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Association Between Race/Ethnicity and Survival of Melanoma Patients in the United States Over 3 Decades

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Association Between Race/Ethnicity and Survival of Melanoma Patients in the United States Over 3 Decades

A Secondary Analysis of SEER Data

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Abstract: Melanoma is a treatable and preventable skin cancer. It is responsible for 75% of deaths among all skin cancers. Previous studies have found that race/ethnicity may play a role in survival among melanoma patients. However, there are no studies that cover 30 years and take race into account for the U.S. population.

This study is a secondary analysis of the National Cancer Institute's Surveillance, Epidemiology, and End Result (SEER) Program. Adults with primary cutaneous melanoma from 1982 to 2011 were included; the final sample size was 185,219. The outcome was survival; both cause-specific and all-cause mortality were examined. The main exposure was race/ethnicity. Kaplan–Meier survival analysis was used to estimate overall survival. Cox proportional hazards regression was used to estimate unadjusted and adjusted hazard ratios (HRs). A *P*-value less than 0.05 was considered statistically significant.

More than 50% of patients in all races/ethnicities were diagnosed at the in situ or localized stage. Non-Hispanic White patients were more frequently diagnosed at the in situ stage. Overall, more men were diagnosed than women. The majority of cases among all races were men. Non-Hispanic Black females represented the smallest percentage of melanoma cases among all races. The smallest number of diagnoses across all races/ethnicities was made from 1982 to 1991. Median follow-up was 81 months and no collinearity was observed in the adjusted models. When examining cause-specific mortality and controlling for site and stage at diagnosis, gender, age and decade of diagnosis, the HR for non-Hispanic Black patients was lower than that for non-Hispanic White patients (HR 0.7; 95% confidence interval (CI): 0.6–0.8). However, when examining all-cause mortality, this difference disappeared (HR 1.1; 95% CI: 1.0–1.2). Stage at diagnosis impacted HR; patients diagnosed with distant metastases had significantly worse survival.

When taking cause-specific mortality into consideration and after controlling for stage and site at diagnosis, gender, and age and decade of diagnosis, non-Hispanic Black patients had a lower HR compared to non-Hispanic White patients. However, this difference disappeared when examining all-cause mortality. Further research is needed to explore this finding and to determine what factors may be associated with late-stage melanoma diagnosis.

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Abbreviations: CI = confidence interval, HR = hazard ratio, SEER = National Cancer Institute's Surveillance, Epidemiology, and End Results Program, U.S. = United States.

INTRODUCTION

Melanoma is an aggressive skin cancer originating from melanocytes, the cells which are normally responsible for the production of pigments in the basal layer of epidermis. Of the various skin cancers that are known, melanoma is the most aggressive type. While it accounts for only around 5% of all skin cancers, it is responsible for 75% of deaths among skin cancer patients.[1]

Melanoma is preventable and treatable. It is often caused by ultraviolet radiation from sunshine or tanning beds. Certain factors have been shown to increase the lifetime risk to develop melanoma such as light eyes, red hair, fair skin, abundance of freckles, and multiple or dysplastic moles.[2] There were around 55,000 deaths from malignant melanoma worldwide in 2012 (0.7% of total cancer deaths).[3] Globally, Australia and New Zealand have the highest melanoma incidence.[4] In the United States (U.S.), melanoma incidence is increasing.[5] According to Sandru et al,[6] the likelihood of getting melanoma has increased from 1:1500 in 1935 to 1:50 in 2011. Melanoma-related mortality rates are increasing as well.[5]

The highest incidence according to SEER was in Caucasians (29.7 males and 19.1 females per 100,000), followed by Hispanics (4.4 males and 4.7 females per 100,000), then by Asians and Blacks (1.1 males and 1.0 females per 100,000).[7] Previous studies have found that race/ethnicity may play a role in survival among melanoma patients.[8] Stage at diagnosis is an important factor when determining prognosis; site may also play a role in survival.[5]

To our knowledge, there are no studies available which examined differences in survival among melanoma patients by race/ethnicity over a period of 30 years in the U.S. The objective of this study was to examine the differences in survival by race/ethnicity, taking stage and site at diagnosis into account, among U.S. melanoma patients over 3 decades.

