultaneous downward trends for distant-stage tumors were seen in ages under 40 years (Table 1). This may partly explain the divergence of incidence and mortality among the young birth cohorts. For the older-aged groups, improvements in survival may have contributed to the moderation of the slopes in mortality.

Our analysis of the incidence data by tumor stages and thickness categories agreed with previous reports (25,26). Between 1974-1975 and 1988-1989, overall rates increased statistically significantly ( $P < .05$ ) for every tumor stage among males and for only local-stage tumor among females (Table 1). In the more recent time period, however, the overall rates increased statistically significantly for local- and regional-stage tumors among males but not among females. In general, age-specific rates among males stabilized or declined less for distant-stage tumors for those aged under 60 years and increased more for those aged 60 years and older compared with females. Rates statistically significantly increased for all thickness categories except for the thick lesions among females (Table 2). Because of lower survival rates of patients with distant-stage and thick tumors (27), the preceding trends may explain why overall mortality from melanoma in the United States is still increasing among males but is stabilizing or declining among females. It is also worth noting that improved detection and documentation of tumor thickness, as reflected on proportional reductions in unstaged and unknown thickness categories over time, to some extent may have contributed to the increased incidence in local-stage and thin lesions.

Many reviewers have examined whether improved detection or real occurrence or both have led to the increase in melanoma incidence (8,25,28,29). Earlier detection, resulting mainly from increased awareness by health providers and the general public, has indeed had an impact, as seen in the higher rate of increase in localized tumors compared with regional and metastatic diseases. However, on the basis of our findings and others, there is supporting evidence to suggest that the trends reflect real changes more than increased diagnosis: 1) Incidence increased more rapidly in the 1970s when there was little awareness of melanoma; educational programs to enhance early detection of melanoma at the national level started in 1985 (30). 2) Sun exposure as measured by sunburning and regular use of a tanning booth increased in the past decade (18). 3) In the time period covered by our analyses, 1974-1997, the rise in incidence was not limited to local-stage and thin tumors, with potential misclassifications; distant-stage and thick tumors, with little misclassification, also increased statistically significantly (Fig. 4; Tables 1 and 2). 4) Most important, mortality increased for decades (8,17,25), and there was no major change in the International Causes of Death code for melanoma (31) to account for

its increase. 5) It is also noteworthy that melanoma is increasingly diagnosed in nonhospital medical settings, with underreporting as high as 20% of the total cases in some cancer registries (32,33). This, if it did not underestimate the recent trend, may potentially offset misclassification of nevi as invasive melanoma that may have occurred.

In summary, the recent melanoma trends in the United States may reflect increased sun exposure more than increasing diagnosis. Incidence likely will continue to increase, at least until the majority of the current middle-aged population becomes the oldest population. The rise of risk in the more recent birth cohort calls for increased support for primary and secondary prevention programs. However, the current decline or stabilization of rates in distant-stage and thick tumors in males less than 60 years of age may be early indications for peaking of mortality among males in the near future, since it has already been seen among females.

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## NOTES

<sup>1</sup>Editor's note: SEER is a set of geographically defined, population-based, central cancer registries in the United States, operated by local nonprofit organizations under contract to the National Cancer Institute (NCI). Registry data are submitted electronically without personal identifiers to the NCI on a biannual basis, and the NCI makes the data available to the public for scientific research.

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