HHS Public Access

Author manuscript

Prev Med. Author manuscript; available in PMC 2017 October 01.

Published in final edited form as:

Prev Med. 2016 October; 91: 294–298. doi:10.1016/j.ypmed.2016.08.032.

Melanoma burden and recent trends among non-Hispanic whites aged 15–49 years, United States

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Abstract

Melanoma is among the most common cancers for adolescents and young adults. Updated information on melanoma among adults < 50 is needed. The objective of this study was to examine invasive melanoma in the United States among people aged 15–49 years for the group at highest risk, non-Hispanic whites. In 2015, we analyzed population-based cancer registry data from the Centers for Disease Control and Prevention's National Program of Cancer Registries and the National Cancer Institute's Surveillance, Epidemiology, and End Results program to examine melanoma incidence and death rates and trends among non-Hispanic whites aged 15-49 years by sex and age. We also present incidence trends with regard to thickness and site on the body. Among non-Hispanic whites aged 15-49 years, rates were higher among females. Thin melanomas increased among both sexes during 1992–2006 and stabilized during 2006–2012. For the period 1992-2012, melanomas thicker than 4 mm increased among males and melanomas 1.01–2.00 mm thick increased among females. Melanomas were most commonly diagnosed on the trunk and lower extremity among females and on the trunk and upper extremity among males. Increases in melanoma incidence among non-Hispanic whites aged 15-49 years across various thicknesses suggest that melanoma trends are not solely related to increased screening but are, in part, related to true increases. Declines in melanoma rates of about 3% a year from the mid-2000s

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Conflicts of Interests: The authors declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

The findings and conclusions in this report are those of the authors and do not necessarily represent the official position of the Centers for Disease Control and Prevention or the National Cancer Institute.

Funding Sources: None. The authors of this paper reported no financial disclosures.

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to 2012 in the youngest age groups offer hope that melanoma incidence may decline in future generations.

Keywords

Melanoma; cancer incidence; cancer mortality; trends; adolescent and young adult

INTRODUCTION

The recent *Surgeon General's Call to Action to Prevent Skin Cancer* characterized skin cancer as a "major public health problem" because despite known effective prevention strategies, incidence continues to increase. These increases are resulting in significant burdens in the United States, with over 5 million people treated for skin cancer each year at a cost of \$8.1 billion. Melanoma is the skin cancer responsible for the most deaths, and the most common skin cancer for which incidence and mortality data are systematically tracked in the United States. Over 67,000 cases of invasive melanoma and over 9,000 deaths from the disease occurred in 2012.

Melanoma is among the most common cancers for adolescents and young adults, and the second most common cancer among young women aged 20–29 years.³ The highest incidence of melanoma occurs among fair-skinned populations, predominantly non-Hispanic whites, who have about 25 times the melanoma incidence rate of black populations and about 6 times the rate of Hispanic populations.¹ Although the incidence of most other cancers is decreasing in the United States, melanoma incidence continues to increase.⁴

The objective of this study was to examine incidence and mortality data for invasive melanoma among adolescents and adults younger than age 50. Because of our large data set, we were able to characterize the burden of these cancers in the United States. Given the higher rates among fair-skinned groups, we focused on non-Hispanic white males and females aged 15–49 years. We also provide information on trends, including thickness and site on the body, using data including a smaller percentage of the US population.

METHODS

In 2015, we examined population-based cancer registry data from the National Cancer Institute's Surveillance, Epidemiology, and End Results (SEER) program from 1992–2012 (SEER 13) to demonstrate incidence trends for 13% of the U.S. population, respectively. Data from the Centers for Disease Control and Prevention's (CDC's) National Program of Cancer Registries (NPCR) were combined with SEER data, enabling analysis of incidence data on 99.1% of the U.S. population for the years 2008–2012. Cases were coded using the International Classification of Diseases version that was current at the time of diagnosis and later converted to the 3rd edition (ICD-O-3).⁵ We included microscopically confirmed invasive melanomas of the skin, defined as having an ICD-O-3 site code of C440–C449 and ICD-O-3 histology code of 8720–8790. Mortality data covering all deaths in the United States are from the CDC's National Vital Statistics System for the years 2008–2012 (to describe current rates and counts) and for the years 1992–2012 (to describe trends).

Statistical analysis

We used SEER*Stat software version 8.2.1 to calculate age-adjusted rates per 100,000 population (based on the 2000 U.S. standard population), rate ratios, 95% confidence intervals, and average annual percent change. Rates based on a count of <10 cases were not reported. Rate ratios (RRs) were considered to be significant if they differed from 1 at p<0.05.

