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## Prevalence and Mortality of Melanoma in Oklahoma Among Racial Groups, 2000-2008

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## Abstract

**Introduction**—This study assessed the period prevalence (2000-2008) and mortality rates of melanoma, in Oklahoma, among different racial/ethnic strata.

**Methods**—We analyzed incident cases of melanoma from 2000-2008 from the Oklahoma Central Cancer Registry and determined disease duration using Kaplan-Meier survival analysis to calculate period prevalence of melanoma in Oklahoma. Using a series of Chi-Square tests, we compared period prevalence and mortality rates among the racial groups and compared mortality between Oklahoma and the US.

**Results**—White non-Hispanics in Oklahoma have the highest period prevalence (p<0.0001) among the racial strata. American Indian or Alaska Native (AI/AN) individuals have the second highest period prevalence in Oklahoma (p<0.0001). Furthermore, white non-Hispanics (p<0.0001) and AI/AN individuals (p=0.0003) in Oklahoma had higher mortality rates compared to the US.

**Conclusions**—There are disparities in the prevalence and mortality of melanoma among the AI/AN population in Oklahoma, and prevention and education programs should focus on this population.

## INTRODUCTION

Melanoma is a malignancy of the melanocytes, the cells responsible for pigmentation of the skin, visceral organs, eyes and ears.<sup>1</sup> The incidence of melanoma in the United States has

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risen over the last few decades.<sup>2-6</sup> Melanoma incidence has been increasing on average 2.6-2.9% per year since 1981.<sup>7,8</sup> This rise in incidence is concerning since melanoma is considered preventable through proper precautions.<sup>9</sup> Melanoma is a serious condition, with 9,940 individuals in the US estimated to die from melanoma in 2015.<sup>10</sup> Disparities in melanoma incidence, stage, and mortality are evident in the literature among racial groups in the US.9,11-20 Most of these studies are based on national or regional data. Few studies have focused on the disparities in the prevalence and mortality of melanoma among racial groups in a single state, especially in a state with large numbers of American Indian and Alaska Native (AI/AN) individuals like Oklahoma. Oklahoma is unique in that there is a large proportion of AI/AN individuals alone (9% as compared 1.2% nationally).<sup>21</sup> In fact, Oklahoma has the second largest population of AI/AN in the US, after California.<sup>21</sup> A single study has investigated the disparities between the white and AI/AN populations in Oklahoma.<sup>22</sup> That study observed that AI/AN individuals in Oklahoma had significantly higher overall cancer incidence than whites (629.8/100,000 vs. 503.3/100,000), and their disease was diagnosed at a later stage than the white population (14.0% in white vs. 20.0% in AI/AN).<sup>22</sup> It focused on incident data between the white and AI/AN populations, and clearly quantified the disparities between the two racial groups. Although limited to Oklahoma, that study focused on all cancers combined and was not specific to addressing melanoma alone.

Disparities in melanoma mortality among racial groups is also evident, another study reported the mortality from melanoma was significantly higher in white individuals in the South, including Oklahoma.<sup>23</sup> This study focused on mortality in a region with no specific information about individuals in Oklahoma. Due to a different population distribution in Oklahoma, specifically among AI/AN individuals, mortality rates may differ from that study population. Also, a later stage melanoma at diagnosis is linked to higher mortality.<sup>3,6,8</sup> Because of this, melanoma stage at diagnosis for the different racial groups is examined along with mortality.

The purpose of this study was to describe the burden of melanoma by estimating the stage at diagnosis, period prevalence, and mortality from 2000-2008 by race in Oklahoma. This is the first study that has estimated race-specific prevalence proportions in Oklahoma. Additionally, we investigated racial disparities in melanoma mortality rates in Oklahoma and compared those rates to national mortality rates.

