

# Incidence, Survival, and Mortality of Malignant Cutaneous Melanoma in Wisconsin, 1995-2011

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## ABSTRACT

**Objective:** To assess trends in malignant melanoma incidence, survival, and mortality in Wisconsin.

**Methods:** Incidence data for Wisconsin were obtained from the Wisconsin Cancer Reporting System Bureau of Health Information using Wisconsin Interactive Statistics on Health, while incidence data for the United States were obtained from the Surveillance, Epidemiology, and End Results system (SEER). The mortality to incidence ratio [ $1 - (\text{mortality}/\text{incidence})$ ] was used as a proxy to estimate relative 5-year survival in Wisconsin, while observed 5-year survival rates for the United States were obtained from SEER. Mortality data for both Wisconsin and the United States were extracted using the Centers for Disease Control and Prevention Wide-ranging Online Data for Epidemiologic Research.

**Results:** During the past decade, malignant melanoma incidence rates increased 57% in Wisconsin (from 12.1 to 19.0 cases per 100,000) versus a 33% increase (from 20.9 to 27.7 cases per 100,000) in the United States during the same time period. The greatest Wisconsin increase in incidence was among women ages 45-64 years and among men ages 65 years and older. Overall relative percent difference in 5-year survival in Wisconsin rose 10% (from 77% to 85%) and was unchanged (82%) for the United States. Wisconsin overall mortality rates were unchanged at 2.8 deaths per 100,000, compared to a 10% increase in the United States (from 3.1 to 3.4 deaths per 100,000). Wisconsin mortality rates improved for women ages 45-64 and for men ages 25-44.

**Conclusion:** Despite improvements in malignant melanoma survival rates, increases in incidence represent a major public health challenge for physicians and policymakers.

## INTRODUCTION

According to the Centers for Disease Control and Prevention (CDC), skin cancer is the most common form of cancer in the United States.<sup>1</sup> Malignant melanoma is the least common but deadliest of the 3 most common skin cancers and is associated

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with exposure to ultraviolet light<sup>2</sup> (UV) and genetic factors that control characteristics such as lighter skin color, many large nevi, blue eye color, and red or blonde hair color.<sup>3</sup> Alarming, despite decreased incidence rates of most other types of cancer, melanoma incidence and mortality rates have increased rapidly in recent decades.<sup>4</sup>

In a previous analysis of melanoma trends in Wisconsin for the period 1979-1997, incidence rates rose 25% among men and 11% among women, while rates for the United States rose 61% and 43%, respectively.<sup>5</sup> Though Wisconsin seemingly has fared better than the United States in relation to incidence and incidence trends, this advantage did not hold up for mortality rates. In the same time period, Wisconsin mortality rates rose 26% among men and 17% among women, while US rates remained relatively stable among women and rose 10% among men.<sup>5</sup> Such trends are of great concern to Wisconsin, and highlight why continued monitoring of melanoma incidence, survival, and mortality is essential.

The purpose of this study is to extend previous comparisons of Wisconsin and the United States to include more recent data. Unlike earlier studies, this analysis also assessed 5-year survival trends. Incidence, survival, and mortality are interrelated, yet distinct population-based indicators of cancer burden and analysis of all 3 measures is necessary to fully interpret progress in cancer control. Considering that melanoma is an increasingly common disease with known risk factors, it is important to carefully monitor trends to identify opportunities for prevention, early detection, and treatment.