Trends in age-adjusted incidence and death rates were analyzed using the Joinpoint Regression Program, which tests whether or not apparent changes in trends are statistically significant.⁶ Joinpoint regression allowing 4 segments was used to fit age-adjusted trends for 1992–2012. Annual percent change calculated using Joinpoint was considered significant when the regression line slope differed from zero (p<0.05).

Cases were limited to non-Hispanic whites only, for the periods 1992–2012 (SEER 13) and 2008–2012 (NPCR + SEER), using the North American Association of Central Cancer Registries Hispanic Identification Algorithm (NHIA) version 2 (NHIAv2.2) and race as coded in the medical record. NHIAv2.2 was not available for deaths due to melanoma; these analyses were limited to white race only.

RESULTS

Current Melanoma Incidence Rates and Recent Trends (2008–2012)

Table 1 shows current incidence and mortality rates (2008–2012) among non-Hispanic whites aged 15–49 years. An average of 13,387 invasive melanomas were diagnosed in this population each year, 7,831 among females and 5,556 among males. Incidence rates among females aged 15–29 years were more than twice as high as males in the same age group (RR 2.32; p <0.05). Although rates among females were higher in every age group <50 years, rates among both sexes increased with age, and differences between them were attenuated with older age (RR 1.59 and 1.17, respectively, for age groups 30–39 and 40–49 years). Among females aged 15–49 years, approximately 50% of cases were diagnosed among those aged 40–49 years. Trends from 1992–2012, also shown in Figure 1, demonstrate that melanoma incidence increased during the time period. The steepest increase was among females aged 15–29 years from 1992–2005, with a 4.2% increase each year. Melanoma rates for the 15–29 year age group decreased by 3.6% annually from 2004–2012 among males (p<0.05), and by 3.3% annually from 2005–2012 among females (p<0.05) (Table 1).

Melanoma Incidence Rates and Trends by Thickness

Table 2 displays rates and trends in melanoma thickness at diagnosis during 1992–2012. The majority of melanomas diagnosed were thin lesions, up to 1 mm thick. Thin lesions increased among both males and females during 1992–2006 (3.0% and 4.5% per year, respectively) and leveled off between 2006 and 2012. However, lesions 1.01–2.00 mm thick increased an average of 2.8% per year among females, and lesions thicker than 4 mm

increased by 1.8% each year among males. The rate of melanomas with unknown thickness declined for both males and females. Other trends were not statistically significant.

Melanoma Incidence Rates and Trends by Site on Body

Table 3 displays rates and trends in melanoma incidence by body site. Among males, rates were highest on the trunk and upper extremities (6.9 and 3.0 per 100,000, respectively); among females, rates were highest on the lower extremity, trunk, and upper extremities (6.5, 6.3, and 4.4, respectively). Increases were most pronounced for melanomas of the trunk and lower extremity among females. Among females, melanoma of the trunk increased by 3.9% each year during 1992–2005 and melanomas of the lower extremity increased by 3.7% annually during 1992–2006.

Current Melanoma Death Rates and Recent Trends

Deaths from melanoma also increased with age, and contrary to incidence, were slightly higher among males than females for each age group (Table 1). An average of 1,027 deaths occurred among non-Hispanic whites aged 15–49 years each year from 2008–2012, 405 among females and 622 among males. Death rates decreased during 1992–2012 for both sexes and all ages except among males aged 15–29 years, for whom death rates remained stable. Melanoma deaths were more common among males than females for all age groups, despite higher incidence among females.

DISCUSSION

From 2008–2012, an average of 13,387 melanomas were diagnosed each year among non-Hispanic whites aged 15–49 years. Rates were higher among females and increased with age among both sexes, although age distribution was generally younger among females than males. Our analysis examining trends in melanoma incidence from 1992–2012 identified increases in incidence across groups, but also identified stabilization or decreases among those 15–29 in the most recent years. The decreases in the most recent years may reflect a cohort effect, or possibly delayed reporting of melanomas to central cancer registries.^{7,8}

Higher rates among young women, as well as steeper increases, suggest a potential effect of intentional tanning, both outdoors and indoors, as has been documented elsewhere. 9–12 For example, Bradford et al. examined increases in melanoma by age cohort among young women and found preferential increases among trunk melanomas diagnosed at younger ages. 9 This is consistent with studies that have hypothesized that melanoma at different sites on the body is associated with different patterns of UV exposure; for example, melanomas appearing on the head and neck have been shown to be more strongly associated with occupational exposure, while those on the trunk are more strongly associated with intermittent exposure. 10,11

Higher death rates and higher percentages of thicker tumors diagnosed among males indicate that young men may be diagnosed later. Melanoma thickness at diagnosis is strongly correlated with melanoma prognosis, as those diagnosed with thicker or later-stage melanomas consistently have poorer survival rates. ¹³ Gender differences in stage at diagnosis may be related to fewer encounters with health care providers among males than

females, or to less awareness of skin lesions generally. ^{14,15} Later diagnosis among males, together with higher death rates, may indicate lack of awareness of skin in general and melanoma in particular, and highlight opportunities for increased education and awareness efforts, related to both primary prevention and awareness of abnormal lesions.