## METHODS

This study used data from the Oklahoma Central Cancer Registry (OCCR), which is coded according to the North American Association of Central Cancer Registries (NAACCR) standards. All statistical testing and calculations were performed with SAS 9.3 statistical software. The registry data were limited to incident cases of melanoma diagnosed between the years 2000 and 2008 among Oklahoma residents. We included those with SEER ICD-O-3 histology codes between 8720 to 8790 and site codes of skin of the lip, eyelid, ear, head, neck, trunk, and extremities (C44.0-C44.9); labia and clitoris (C51.0-C51.2); vulva (C51.8-C51.9); penis (C60.0-C60.2, C60.8-C60.9); and scrotum (C63.2) according to SEER site

codes.<sup>24</sup> Individuals with unknown ICD-O-3 codes were excluded from the analysis. Cases diagnosed upon autopsy or from a death certificate only were also excluded.

The registry data were recoded for race and ethnicity, using the following race and ethnic groups: White non-Hispanic, White Hispanic, African American, AI/AN, and Asian and Pacific Islander. To ensure correct classification of AI/AN individuals, each incident case in the OCCR data was cross referenced with the Indian Health Service (IHS) registration database and those that matched were reported as AI/AN. Individuals whose racial classification was unknown or missing were excluded from the analysis.

We determined the percent of OCCR incident cases diagnosed at each SEER stage, and the percentage of individuals among the racial strata diagnosed with a late stage of melanoma. Late stage melanoma was defined as anyone that had regional or distant stage according to SEER staging guidelines.<sup>25</sup> The proportions of each racial strata diagnosed at late stage were compared using a series of Chi-Square tests.

To estimate prevalence from the OCCR incidence data, the mean duration of melanoma was determined for individuals within each race/ethnicity. We estimated duration for individuals by determining the number of days between last follow-up date obtained by the OCCR and date of diagnosis. Individuals who lived through the entirety of the OCCR study period were assumed to be alive as of November 1, 2014. We used the Kaplan-Meier estimates of mean survival time to estimate the duration of melanoma for each racial/ethnic stratum. To determine whether the mean survival time differed by race/ethnicity, we used the log-rank test for Kaplan-Meier analysis. We found mean survival did differ by race, so the mean survival time was determined by racial strata, and used as an estimation of the duration of melanoma. Since we used the mean survival to calculate prevalent cases, all-cause mortality was included in the individuals who died during the period.

The number of prevalent cases for each race/ethnic group during the period from 2000 to 2008 was estimated using the relationship between incidence and duration in a steady state population: **Prevalence**  $\approx$  **Incidence**  $\times$  **Duration**.<sup>26</sup> The number of prevalent cases of melanoma in Oklahoma was estimated using the OCCR incident cases from 2000 to 2008, and the estimated duration from the mean survival in the Kaplan-Meier analysis. Similarly, the product of the estimated duration and the total incident cases rendered estimates of the prevalent cases in each race/ethnic group over the period. To arrive at an estimated period prevalence per 100,000 persons, the estimated number of prevalent cases was divided by the population in each racial category over the 9-year period. Denominators for period prevalence came from SEER's annual estimates of Oklahoma's population from 2000 to 2008.<sup>27</sup> The annual population in each racial category was totaled over the 9-year period. Period prevalence for each racial category was calculated by dividing the group's prevalent cases by the group's total period population. Finally, we calculated 95% confidence intervals on each estimated population proportion.<sup>28</sup> Period prevalence for each of the racial categories were compared using Chi-Square tests.

The crude and age-adjusted melanoma mortality rates by race in Oklahoma, over the same period, were determined using the final cancer mortality statistics from the Oklahoma State

Department of Health website, OK2Share.<sup>29</sup> Crude and age-adjusted mortality rates were reported in the same race/ethnicity categories used in the prevalence calculations, and all individuals were IHS-linked to ensure more accurate classification of individuals who were AI/AN by adjusting for racial misclassification. The national crude and age-adjusted mortality rates were obtained from the CDC's WONDER cancer statistics, from 2000-2008.<sup>30</sup> The Oklahoma mortality rates were then compared to national mortality rates using a series of Chi-Square tests in the same racial categories. Asian or Pacific Islander mortality rates in Oklahoma could not be compared due to the suppressed Oklahoma state data (n<5).