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METHODS

Study Design

This study was a secondary analysis of publicly available data from the National Cancer Institute's Surveillance, Epidemiology, and End Results (SEER) Program, which collects incidence and survival data for patients with malignant tumors through selected population-based cancer registries across the United States (U.S.), representative of approximately 30% of the American population.[9] Adults (18 years or older) diagnosed with primary cutaneous melanoma from 1982 to 2011 were included in the study. After excluding duplicate patients, patients below 18 years, patients diagnosed before 1982, and patients missing survival information, the final sample size was 185,219.

The outcome of interest was overall survival, for both cause-specific and all-cause mortality. The main exposure of interest was race/ethnicity. Possible confounders included stage at diagnosis, site at diagnosis, gender, age at diagnosis, and decade of diagnosis. Race/ethnicity was grouped as non-Hispanic White, non-Hispanic Black, Hispanic, or Other (Asian or Pacific Islander, American Indian/Alaska Native, and other unspecified). Stage at diagnosis was categorized as in situ, localized, regional, and distant. Site was classified into head and neck, trunk, upper limb, and lower limb. Eyelid and ears were considered part of the head and neck category.[10] Age at diagnosis was categorized as less than 30 years, 30 to 39, 40 to 49, 50 to 59, 60 to 69, or 70 years or older. Decade of diagnosis was categorized as 1982 to 1991, 1992 to 2001, and 2002 to 2011.

Statistical Analysis

The Chi-square test was used to study bivariate associations between categorical variables. Kaplan–Meier survival analysis was used to estimate the unadjusted survival curves by race for both cause-specific and all-cause mortality. Cox proportional hazards regression was used to estimate unadjusted and adjusted hazard ratios (HRs). Collinearity was assessed using Pearson correlation. Three different adjusted models were estimated for both cause-specific and all-cause mortality: 1 which included site at diagnosis, gender, age and decade of diagnosis; 1 which substituted stage at diagnosis for site; and 1 which included both site and stage at diagnosis. A *P*-value less than 0.05 was considered statistically significant. Statistical analysis was completed using SPSS version 22 (IBM, Armonk, NY). This secondary data analysis utilized data that is publicly available through the SEER website. Ethical approval was waived since the analysis was considered nonhuman subjects research by the Florida International University Health Sciences IRB.

RESULTS

Table 1 describes the demographic and clinical characteristics of adult patients with primary cutaneous melanoma present in the SEER registry from 1982 to 2011. More than 50% of patients in all races/ethnicities groups were diagnosed at the in

TABLE 1. Demographic Characteristics of U.S. Adult Patients With Primary Cutaneous Melanoma, 1982–2011 (N = 185,219)

	Race/Ethnicity				
Characteristics	**NHW 169,844 (%)**	**NHB 3070 (%)**	**Hispanic 4616 (%)**	**Other† 2303 (%)**	***P***
Stage at diagnosis					<0.001
In situ	33.4	12.1	27.9	23.7	
Localized	56.9	53.1	56.2	52.5	
Regional	7.3	27.6	12.1	18.5	
Distant	2.3	7.1	3.8	5.3	
Site at diagnosis					<0.001
Head and neck	26.5	14.5	24.7	25.7	
Trunk	31.0	25.2	25.8	28.1	
Upper limb	23.9	17.1	20.6	17.7	
Lower limb	18.6	43.2	28.9	28.5	
Gender					<0.001
Male	56.8	71.9	55.1	56.6	
Female	43.2	28.1	44.9	43.4	
Age at diagnosis					<0.001
<30 years old	5.7	14.7	10.2	8.6	
30–39 years old	13.1	33.3	25.8	17.4	
40–49 years old	17.9	22.8	20.6	18.5	
50–59 years old	19.7	10.4	14.1	17.2	
60–69 years old	18.9	8.2	12.7	13.2	
≥70 years old	24.7	10.7	16.7	25.1	
Decade of diagnosis					<0.001
1982–1991	20.9	27.4	24.9	19.8	
1992–2001	32.8	39.9	33.5	37.1	
2002–2011	46.3	32.7	41.6	34.1	