Although 68% of melanomas among our study population were diagnosed at an early stage, with a thickness of 1 mm or less, 21% of cases were diagnosed at later stages. Increases in melanoma incidence may be, in part, related to overdiagnosis of potentially indolent lesions. 16 Screening for skin cancer has become more common in recent years. 17 However, our study describes increases in both thick and thin lesions, strengthening evidence that while some increases in melanoma are likely attributable to increased surveillance and diagnosis of in situ or early-stage lesions, increases in 1.01 to 2.00 mm melanomas in women and thicker than 4.00 mm melanomas in men are clinically significant and may eventually lead to increasing mortality. 18,19 Although our study did not show increases in mortality among younger men, melanoma mortality is increasing slowly, at about 1% a year, among white males in the United States of all ages. Since these increases were not apparent among younger males, it is likely that they are driven by trends among middle-aged and older males. Also, although diagnosis at an early stage improves prognosis, even those diagnosed early are at increased risk throughout life. People who are diagnosed with melanoma have a nearly 9-fold increased risk of developing a second melanoma, with even higher risks for younger people or for those recently diagnosed.²⁰

Declines in melanoma rates of about 3% a year from the mid-2000s to 2012 in the youngest age groups offer hope that melanoma incidence may decline in future generations. Evidence from Australia has suggested stabilization and declines in melanoma incidence among young adolescents and young adults, also primarily limited to early-stage lesions. ²¹ Australia has invested significant resources in addressing primary prevention and awareness of melanoma. Ongoing analysis to determine whether these declines continue in the United States, or if they are potentially related to data collection issues or other reasons, will be important. If these trends are sustained into the future, this will be the first manuscript to document such stabilization or declines.

In order to further examine whether recent stabilization or downward trends were related to delays in reporting, we examined delay-adjusted SEER 18 data (not shown). Delay-adjusted factors are estimated for broad age groups and do not include Hispanic ethnicity, so we were not able to calculate delay adjustment for our data among non-Hispanic whites. However, analysis of delay-adjusted data among whites of all ethnicities also demonstrated declines among the youngest age groups. These declines were not observed among older populations, either in our data or in SEER delay-adjusted data. Using delay-adjusted data allowed us to estimate that our 2012 data were undercounted by about 5%. Delay-adjusted rates from SEER 13 areas showed less steep increases in melanoma among males and stabilization in rates among females in recent years, but information about specific age groups was not available. Future analyses incorporating delay adjustment methods are needed to clarify recent trend data.

Limitations

Our study is subject to certain limitations. Melanomas, especially those diagnosed at early stages, are often diagnosed and treated in outpatient settings and therefore are prone to underreporting and reporting delays. 7,23,24 Despite efforts to increase reporting, 24 trends in the most recent years of our analysis may be affected by these reporting delays. Unknown tumor size became less common during our years of study. Increases by tumor size could have partially reflected tumors being assigned a size code, rather than unknown. In addition to uncertainty related to reporting issues, we were unable to examine skin type, sun sensitivity, or behavioral risk factors in this analysis, because those data are not available in cancer registries. Finally, although we examined melanomas diagnosed among young non-Hispanic white adults aged 15–49 years, we used fairly broad age groups to enhance the stability of rates. There are substantial differences in incidence within age groups, particularly those aged 15–29 years.

CONCLUSION

In conclusion, this analysis provides a detailed look at trends in melanomas diagnosed among young non-Hispanic whites in the United States. Increases in melanoma incidence across various thicknesses suggest that melanoma trends are not solely related to increased screening but are, in part, true increases. Decreases in melanoma incidence from the mid-2000's to 2012 for both males and females aged 15–29 could indicate the first signs of stabilization in increasing melanoma rates. Later stage at diagnosis and higher death rates among males are concerning and indicate the need for increased awareness.