## METHODS

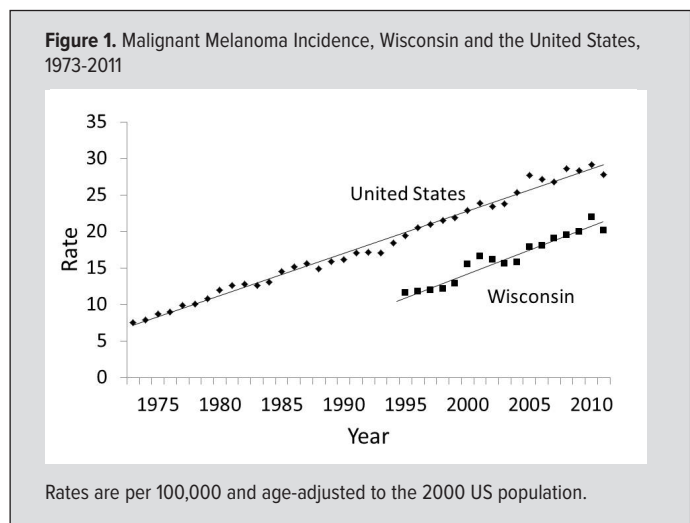
Malignant melanoma incidence data for Wisconsin were obtained from the Wisconsin Cancer Reporting System Bureau of Health

Information using the Wisconsin Interactive Statistics on Health (WISH) online database (<http://www.dhs.wisconsin.gov/wish/cancer/>) for the period 1995-2011. Because of varied reporting methods and incomplete data collection from nonhospital sources prior to 1995, incidence data before 1995 are not included in the analysis. Incidence data for the US population for the period 1973-2011 were extracted from the Surveillance, Epidemiology, and End Results (SEER) system using SEER\*Stat 8.1.5 (National Cancer Institute, Bethesda, Maryland). SEER routinely collects patient statistics from 12 cancer registries, including Oakland and San Francisco, San Jose, and Los Angeles, California; Seattle, Washington; Detroit, Michigan; Atlanta, Georgia; rural Georgia; Connecticut; Iowa; New Mexico; Utah; and Hawaii. These data are considered representative of the entire United States.

Due to limited availability of cancer-specific survival data in Wisconsin, we used the melanoma mortality to incidence ratio  $[1 - (\text{mortality}/\text{incidence})]$  to approximate survival. The ratio is defined as the number of deaths from a specific disease within a specified time period to the number of new cases of the same disease during the same time period. This method produces comparable estimates of 5-year relative survival for most tumor sites.<sup>6</sup> For the United States, 5-year survival data were obtained from SEER. The site was coded as “melanoma of the skin” (ICD-O-3/WHO 2008). We included only malignant cases of known age that were actively followed in the research database. Death certificate only and autopsy only cases, as well as cases alive with no survival time, were excluded from the analysis.

Malignant melanoma mortality data for both Wisconsin and the United States for the period 1968-2010 were collected from the National Center for Health Statistics using CDC Wides-ranging Online Data for Epidemiologic Research (WONDER). Neoplasm cases coded as “malignant melanoma of skin” (172) and “malignant melanoma of skin” (C43) were included, based on the *International Statistical Classification of Disease*, 8th, 9th, and 10th Revisions (ICD-8, ICD-9, ICD-10, respectively). Non-cutaneous melanoma and melanomas in genital regions are coded separately and thus were not included in this study. In order to examine long-term trends, we used all available data from the earliest time period to the most recently available for each measure of cancer burden.

Incidence, survival, and mortality rates were stratified by age and gender to compare trends over time and identify subgroups at greatest risk. To provide more stable rate estimates and trends, data were compiled for two 5-year time periods (1995-1999 and 2005-2009). The same 5-year time periods were chosen to permit comparison of all 3 metrics in the last decade. The percent change in the rates from 1995-1999 to 2005-2009 was calculated for each age group to compare age-specific trends in malignant melanoma between women and men in the past decade. When comparing rates, standard errors (SE = rate/square root of num-



ber of deaths) and 95% confidence intervals were calculated. All incidence and mortality rates were age-adjusted to the 2000 US standard population using 19 age groups (<1, 1-4, 5-9, 10-14, 15-19, ... ≥85 years). This study was restricted to non-Hispanic whites because they comprise over 90% of all patient cases in the United States.<sup>7</sup>

## RESULTS

### Incidence

In Wisconsin, overall incidence rates linearly increased 6.3 cases per 100,000 every 10 years ( $R^2=0.94$ ), reaching 20.2 cases per 100,000 in 2011. For the United States, incidence rates increased 5.7 cases per 100,000 every 10 years ( $R^2=0.99$ ), reaching 27.8 cases per 100,000 in 2011 (Figure 1). Despite greater increases in incidence, Wisconsin's total incidence remains 27% below the US average.