NHB = non-Hispanic Black, NHW = non-Hispanic White.
†Other race/ethnicity includes Asian or Pacific Islander, American Indian/Alaska Native, and other unspecified.

situ or localized stage. Non-Hispanic White patients were more frequently diagnosed at the in situ stage. The highest percentage of patients diagnosed at distant stage were non-Hispanic Blacks at 7.1%, followed by patients of other races at 5.3%. Melanoma was commonly located in the lower limb for non-Hispanic Black, Hispanic, and patients of other races (43.2%, 28.9%, and 28.5%, respectively), while melanoma in non-Hispanic White patients was most frequently located in the trunk (31.0%).

The majority of cases among all races were men. Non-Hispanic Black females represented the smallest percentage of melanoma cases among all races/ethnicities. Patients less than 30 years old at diagnosis contributed the smallest proportion in each race, except for non-Hispanic Black patients, for whom the smallest proportion was diagnosed at 60 to 69 years of age. Non-Hispanic White and patients of other races were more frequently diagnosed at age of 70 years or above, while most Hispanic and non-Hispanic Black patients were diagnosed at 30 to 39 years. The smallest number of diagnoses across all races/ethnicities was made from 1982 to 1991.

The unadjusted overall survival curves by race are shown for cause-specific and all-cause mortality in Figures 1 and 2, respectively. Median follow-up time was 81 months. Non-Hispanic Blacks had the worst unadjusted survival compared to other races.

Table 2 shows the unadjusted and adjusted HRs of cause-specific mortality for primary cutaneous melanoma among U.S. adult patients, 1982 to 2011. In the unadjusted model, non-Hispanic Black patients had the highest HR of 4.3 (95% confidence interval (CI): 4.0–4.5) in comparison with the reference group of non-Hispanic White patients. No collinearity was observed in the adjusted models. In Adjusted Model 1a, which adjusted for site at diagnosis, gender, and age and decade of diagnosis, the HR for non-Hispanic Black patients remained high compared to non-Hispanic Whites (HR 3.0; 95% CI: 2.7–3.3). In Adjusted Model 2a, which substituted stage at diagnosis for site, the HR for non-Hispanic Black patients was 30% better compared to non-Hispanic White patients (HR 0.7; 95% CI: 0.6–0.8). In Adjusted Model 3a, which included both site and stage at diagnosis, the HR for non-Hispanic Black patients remained virtually unchanged (Figure 3). Stage at diagnosis had an important impact on HR. Those diagnosed with localized melanoma had an HR of 5.8 (95% CI: 5.3–6.3), those diagnosed with regional melanoma had an HR of 31.5 (95% CI: 28.9–34.2), and those diagnosed with distant metastases had an HR of 169.6 (95% CI: 154.2–186.6), compared to the reference group of in situ diagnosis. Women had a lower hazard of death compared to men (HR 0.6; 95% CI: 0.6–0.7). Patients diagnosed in 1982 to 1991 had a higher HR compared to those diagnosed in 2002 to 2011 (HR 1.7; 95% CI: 1.6–1.8).

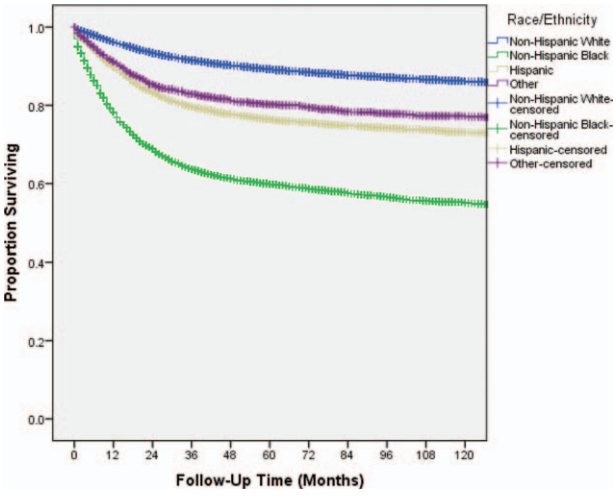

FIGURE 1. Unadjusted survival curve by race/ethnicity, cause-specific mortality, among U.S. adult patients with primary cutaneous melanoma, 1982–2011 (N = 185,219).