## RESULTS

From the OCCR, we identified 6,962 incident cases of melanoma in Oklahoma from 2000-2008. Of those cases, 88 had missing or unknown racial status and were eliminated, leaving 6,874 for the prevalence analysis. The data included 6,418 white individuals (93.4%), 341 AI/AN individuals (5.0%), 62 white Hispanic individuals (1.0%), 36 African American individuals (0.5%), and 17 Asian/Pacific Islanders (0.3%). The population of incident cases over the period consisted of 59% male and 41% female individuals (**Table 1**).

Among the incident cases of melanoma over the period, 1,676 (28.8%) were staged as in situ, 3,246 (55.8%) as localized, 469 (8.1%) as regional, and 426 (7.3%) as distant. A series of Chi-Square tests indicated that white Hispanics (21.2%, p=0.22), African Americans (17.2%, p=0.74), and Asian/Pacific Islanders (14.3%, p=0.93) did not differ from white non-Hispanics (15.1%) in the proportion diagnosed at late stage melanoma. However, AI/AN individuals (20.1%, p=0.02) had a higher proportion of individuals diagnosed at late-stage of melanoma compared to white non-Hispanics. We were unable to analyze 1,057 individuals for stage at diagnosis because of missing staging information, although these individuals were included in the prevalence estimates.

#### **Prevalence Estimates**

Of the 6,874 incident cases, 6,846 cases were included in the Kaplan-Meier analysis, 2,381 (34.8%) died from all causes over the period from 2000-2008. We excluded 26 individuals from the survival analysis with unknown or missing follow up information. Overall survival did differ among racial groups (p from log rank test=0.03) (**Figure 1**). Estimated period prevalence for each racial stratum along with confidence interval are reported in **Table 2**.

White non-Hispanic individuals had a significantly higher period prevalence (233.0 per 100,000; 95% CI: 231.3, 235.0) than any other racial strata (p<0.0001). African Americans had the lowest period prevalence (8.0 per 100,000; 95% CI: 7.2, 9.2) when compared to the other racial categories (p<0.0001). We observed a period prevalence of 88.0 (95% CI: 85.1, 91.4) per 100,000 among AI/ANs, which was significantly higher than white Hispanics, African Americans, and Asian/Pacific islanders (p<0.0001).

#### Mortality

Regarding mortality, there were 1,141 melanoma deaths over the period 2000-2008.<sup>29</sup> Of the total deaths in the period, 1,091 (95.6%) where in white non-Hispanic individuals, 8 (0.7%)

in white Hispanic individuals, 7 (0.6%) in African American individuals, and 35 (3.1%) were in AI/AN individuals. Both crude and age adjusted melanoma mortality rates among racial categories in Oklahoma and the United States are presented in **Table 3**. The crude melanoma mortality rate for Oklahoma white non-Hispanics was 4.6 deaths per 100,000, which was higher than the national white non-Hispanic crude mortality rate of 3.9 deaths per 100,000 (p<0.0001). The age adjusted mortality rate in Oklahoma was also higher than age adjusted national rate. The crude melanoma mortality rates for white Hispanics (p=0.99) and African Americans (p=0.66) in Oklahoma did not differ from the national crude mortality rate share the national crude melanoma mortality rate (p=0.0003). The age adjusted mortality rate (p=0.0003). The age adjusted mortality rate was also higher among AI/AN individuals in Oklahoma compared to the national age adjusted rate. Also, AI/AN individuals in Oklahoma had a higher crude melanoma mortality rate than white Hispanics (p=0.0053) and African Americans (p<0.0001) in Oklahoma.