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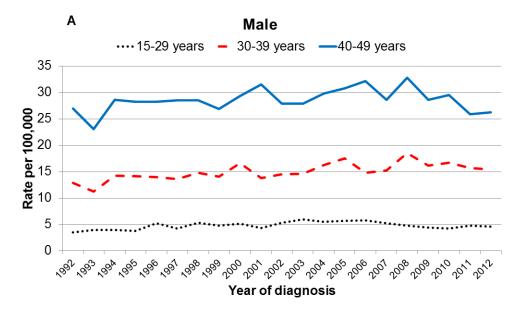
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Highlights

• Over 13,000 invasive melanomas are diagnosed annually among young non-Hispanic whites.

- Most diagnoses are thin lesions, but some thicker lesions are increasing.
- Young women had higher rates and steeper increases of melanoma incidence.
- Recent trends among those age 15–29 may suggest stabilization in rates.



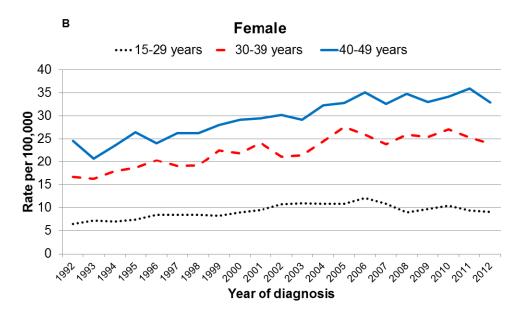


Figure 1. Melanoma incidence rates by age and year of diagnosis among non-Hispanic whites aged 15–49, SEER, 1992–2012

Rates are per 100,000 persons and are age-adjusted to the 2000 U.S. standard population (19 age groups – Census P25–1130).

Source for trend data: Surveillance, Epidemiology, and End Results (SEER) Program (www.seer.cancer.gov) SEER*Stat Database: Incidence - SEER 13 Regs Research Data, Nov 2014 Sub (1992–2012) <Katrina/Rita Population Adjustment> - Linked To County Attributes - Total U.S., 1969–2012 Counties, National Cancer Institute, DCCPS,

Surveillance Research Program, Surveillance Systems Branch, released April 2015, based on the November 2014 submission.

Table 1

Melanoma incidence and death rates (2008–2012) and trends (1992–2012) among non-Hispanic whites aged 15–49, United States

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			Rate	Rate (2008–2012)		Trend 1	1	Trend 2	2
	Sex	Age in years	Average annual count	Rate per 100,000	95% CI	Year	APC	Year	APC
Incidence	Male	15–29	654	3.4	(3.3, 3.5)	1992–2004	3.7*	2004–2012	-3.6*
	Male	30–39	1508	12.8	(12.5, 13.1)	1992–2012	1.3*		
	Male	40-49	3393	23.3	(23.0, 23.7)	1992–2008	1.1*	2008-2012	8.8
Incidence	Female	15–29	1489	7.8	(7.6, 8.0)	1992–2005	*2.4	2005-2012	-3.3 *
	Female	30–39	2382	20.4	(20.0, 20.7)	1992–2005	3.4*	2005–2012	-0.2
	Female	40-49	3960	27.4	(27.1, 27.8)	1992–2012	2.3 *		
Mortality	Male	15–29	54	0.3	(0.2, 0.3)	1992–2010	0.2	2010-2012	-22.7
	Male	30–39	143	1.2	(1.1, 1.3)	1992–2012	-2.5*		
	Male	40-49	424	2.9	(2.8, 3.0)	1992–2012	-1.9		
Mortality	Female	15–29	35	0.2	(0.2, 0.2)	1992–2012	-2.2*		
	Female	30–39	110	6.0	(0.9, 1.0)	1992–2012	-1.2		
	Female	40-49	260	1.8	(1.7, 1.9)	1992–2012	-1.4		

APC=Annual percent change, calculated using Joinpoint Regression Program, available at http://surveillance.cancer.gov/joinpoint/

Rates are per 100,000 persons and are age-adjusted to the 2000 U.S. standard population (19 age groups - Census P25-1130).

2012 and were reported to the National Program of Cancer Registries (CDC) and the Surveillance, Epidemiology and End Results (SEER) program (NCI). They cover about 99.1% of the U.S. population. Source for 2008–2012 incidence rates: Data are from population areas that meet United States Cancer Statistics publication crietia (www.cdc.gov/cancer/npcr/uscs/technical_notes/crietra.htm) for 2008–2012 incidence rates:

Source for 2008-2012 mortality data: Surveillance, Epidemiology, and End Results (SEER) Program (www.seer.cancer.gov) SEER*Stat Database: Mortality - All COD, Aggregated With State, Total U.S. (1969-2012) «Katrina/Rita Population Adjustment», National Cancer Institute, DCCPS, Surveillance Research Program, Surveillance Systems Branch, released April 2015. Underlying mortality data provided by NCHS (www.cdc.gov/nchs).