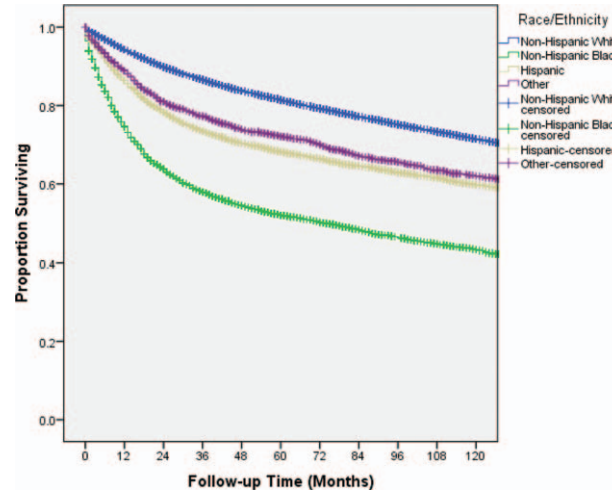

FIGURE 2. Unadjusted survival curve by race/ethnicity, all-cause mortality, among U.S. adult patients with primary cutaneous melanoma, 1982–2011 (N = 185,219).

Table 3 shows the unadjusted and adjusted HRs of all-cause mortality for primary cutaneous melanoma among U.S. adult patients, 1982 to 2011. In the unadjusted model, non-Hispanic Black patients had the highest HR of 2.6 (95% CI: 2.5–2.7) in comparison with the reference group of non-Hispanic White patients. No collinearity was observed in the adjusted models. In Adjusted Model 1b, which adjusted for site at diagnosis, gender, and age and decade of diagnosis, the HR for non-Hispanic Black patients remained high compared to non-Hispanic Whites (HR 2.5; 95% CI: 2.4–2.7). However, in Adjusted Model 2b, which substituted stage at diagnosis for site, there was no significant difference between non-Hispanic Blacks and the reference group of non-Hispanic Whites (HR 1.0; 95% CI: 0.9–1.1). Similarly, in Adjusted Model 3b, which included both site and stage at diagnosis, no significant difference was observed between non-Hispanic Blacks and non-Hispanic Whites (Figure 4). Stage at diagnosis had an important impact on HR. Those diagnosed with localized melanoma had an HR of 1.5 (95% CI: 1.5–1.5), those diagnosed with regional melanoma had an HR of 3.9 (95% CI: 3.8–4.1), and those diagnosed with distant metastases had an HR of 15.8 (95% CI: 14.9–16.7), compared to the reference group of in situ diagnosis. Individuals diagnosed with melanoma in the trunk, upper limb, and lower limb had a slightly better HR compared to individuals diagnosed with melanoma in the head and neck. Women had a lower hazard of death compared to men (HR 0.7; 95% CI: 0.7–0.7). Patients diagnosed in 1982 to 1991 had a higher HR compared to those diagnosed in 2002 to 2011 (HR 1.5; 95% CI: 1.4–1.5).

TABLE 2. Unadjusted and Adjusted Hazard Ratios, Cause-Specific Mortality, Among U.S. Adult Patients With Primary Cutaneous Melanoma, 1982–2011 (N = 185,219)