#### DISCUSSION

The majority of cases of melanoma were in the white non-Hispanic population, with approximately 6% of the incident cases over the nine years occurring in other racial groups. This distribution of melanoma in the population of Oklahoma was similar to data from other studies on melanoma, indicating that fairer skin is a risk factor in the development of melanoma.<sup>2-4,9,13,15,19</sup> More cases were seen among men than among women, which also followed the distribution of melanoma studied in previous studies.<sup>2-3,9,13</sup> We found that AI/AN individuals demonstrated the second highest prevalence of melanoma, after whites non-Hispanics.

Members of non-white populations are typically diagnosed with melanoma at later stages than white individuals. <sup>2,4,11-15,18,31</sup> Similar to previous results of we observed that AI/AN individuals in Oklahoma are diagnosed at a significantly higher stage of melanoma than white non-Hispanics. These studies reinforce the need for enhanced melanoma education at the individual and primary care physician level for AI/AN individuals. Korta and his colleagues stated that whites differ from other racial groups in their ability to identify melanoma visual characteristics on a self-exam.<sup>14</sup> Continued research among the AI/AN population in effective educational programs for skin lesion identification, and melanoma prevention strategies or educational programs through the extensive Indian Health Service, Tribal health programs, and urban clinics throughout Oklahoma.

In our analysis, we observed the crude mortality rate of white non-Hispanics in Oklahoma was significantly higher than the crude mortality rate for white non-Hispanics in the United States. Also, we observed the white non-Hispanic age-adjusted mortality rates were higher in Oklahoma compared to the U.S. This could indicate that Oklahoman white non-Hispanics were diagnosed at a later stage than white non-Hispanics in other parts of the United States. In addition, these cases may reflect the high proportion of rural residents of Oklahoma and may indicate problems with access to medical care. Further studies should be conducted to determine the stage of melanoma at diagnosis in Oklahoman white non-Hispanics and the

rest of the country. If the disparity in stage exists, it may also be evidence of lack of education and prevention knowledge, or failure to comply with personal safety practices.

Furthermore, we observed that AI/AN individuals of Oklahoma have a significant difference in crude melanoma mortality when compared to the U.S., and the age-adjusted rate is higher as well. Much like the prevalence data reported, melanoma mortality is approximately 2-3 times higher in AI/AN individuals in Oklahoma than other non-white racial groups, which is also evident in the national data. This could indicate a disparity in melanoma early detection in the AI/AN population, not just in Oklahoma but nationally as well. We observed that melanoma was diagnosed at a later stage in AI/AN individuals in Oklahoma compared to non-Hispanic whites.<sup>22</sup>

Due to the higher prevalence and mortality rates of melanoma in Oklahoma, research into melanoma educational and prevention tactics in Oklahoma is important to determine whether Oklahomans are being undereducated compared to individuals in other states. Development of educational opportunities and programs to increase awareness of melanoma could positively impact the mortality among all racial groups in Oklahoma. Increased research into educational programs or even screening/prevention programs in the white non-Hispanic and AI/AN population is recommended to determine if different programs could decrease the prevalence and mortality of melanoma in these Oklahomans.