-Katrina/Rita Population Adjustment> - Linked To County Attributes - Total U.S., 1969-2012 Counties, National Cancer Institute, DCCPS, Surveillance Research Program, Surveillance Systems Branch, Source for trend data: Surveillance, Epidemiology, and End Results (SEER) Program (www.seer.cancer.gov) SEER*Stat Database: Incidence - SEER 13 Regs Research Data, Nov 2014 Sub (1992-2012) released April 2015, based on the November 2014 submission. Page 11

^{*} denotes statistical significance (p<0.05).

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Rates and trends in melanoma thickness at diagnosis among non-Hispanic whites aged 15-49, SEER, 1992-2012

Table 2

		Z	N Rate per 100,000	%	Trend 1	1	Trend 2	2
					Year	APC	Year	APC
Male	Thin (0.01–1.00 mm)	11,463	9.5	63.5	1992–2006	3.0*	2006–2012	-2.5
	1.01-2.00 mm	2,615	2.2	14.5	1992–2012	0.3		
	2.01-4.00 mm	1,165	1.0	6.5	1992–2012	8.0		
	>4.00 mm	069	9.0	3.8	1992–2012	*8.1		
	Unknown/no tumor found	2,118	1.8	11.7	1992–2012	* 4.4		
Female	Female Thin (0.01–1.00 mm)	16,118	13.8	72.2	1992–2006	4.5*	2006–2012	-1.0
	1.01–2.00 mm	2,568	2.2	11.5	1992–2012	2.8		
	2.01-4.00 mm	991	0.0	4.4	1992–2012	0.7		
	>4.00 mm	395	0.3	1.8	n/a			
	Unknown/no tumor found	2,261	1.9	10.1	1992–2003	-2.0*	$1.9 10.1 1992-2003 _{-2.0}^{*} 2003-2012 _{-7.4}^{*}$	* 4.7-

APC=Annual percent change, calculated using Joinpoint Regression Program, available at http://surveillance.cancer.gov/joinpoint/

Rates are per 100,000 persons and are age-adjusted to the 2000 U.S. standard population (19 age groups - Census P25-1130).

N denotes the total number of cases included in the analysis for all years 1992–2012. The dataset includes cases diagnosed from about 13% of the US population.

Data Source: Surveillance, Epidemiology, and End Results (SEER) Program (www.seer.cancer.gov) SEER*Stat Database: Incidence - SEER 13 Regs Research Data, Nov 2014 Sub (1992–2012) - Katrina/ Rita Population Adjustment> - Linked To County Attributes - Total U.S., 1969-2012 Counties, National Cancer Institute, DCCPS, Surveillance Research Program, Surveillance Systems Branch, released April 2015, based on the November 2014 submission. Page 12

[#] denotes statistically significant (p<0.05).

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Rates and trends in melanoma by site on body among non-Hispanic whites aged 15-49, SEER, 1992-2012

Table 3

					Trend 1	_	Trend 2	2
		Rate per 100,000 N*	* Z	%	Year	APC	Year	APC
Male	Trunk	6.9	8,334	46.2	1992–2006	1.1^*	2006–2012	-3.24*
	Head and neck	2.4	2,941	2,941 16.3	1992–2012	1.9*		
	Upper extremity	3.0	3,674	20.4	1992–2012	1.2*		
	Lower extremity	2.0	2,435	13.5	1992–2008	2.7*	2008-2012	-7.60
	Overlapping or NOS	9.0	299	3.7	1992–2012	-1.9		
Female	Trunk	6.3	7,366 33.0	33.0	1992–2005	3.9*	2005-2012	0.03
	Head and neck	1.6	1.6 1,816 8.1	8.1	1992–2012	2.1*		
	Upper extremity	4.4	5,126	5,126 23.0	1992–2012	2.1*		
	Lower extremity	6.5	7,592	34.0	1992–2006	3.7*	2006–2012	-2.97*
	Overlapping or NOS	0.4	0.4 433	1.9 N/A	N/A			

APC=Annual percent change, calculated using Joinpoint Regression Program, available at http://surveillance.cancer.gov/joinpoint/

NOS=Not otherwise specified.

* denotes statistical significance (p<0.05).

N denotes the total number of cases included in the analysis for all years 1992–2012. The dataset includes cases diagnosed from about 13% of the US population.

Rates are per 100,000 persons and are age-adjusted to the 2000 U.S. standard population (19 age groups - Census P25-1130).

Trends and APC calculated using Joinpoint Trend Analysis Software.

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