

# Increasing Incidence of Melanoma Among Middle-Aged Adults: An Epidemiologic Study in Olmsted County, Minnesota

Garrett C. Lowe, MD; Alexandra Saavedra, BS; Kurtis B. Reed, MD; Ana I. Velazquez, BS; Roxana S. Dronca, MD; Svetomir N. Markovic, MD, PhD; Christine M. Lohse, MS; and Jerry D. Brewer, MD

## Abstract

**Objective:** To identify changes in the incidence of cutaneous melanoma over time in the fastest-growing segment of the US population—middle-aged adults.

**Patients and Methods:** By using the Rochester Epidemiology Project resource, we identified patients aged 40 to 60 years who had a first lifetime diagnosis of melanoma between January 1, 1970, and December 31, 2009, in Olmsted County, Minnesota. The incidence of melanoma and overall and disease-specific survival rates were compared by age, sex, year of diagnosis, and stage of disease.

**Results:** Between 1970 and 2009, age- and sex-adjusted incidence increased significantly over time ( $P < .001$ ) from 7.9 to 60.0 per 100,000 person-years, with a 24-fold increase in women and a 4.5-fold increase in men. Although not significant ( $P = .06$ ), the incidence of melanoma increased with age. Overall and disease-specific survival improved over time, with hazard ratios of 0.94 ( $P < .001$ ) and 0.93 ( $P < .001$ ) for each 1-year increase in the year of diagnosis, respectively. Each 1-year increase in the age at diagnosis was associated with an increased risk of death from any cause (hazard ratio, 1.07;  $P = .01$ ) but was not significantly associated with disease-specific death ( $P = .98$ ). Sex was not significantly associated with death from any cause ( $P = .81$ ) or death from disease ( $P = .23$ ). No patient with malignant melanoma in situ died from disease. Patients with stage II, III, and IV disease were more than 14 times more likely to die from disease than were patients with stage 0 or I disease ( $P < .001$ ).

**Conclusion:** The incidence of cutaneous melanoma among middle-aged adults increased over the past 4 decades, especially in middle-aged women, whereas mortality decreased.

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From the Department of Dermatology (G.C.L., A.S., K.B.R., J.D.B.), Division of Medical Oncology (A.I.V., R.S.D., S.N.M.), Division of Hematology (S.N.M.), Division of Clinical Immunology and Immunotherapeutics (S.N.M.), and Division of Biomedical Statistics and Informatics (C.M.L.), Mayo Clinic, Rochester, MN.

Skin cancer affects more people in the United States than does any other malignancy, with cutaneous melanoma (hereafter called melanoma) being particularly deadly. Melanoma is diagnosed in more than 75,000 Americans each year, and more than 9000 die from it annually.<sup>1</sup> Melanoma is the sixth most frequently diagnosed cancer in developed countries,<sup>2</sup> with the burden carried mainly by fair-skinned populations. It is within this demographic group that melanoma incidence is the highest and is well documented across Australia and New Zealand,<sup>3,4</sup> Europe,<sup>5-9</sup> and North America.<sup>10,11</sup> In the United States, the incidence of many common cancers, including prostate, colon, and breast cancer, either remains steady or has declined over time.<sup>12</sup> However, the incidence of melanoma steadily increases from year to year

in non-Hispanic white men and women of all age groups and tumor thickness categories.<sup>12,13</sup> In addition, melanoma has previously been shown to have a higher incidence rate among women younger than 45 years and in men older than 45 years.<sup>14,15</sup>