There are multiple limitations to this study. The mean duration used in the calculation of estimated prevalence was a limiting factor. First of all, if the mean survival is not a good indicator of duration then this would affect the prevalence results either positively or negatively. Also, there were many individuals categorized as alive by the survival analysis that had a last follow up in excess of a year prior to the end of the follow-up period. The OCCR does passive linkage with state and national death data, and use of a passive system has been shown to over- estimate survival data for some groups, but generally estimates survival with similar quality as SEER methodology.<sup>32,33</sup> Treating censored observations in this manner may have overestimated survival times, which would consequently overestimate prevalence. Of concern is that NDI linkage is not completed each year at OCCR. The large majority of cases will be updated with Oklahoma Mortality Data and the Social Security Death Index to identify those who are deceased. It is possible that this resulted in an artificial inflation of the rates for recent years. Another limitation to between-group comparisons of the mean duration was the small sample sizes for African Americans, Asian and Pacific Islanders, and Hispanics. The Kaplan Meier log rank test did indicate a difference in the mean survival between races. Much of the literature focused on melanoma does indicate that minorities are usually diagnosed at a later stage of melanoma when compared to whites.<sup>2,4,11-15,18,31</sup> Later stage at diagnosis would affect survival, and that duration would follow and be different among racial strata. However, due to small sample sizes in the African American, White Hispanic, and Asian and Pacific Islander populations these mean survival times may be skewed toward longer survival. If this is the case, we may have assumed falsely longer durations for these racial stratum. One possible remedy for this is to conduct a regional study including states surrounding Oklahoma, which would increase the sample size overall and enhance the precision. Including a larger sample size could

possibly allow us to detect a more accurate difference in survival in each race/ethnicity, thus making the prevalence estimates more accurate.

This study approximated prevalence by combining incidence and the duration of melanoma. This calculation is based off the relationship between incidence, duration, and prevalence in a steady state population, which is when the rate of immigration equals the rate of emigration.<sup>26</sup> Oklahoma was assumed to be under this steady state for the time period 2000-2008. From 2000-2008, Oklahoma's population grew at a rate of 5.6%, indicating that the population was not in steady state.<sup>21,34</sup> Violation of this assumption would skew period prevalence estimated by the steady state population relationship.

Racial misclassification is also a limitation to this study. Steps were taken to adjust for AI/AN racial misclassification through linkage with IHS records. If the individual was unaware of family history, or have never been registered at an IHS, tribal facility, or urban AI/AN facility, then these individuals may continue to be misclassified.

Furthermore, socioeconomic status or access to health care was not taken into consideration for the mortality data. Many Oklahomans (n=1,266,322; 33.8%) live in small rural communities with limited access to health care.<sup>35</sup> Also, these individuals may be required to travel to one of the major metropolitan areas to have access to specialized health care services. Future studies focusing on the prevalence, incidence, and mortality from melanoma in Oklahoma or the United States that address these confounders could prove advantageous.

This study was the first study to estimate the prevalence of melanoma in the population of a state with a high proportion of AI/AN. Furthermore, this study was the only study that focuses on racial differences in the prevalence and mortality of melanoma in Oklahoma, while attempting to reduce misclassification of AI/AN individuals through the IHS linkage. In conclusion, we observed a higher prevalence of melanoma among AI/AN individuals in Oklahoma than among other non-white racial groups. Oklahoma and national melanoma mortality rates were significantly different in the AI/AN population, also we found differences in mortality among the white non-Hispanic individuals in Oklahoma and the U.S. With the growing incidence of melanoma,<sup>2-8</sup> research should be intensified to determine more effective methods to use in educational programs for both the public and health care providers. In addition, continued research into the burden of all cancers should be conducted in populations with high proportions of AI/AN individuals.

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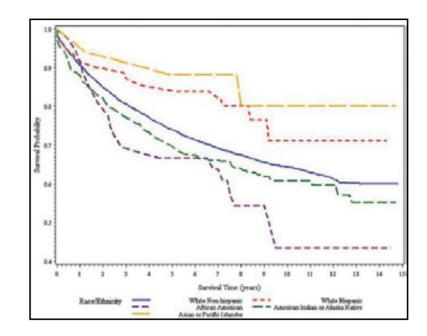
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#### Figure 1.

Overall survival among those with incidence cases of melanoma (n=6,846) by race/ethnicity in Oklahoma, 2000-2008.