Wisconsin and United States malignant melanoma incidence rates, stratified by age and gender, are presented in Table 1. In Wisconsin, incidence rates for all ages increased 57% from 1995-1999 to 2005-2009 (from 12.1 to 19.0 cases per 100,000), with greater increases for people over 65 years of age. For women of all ages, incidence rates increased 65% (from 10.1 to 16.7 cases per 100,000) versus a 49% increase for men (from 15.0 to 22.4 cases per 100,000). Women age 45-64 experienced the highest percent change of 72% (from 15.1 to 26.0 cases per 100,000). In the United States, overall incidence rates increased 33% (from 20.9 to 27.7 cases per 100,000). Incidence rates rose 31% for women over 65 years of age, compared to a 35% increase for men. Although incidence data for Wisconsin are unavailable prior to 1995, the trends in incidence rates among men and women in Wisconsin are similar to those observed in the United States (Figure 2).

### Survival

For Wisconsin, overall survival from 1995-1999 to 2005-2009 increased 10% (from 77% to 85%). Though men and women

**Table 1.** Trends in Malignant Melanoma Incidence, Survival, and Mortality, by Age and Gender, Wisconsin and the United States

	Age	1995-1999	2005-2009	Percent Change <sup>a</sup>		Age	1995-1999	2005-2009	Percent Change <sup>a</sup>
<b>Incidence Rates: Wisconsin</b>					<b>Incidence Rates: United States</b>				
Women	25-44	11.9	18.9	59%	Women	25-44	18.7	22.9	22%
	45-64	15.1	26.0	72%		45-64	29.1	38.0	31%
	65+	21.5	35.5	65%		65+	38.8	54.9	41%
	All ages	10.1	16.7	65%		All ages	17.6	23.1	31%
Men	25-44	8.8	11.0	25%	Men	25-44	13.7	14.8	8%
	45-64	23.1	33.4	45%		45-64	42.8	50.6	18%
	65+	55.1	89.7	63%		65+	91.5	144.7	58%
	All ages	15.0	22.4	49%		All ages	25.5	34.4	35%
Overall		12.1	19.0	57%	Overall		20.9	27.7	33%
<b>Survival<sup>b</sup> Rates: Wisconsin</b>					<b>Survival Rates: United States</b>				
Women	25-44	92%	95%	3%	Women	25-44	96%	96%	0%
	45-64	83%	90%	8%		45-64	91%	92%	1%
	65+	65%	79%	22%		65+	68%	70%	3%
	All ages	81%	89%	10%		All ages	86%	87%	1%
Men	25-44	82%	87%	6%	Men	25-44	89%	90%	1%
	45-64	78%	84%	8%		45-64	84%	85%	1%
	65+	67%	79%	18%		65+	64%	66%	3%
	All ages	74%	82%	11%		All ages	78%	78%	0%
Overall		77%	85%	10%	Overall		82%	82%	0%
<b>Mortality Rates: Wisconsin</b>					<b>Mortality Rates: United States</b>				
Women	25-44	1.0	1.0	0%	Women	25-44	1.1	1.0	-9%
	45-64	2.6	2.5	-4%		45-64	3.1	3.1	0%
	65+	7.5	7.6	1%		65+	8.2	9.0	10%
	All ages	1.9	1.8	-5%		All ages	2.1	2.1	0%
Men	25-44	1.6	1.4	-13%	Men	25-44	1.6	1.5	-6%
	45-64	5.1	5.3	4%		45-64	6.5	6.3	-3%
	65+	18.2	19.0	4%		65+	19.9	24.5	23%
	All ages	3.9	4.0	3%		All ages	4.4	5.0	14%
Overall		2.8	2.8	0%	Overall		3.1	3.4	10%