	Unadjusted		Adjusted 1a		Adjusted 2a		Adjusted 3a	
Characteristics	**HR (95% CI)**	***P***	**HR (95% CI)**	***P***	**HR (95% CI)**	***P***	**HR (95% CI)**	***P***
Race/ethnicity								
Non-Hispanic White	Ref		Ref		Ref		Ref	
Non-Hispanic Black	4.3 (4.0–4.5)	<0.001	3.0 (2.7–3.3)	<0.001	0.7 (.6-.8)	<0.001	0.7 (0.6–0.8)	<0.001
Hispanic	2.2 (2.0–2.3)	<0.001	1.8 (1.6–2.0)	<0.001	1.1 (.9–1.2)	0.38	1.1 (1.0–1.2)	0.26
Other†	1.8 (1.6–1.9)	<0.001	1.6 (1.4–1.8)	<0.001	0.9 (.8–1.0)	0.03	0.9 (0.8–1.0)	0.14
Stage at diagnosis								
In situ	Ref		—		Ref		Ref	
Localized	5.3 (5.0–5.8)	<0.001	—		5.7 (5.3–6.2)	<0.001	5.8 (5.3–6.3)	<0.001
Regional	31.3 (28.8–34.0)	<0.001	—		31.7 (29.2–34.4)	<0.001	31.5 (28.9–34.2)	<0.001
Distant	202.4 (186.2–22.1)	<0.001	—		189.8 (174.4–206.5)	<0.001	169.6 (154.2–186.6)	<0.001
Site at diagnosis								
Head and neck	Ref		Ref		—		Ref	
Trunk	1.0 (0.9, 1.0)	0.02	1.1 (1.0–1.1)	<0.001	—		1.0 (1.0–1.1)	0.15
Upper limb	0.8 (0.7, 0.8)	<0.001	0.95 (0.91–1.00)*	0.04	—		0.8 (0.7–0.8)	<0.001
Lower limb	1.1 (1.0, 1.1)	0.001	1.6 (1.5–1.6)	<0.001	—		1.0 (1.0–1.1)	0.75
Gender								
Male	Ref		Ref		Ref		Ref	
Female	0.4 (0.3–0.4)	<0.001	0.4 (0.4–0.5)	<0.001	0.7 (0.6–0.7)	<0.001	0.6 (0.6–0.7)	<0.001
Age at diagnosis								
<30 years old	Ref		Ref		Ref		Ref	
30–39 years old	1.6 (1.5–1.7)	<0.001	1.4 (1.3–1.5)	<0.001	1.3 (1.1–1.4)	<0.001	1.3 (1.2–1.4)	<0.001
40–49 years old	1.1 (1.0–1.1)	0.48	1.2 (1.1–1.3)	<0.001	1.6 (1.4–4.7)	<0.001	1.6 (1.4–1.8)	<0.001
50–59 years old	0.7 (0.7–0.8)	<0.001	1.1 (1.0–1.2)*	0.006	1.9 (1.8–2.1)	<0.001	2.0 (1.8–2.2)	<0.001
60–69 years old	0.8 (0.8–0.9)	<0.001	1.3 (1.2–1.4)	<0.001	2.4 (2.2–2.6)	<0.001	2.5 (2.3–2.8)	<0.001
≥70 years old	1.2 (1.1–1.2)	<0.001	2.2 (2.0–2.4)	<0.001	3.5 (3.2–3.9)	<0.001	4.0 (3.6–4.4)	<0.001
Decade of diagnosis								
1982–1991	3.5 (3.3–3.6)	<0.001	2.6 (2.4–2.7)	<0.001	1.6 (1.5–1.7)	<0.001	1.7 (1.6–1.8)	<0.001
1992–2001	2.0 (1.9–2.1)	<0.001	1.6 (1.5–1.7)	<0.001	1.3 (1.2–1.3)	<0.001	1.3 (1.2–1.4)	<0.001
2002–2011	Ref		Ref		Ref		Ref	

CI = confidence interval, HR = hazard ratio, NHB = non-Hispanic Black, NHW = non-Hispanic White.
*95% confidence interval includes 1 due to rounding.
†Other race/ethnicity includes Asian or Pacific Islander, American Indian/Alaska Native, and other unspecified.