#### Table 1

Number of Incident Cases of Melanoma, by Sex and Race/Ethnic group, in Oklahoma, 2000-2008

| Race/Ethnicity                                   | Male<br>N (%) | Female<br>N (%) | Total |
|--------------------------------------------------|---------------|-----------------|-------|
| White Non-Hispanic                               | 3831 (94.7)   | 2587 (91.5)     | 6418  |
| White Hispanic                                   | 16 (0.4)      | 46 (1.6)        | 62    |
| African American                                 | 23 (0.6)      | 13 (0.5)        | 36    |
| American Indian or<br>Alaska Native <sup>a</sup> | 170 (4.2)     | 170 (6.0)       | 340   |
| Asian or<br>Pacifc Islander                      | 6 (0.2)       | 11 (0.4)        | 17    |
| Total                                            | 4046 (58.9)   | 2827 (41.1)     | 6873  |

<sup>a</sup>1 individual missing gender information

#### Table 2

Incident cases, Estimated Duration, Prevalent Cases, and Period Prevalence (2000-2008) of Melanoma by Race in Oklahoma

| Race                             | Incident<br>Cases | Median Duration,<br>Years (95%CI) <sup><i>a</i></sup> | Prevalent<br>Cases | Total<br>Population<br>(2000-<br>2010) | Period Prevalence<br>per 100,000 (95%CI) |
|----------------------------------|-------------------|-------------------------------------------------------|--------------------|----------------------------------------|------------------------------------------|
| White Non-Hispanic               | 6,418             | 9.6 (9.5, 9.7)                                        | 61,613             | 26,424,019                             | 233 (231.3, 235.0)                       |
| White Hispanic                   | 62                | 7.9 (7.2, 8.6)                                        | 490                | 2,144,709                              | 23 (20.8, 24.7)                          |
| African American                 | 36                | 6.7 (5.5, 7.9)                                        | 241                | 2,944,772                              | 8 (7.2, 9.2)                             |
| American Indian or Alaska Native | 341               | 8.9 (8.4, 9.5)                                        | 3,035              | 3,437,654                              | 88 (85.1, 91.4)                          |
| Asian or Pacifc Islander         | 17                | 7.4 (6.4, 8.4)                                        | 126                | 653,100                                | 19 (15.9, 22.7)                          |

<sup>a</sup>Estimated mean survival from Kaplan-Meier analysis.

#### Table 3

Crude and Age-Adjusted Melanoma Mortality Rates in Oklahoma and the United States, 2000-2008 (per 100,000).

| Race/Ethnicity                        | Crude Mortality<br>Rate Oklahoma <sup>a</sup> | Age-Adjusted<br>Mortality Rate<br>Oklahoma <sup>a</sup> | Crude Mortality<br>Rates United<br>States <sup>b</sup> | Age-Adjusted<br>Mortality Rates<br>United States <sup>b</sup> |
|---------------------------------------|-----------------------------------------------|---------------------------------------------------------|--------------------------------------------------------|---------------------------------------------------------------|
| White Non-Hispanic                    | 4.6 (4.3, 4.9)                                | 3.9                                                     | 3.9 (3.8, 3.9)                                         | 3.3                                                           |
| White Hispanic                        | 0.4 (0.1, 0.7)                                | 0.8                                                     | 0.4 (0.4, 0.5)                                         | 0.8                                                           |
| African American                      | 0.3 (0.1, 0.5)                                | 0.4                                                     | 0.3 (0.3, 0.3)                                         | 0.5                                                           |
| American Indian or Alaska Native      | 1.2 (0.8, 1.6)                                | 1.7                                                     | 0.7 (0.5, 0.7)                                         | 1.0                                                           |
| Asian or Pacifc Islander <sup>C</sup> | NA                                            | NA                                                      | 0.3 (0.2, 0.3)                                         | 0.4                                                           |

<sup>a</sup>Age-Adjusted Mortality Rate data from OK2Share<sup>29</sup>

<sup>b</sup>Data from CDC WONDER<sup>30</sup>

 $^{\it C}$  Asian or Pacific Islander deaths suppressed by OK2S hare due to low numbers (n<5)