<sup>a</sup>Percent Change = [(2005-2009) - (1995-1999)] / (1995-1999)

<sup>b</sup>Estimated 5-year survival based on [1 - (mortality/incidence)]<sup>6</sup>

All incidence and mortality rates are per 100,000 population and all-ages rates are age-adjusted to the 2000 US population.

experienced similar increases in survival rates, survival was considerably lower among men (82%) than women (89%). In the United States, overall survival rates remained fairly constant in the past decade. Similar to Wisconsin, survival rates are lower among men (78%) than women (87%) (Table 1). Notably, we found that observed US survival data from SEER closely matched estimated survival for the United States using the [1 - (mortality/incidence)] approximation. This supports the reliability of estimated survival in Wisconsin.

### Mortality

Total malignant melanoma mortality data for Wisconsin and the United States from 1968 to 2010 are presented in Figure 3. During this time period, Wisconsin total malignant melanoma death rates rose 94% from 1.6 to 3.1 deaths per 100,000, while US death rates rose 70% from 2.0 to 3.4 deaths per 100,000. Mortality rates for both Wisconsin and the United States show some evidence of leveling off in recent years.

Overall mortality rates in Wisconsin stabilized at 2.8 deaths per 100,000 in the past decade. Death rates decreased by 5% from 1.9 to 1.8 deaths per 100,000 for women of all ages and increased 3% from 3.9 to 4.0 for men of all ages. In contrast, overall mortality in the United States increased 10% in the past decade. Death rates remained constant for women of all ages (2.1 deaths per 100,000) compared to a 14% increase in men. Men over 65 years of age had the sharpest increase in mortality over this period of 23% (from 4.4 to 5.0 deaths per 100,000). Age-stratified mortality trends for the United States are presented in Figure 4.

### DISCUSSION

Our analysis of malignant melanoma data in Wisconsin and the United States suggests continued rises in incidence for all age groups, corresponding increases in 5-year survival rates, and improved mortality rates overall. However, the trends in mortality vary by age—with rates increasing progressively for men over

65 years of age, but leveling off or even decreasing for younger adults. These findings are consistent with previous reports of similar trends worldwide.<sup>8-10</sup>

While overall incidence and mortality trends in Wisconsin seem to parallel the United States from 1968 to 2011, several noticeable distinctions have emerged in the past decade. First, overall incidence rates have increased more rapidly in Wisconsin than the United States, especially for younger adults. Second, incidence rates have risen most sharply for women age 45-64, compared to greater increases for men 65+ in the United States. This represents a recent shift in Wisconsin incidence trends. Third, despite less favorable incidence trends in Wisconsin, survival and mortality trends appear to be somewhat more favorable in Wisconsin.

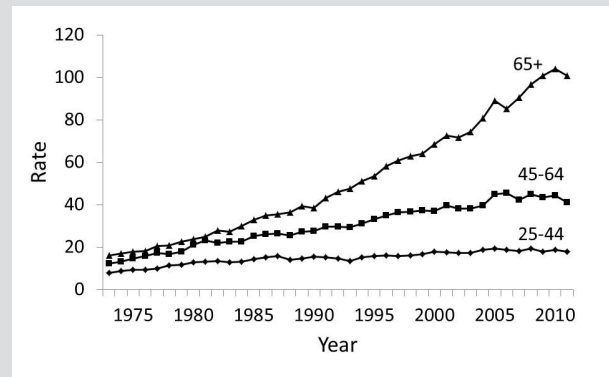
The underlying etiology of melanoma trends is widely debated. Some postulate that continued increases in melanoma incidence rates may be due to increases in natural and artificial ultraviolet radiation exposure.<sup>11,12</sup> In a 2011 study, more than one-third of American adults reported being sunburned in the previous year, with the highest rates among non-Hispanic men.<sup>13</sup> There is also evidence that indoor tanning is increasing among US adults, most of whom are women.<sup>14</sup> According to the 2010 National Health Interview Survey, 32% of women age 18-21, 30% of women age 22-25, 22% of women age 26-29, and 17% of women age 30-34 admitted to using a tanning bed.<sup>15</sup>