The US Census Bureau in 2010 estimated that the group of residents aged between 45 and 64 years has grown more rapidly than any other age group during the preceding decade. Interestingly, this group of individuals has more than 50% of the cases of invasive melanomas diagnosed each year in the United States.<sup>15</sup> To our knowledge, there have been few true population-based epidemiology studies looking at the incidence of malignant melanoma in middle-aged men and women. The studies used to estimate the natural history, distribution

of subtypes, incidence, and disease-related mortality of melanoma among the middle-aged population have been so far limited to those performed in populations that were not very well defined<sup>16</sup> or were biased by the underreporting and delayed reporting that characterize registry-based epidemiology studies.<sup>17-19</sup> Jemal et al<sup>13</sup> recently reported incidence rates of melanoma between 2002 and 2006 in the United States by using data from the Surveillance, Epidemiology, and End Results database of the National Cancer Institute. They estimated incidence rates at 43.5 and 34.0 per 100,000 persons for men and women aged between 40 and 64 years, respectively. The calculated annual percent change in incidence rates from 1992 to 2006 was 3.0%.<sup>13</sup> In 2012, Reed et al<sup>14</sup> estimated the true age- and sex-specific incidence of melanoma from 1970 through 2009 in Olmsted County, Minnesota, in patients aged 18 to 39 years. They found that melanoma among young adults is increasing rapidly, especially among women. The current study aimed to estimate the true age- and sex-specific incidence of melanoma in adults aged 40 to 60 years in Olmsted County over the same period. Univariable and multivariable associations of select features with death from melanoma were assessed in this same population.

## PATIENTS AND METHODS

### Patient Selection

After approval by the institutional review boards of Olmsted Medical Center and Mayo Clinic, 383 adults aged 40 to 60 years who were residents of Olmsted County, Minnesota, at their first lifetime diagnosis of cutaneous melanoma between January 1, 1970, and December 31, 2009, were identified by using the resources of the Rochester Epidemiology Project (REP).<sup>20</sup> The REP was created in 1966, when indexes of diagnoses were created for use by medical professionals in Olmsted County, Minnesota. The result is linkage of medical data from almost all sources of medical care available to the local population of the county. According to the US Census, Olmsted County had a population of 144,000 people in 2010. The majority are non-Hispanic white persons who are socioeconomically similar to the general white population, despite a higher percentage of college graduates in Olmsted County.<sup>21</sup> Approximately

95% of the residents of Olmsted County have given permission to use their medical records for research purposes. The REP allows researchers to estimate the true incidence for almost any disease in the population.<sup>22</sup>

### Statistical Analyses

Incidence rates per 100,000 person-years were calculated overall and by decade by using incident cases of melanoma as the numerator and age- and sex-specific estimates of the population of Olmsted County, Minnesota, as the denominator. The population at risk was estimated by using US Census data from 1970, 1980, 1990, and 2000, with linear interpolation for intercensal years. Incidence rates were age- and sex-adjusted to the structure of the 2000 US white population.

The relationships between the incidence of melanoma and age at diagnosis, sex, and calendar year of diagnosis were assessed by fitting generalized linear models by using the SAS procedure GENMOD (SAS Institute, Inc). Incident cases were grouped into 4 age intervals (40-44, 45-49, 50-54, and 55-60 years) and 4 calendar-year intervals (1970-1979, 1980-1989, 1990-1999, and 2000-2009). The models fit the natural logarithm of crude incidence rates as a linear function of age at diagnosis, sex, and calendar year of diagnosis, with a Poisson distribution used to model the error structure. The significance of the linear trends for the features of interest and interaction terms among these features was assessed by using likelihood ratio statistics.

Changes in features by decade of diagnosis were evaluated by using Kruskal-Wallis and trend tests. Overall survival and disease-specific survival rates were estimated by using the Kaplan-Meier method. The duration of follow-up was calculated from the date of diagnosis to the date of death or last follow-up. Univariable and multivariable associations with death from any cause and death from disease were evaluated by using Cox proportional hazards regression models and summarized with hazard ratios and 95% CIs. The covariates used in the multivariable models included year of diagnosis, age at diagnosis, sex, and pathologic stage.

All analyses were performed by using the SAS software package (version 9.2), and *P* value of less than .05 was considered statistically significant.

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