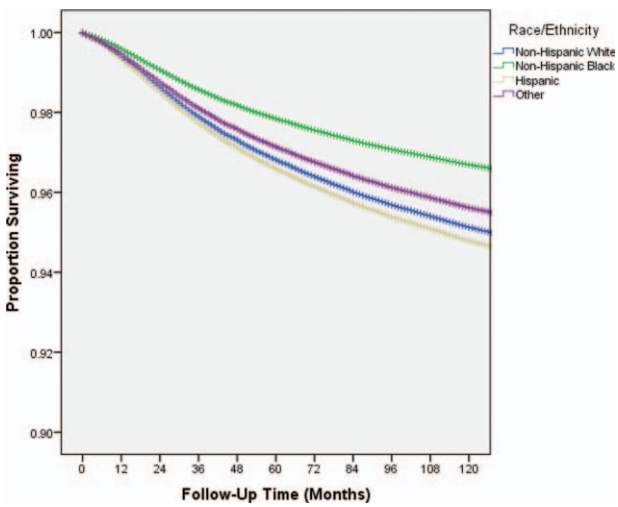

FIGURE 3. Adjusted survival curve by race/ethnicity, cause-specific mortality, among U.S. adult patients with primary cutaneous melanoma, 1982–2011 (N = 185,219).

DISCUSSION

The full adjusted model for cause-specific mortality showed that non-Hispanic Black patients had a 30% better hazard of death compared to non-Hispanic White patients (Adjusted Model 3a). This finding may be related to a biological effect due to the high melanin production in darker skins.[11,12] However, in the full adjusted model for all-cause mortality, the difference between non-Hispanic Black and non-Hispanic White patients disappeared (Adjusted Model 3b). One explanation may be due to social inequities; further research is needed to fully explore this finding.[4,8,13]

The impact of stage at diagnosis remained high in the full adjusted models for both cause-specific and all-cause mortality (Adjusted Models 3a and 3b). The finding that stage at diagnosis is an important prognostic factor aligns with other similar studies in the literature.[5] Future research should explore more fully what demographic factors are associated with late-stage diagnosis among U.S. patients with melanoma, taking socioeconomic status, education, and insurance status into account.[4]

Hispanic and patients of other races were very similar to the non-Hispanic White reference group. Additionally, the

TABLE 3. Unadjusted and Adjusted Hazard Ratios, All-Cause Mortality, Among U.S. Adult Patients With Primary Cutaneous Melanoma, 1982–2011 (N = 185,219)

	Unadjusted		Adjusted 1b		Adjusted 2b		Adjusted 3b	
Characteristics	**HR (95% CI)**	***P***	**HR (95% CI)**	***P***	**HR (95% CI)**	***P***	**HR (95% CI)**	***P***
Race/ethnicity								
Non-Hispanic White	Ref		Ref		Ref		Ref	
Non-Hispanic Black	2.6 (2.5–2.7)	<0.001	0.7 (1.7–0.8)	<0.001	1.0 (0.9–1.1)	0.54	1.1 (1.0–1.2)	0.17
Hispanic	1.5 (1.4–1.6)	<0.001	0.5 (0.5–0.5)	<0.001	1.1 (1.0–1.1)	0.08	1.1 (1.0–1.2)*	0.05
Other†	1.4 (1.3–1.5)	<0.001	Ref	<0.001	0.9 (0.9–1.0)	0.18	1.0 (0.9–1.1)	0.79
Stage at diagnosis								
In situ	Ref		—		Ref		Ref	
Localized	1.1 (1.1–1.1)	<0.001	—		1.4 (1.4–1.5)	<0.001	1.5 (1.5–1.5)	<0.001
Regional	3.4 (3.3–3.5)	<0.001	—		3.8 (3.7–3.9)	<0.001	3.9 (3.8–4.1)	<0.001
Distant	18.4 (17.7–19.1)	<0.001	—		18.0 (17.3–18.7)	<0.001	15.8 (14.9–16.7)	<0.001
Site at diagnosis								
Head and neck	Ref		Ref		—		Ref	
Trunk	0.5 (0.5–0.6)	<0.001	0.9 (0.9–0.9)	<0.001	—		0.9 (0.8–0.9)	<0.001
Upper limb	0.6 (0.6–0.6)	<0.001	0.9 (0.9–0.9)	<0.001	—		0.8 (0.8–0.8)	<0.001
Lower limb	0.5 (0.5–0.5)	<0.001	1.0 (1.0–1.1)	0.006	—		0.8 (0.8–0.8)	<0.001
Gender								
Male	Ref		Ref		Ref		Ref	
Female	0.5 (0.5–0.5)	<0.001	0.6 (0.6–0.6)	<0.001	0.7 (0.7–0.7)	<0.001	0.7 (0.7–0.7)	<0.001
Age at diagnosis								
<30 years old	Ref		Ref		Ref		Ref	
30–39 years old	1.6 (1.6–1.7)	<0.001	1.5 (1.4–1.6)	<0.001	1.3 (1.2–1.5)	<0.001	1.4 (1.2–1.5)	<0.001
40–49 years old	1.2 (1.2–1.3)	<0.001	1.6 (1.4–1.7)	<0.001	2.0 (1.9–2.2)	<0.001	2.1 (1.9–2.3)	<0.001
50–59 years old	1.3 (1.2–1.4)	<0.001	2.1 (2.0–2.3)	0.006	3.4 (3.2–3.7)	<0.001	3.5 (3.2–3.9)	<0.001
60–69 years old	2.3 (2.2–2.4)	<0.001	4.1 (3.8–4.4)	<0.001	6.8 (6.3–7.4)	<0.001	7.2 (6.6–7.9)	<0.001
≥70 years old	5.8 (5.5–6.1)	<0.001	11.6 (10.8–12.4)	<0.001	18.8 (17.3–20.3)	<0.001	20.5 (18.8–22.3)	<0.001
Decade of diagnosis								
1982–1991	0.7 (1.7–0.8)	<0.001	1.9 (1.8–1.9)	<0.001	1.4 (1.4–1.5)	<0.001	1.5 (1.4–1.5)	<0.001
1992–2001	0.5 (0.5–0.5)	<0.001	1.4 (1.4–1.4)	<0.001	1.2 (1.2–1.2)	<0.001	1.2 (1.2–1.2)	<0.001
2002–2011	Ref		Ref		Ref		Ref	