Consistent with prior reports,<sup>4,16</sup> malignant melanoma risk was most prominent for individuals over age 65, particularly men. Age is one of the strongest risk factors for all cancers, likely due to accumulating DNA damage over time.<sup>7</sup> It also has been suggested that melanoma in the elderly may result from different mechanisms causing altered immune response, which could explain increased incidence.<sup>17</sup> Furthermore, higher incidence rates in men may reflect differences in sun exposure, sun protection, and early detection practices. In fact, several studies have found that men are more likely than women to experience sunburn,<sup>14</sup> while they are less likely to practice sun protection<sup>14</sup> and utilize melanoma screening programs.<sup>18,19</sup>

Mortality trends were not uniform across age groups, with continued increases for individuals over 65 and leveling off or even decreasing among younger adults. Increased mortality in the elderly may reflect poor access to medical care and late stage at diagnosis. Explanations for higher mortality among elderly males may be similar to those described earlier for incidence. In contrast, favorable mortality trends for younger adults may reflect improvements in early detection and suggest outcomes related to better treatments. This raises the question whether early detection and education efforts have effectively reached some groups but not others.

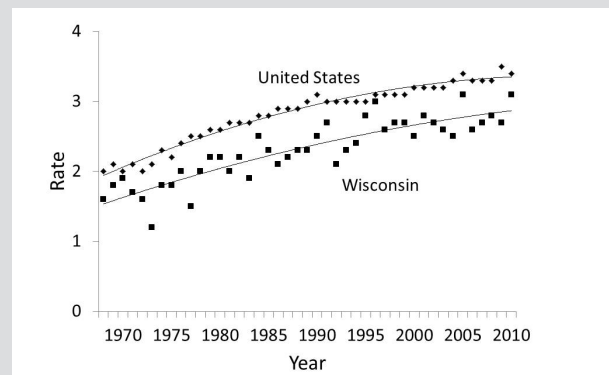
Because malignant melanoma incidence rates have substantially outpaced mortality rates, there has been some debate over

**Figure 2.** Malignant Melanoma Incidence, United States, 1973-2011



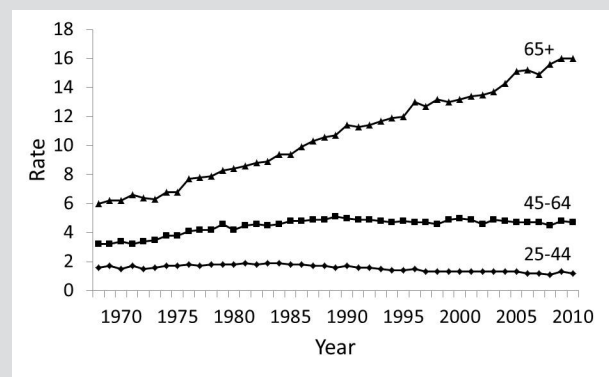
Rates are per 100,000 and age-adjusted to the 2000 US population.

**Figure 3.** Malignant Melanoma Mortality, Wisconsin and the United States, 1968-2010



Rates are per 100,000 and age-adjusted to the 2000 US population.

**Figure 4.** Malignant Melanoma Mortality, United States, 1968-2010



Rates are per 100,000 and age-adjusted to the 2000 US population.

whether increased incidence could be an artifact of improved surveillance,<sup>20</sup> regular screening,<sup>21</sup> or better detection of thinner tumors.<sup>21</sup> Recent evidence, however, suggests that the increase is in fact real.<sup>4,7,16</sup> Differences in diagnostic methods have not changed over time in ways that would be predicted if improved surveillance and increased screening were solely responsible



for higher melanoma rates. Additionally, there is evidence that thicker melanomas, which are less susceptible to misclassification, also are increasing in incidence.<sup>4,7</sup>

Several limitations in the data may affect the interpretation of our findings. First, malignant melanoma data collection procedures have changed significantly over time; thus, observed trends may reflect differences in the thoroughness of case reporting. Traditionally, malignant melanoma cases were reported almost entirely by hospitals. In the past several decades, however, melanoma has been increasingly diagnosed and treated in nonhospital settings. This poses challenges for cancer registries that may not have the resources to collect data from nonhospital sources such as outpatient surgery centers, pathology facilities, and physician offices. Second, comparisons between Wisconsin and US incidence rates may be influenced by variations in the completeness of case reporting between WISH and SEER. Indeed, underreporting<sup>19,22</sup> and delayed reporting<sup>23</sup> of melanoma to cancer registries has been documented and suggests that even the best records of melanoma incidence likely underestimate true incidence. Third, melanoma counts reported by WISH and SEER are based on the number of melanomas in the population, not the number of people with melanoma. Because some people have multiple melanomas, particularly elderly patients, melanoma risks reported here should be interpreted with caution.

Another possible limitation is that changes in disease classifications over time potentially could affect our results. Disease classifications were based on ICD-8, ICD-9, and ICD-10 codes for the time periods 1968-1978, 1979-1998, and 1999-2010, respectively. According to a study by Anderson et al,<sup>24</sup> an estimated 3% fewer deaths were classified to melanoma as the underlying cause of death using the revised ICD-10 rules compared to ICD-9. It is possible that this change could have caused an apparent increase in mortality rates for individuals over 65 years of age. These issues highlight the dependence of melanoma surveillance on complete and accurate reporting to cancer registries.

The findings and associated limitations of this analysis raise appropriate public health concerns regarding screening and prevention efforts. Notably, incidence and mortality rates and trends for men over 65 years of age warrant special attention. Rapid increases in the percentage of the population over 65 years of age may significantly change melanoma burden in the coming years. Therefore, surveillance and future cancer objectives must consider the significant effects of the aging population. Furthermore, recent incidence trends for women in Wisconsin should be of great concern. Because exposure to UV light may be linked to increasing incidence trends, especially among women, primary prevention efforts should emphasize the dangers of indoor tanning.

In order to reduce the burden from malignant melanoma, a comprehensive approach is needed to improve cancer preven-

tion, early detection, and treatment. Unfortunately, the current evidence reviewed by the US Preventive Services Task Force is that there is insufficient data to assess the balance of benefits and harms of using a whole-body skin examination by a primary care clinician or patient skin self-examination for the early detection of cutaneous melanoma in the adult general population.<sup>25</sup> Therefore, it is especially important to promote evidence-based prevention programs, including the use of sunscreen or sun protective clothing, educational interventions in primary and middle schools to increase sun-protective behaviors, and implementation of sun protection policies to increase protection from UV exposure. In addition, multicomponent community-wide interventions should be promoted that include individually oriented strategies, mass media campaigns, and environmental and policy changes across multiple sites.<sup>26</sup>

In summary, our study suggests that treatment outcomes for patients with melanoma are improving, as evidenced by improving survival rates. This could represent improvements in treatment and/or results of treating patients at an earlier stage of disease. Furthermore, while Wisconsin has a lower overall burden compared to the United States, rates appear to be rising more rapidly. Unfortunately, the significant increase in melanoma incidence in all age groups, as well as the continued increase in melanoma mortality rates in some age groups, is a major concern. These findings are a call for more effective prevention efforts and represent a major public health challenge for physicians and policymakers alike.

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