CI = confidence interval, HR = hazard ratio, NHW = non-Hispanic White; NHB = non-Hispanic Black.
*95% confidence interval includes 1 due to rounding.
†Other race/ethnicity includes Asian or Pacific Islander, American Indian/Alaska Native, and other unspecified.

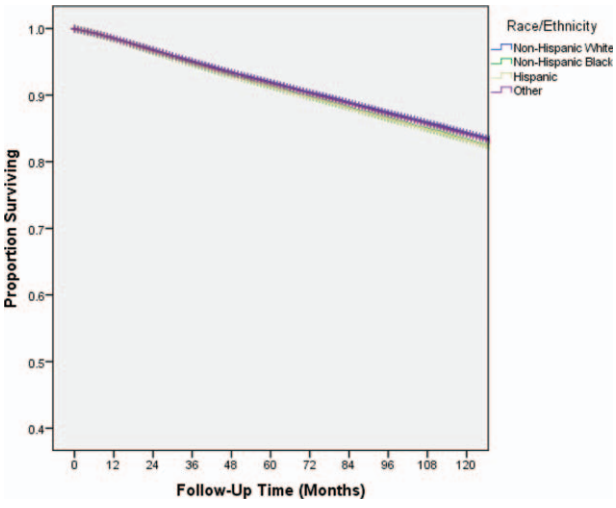

FIGURE 4. Adjusted survival curve by race/ethnicity, all-cause mortality, among U.S. adult patients with primary cutaneous melanoma, 1982–2011 (N = 185,219).

aging process increased HR, which was expected. Observing the number of cases diagnosed from 1982 to 1991, the smallest number of diagnoses across all races/ethnicities were made in that period. This could be due to low screening rates or lower knowledge compared to the present day. While this study did not examine incidence, results showed men were diagnosed more frequently than women overall. In contrast, Wu et al[13] found that melanoma incidence was higher for Hispanic and non-Hispanic Black women younger than 49 compared to men; after the age of 49, incidence was higher for men. The improved HRs for women compared to men were similar to another study which found that, among non-Hispanic White adolescents and young adults with melanoma, men have worse survival after controlling for thickness and other prognostic factors.[14]

The main strength of this study was the use of high-quality SEER data and the large sample size of melanoma cases. One weakness was that about 12% of cases had to be excluded because they were missing information. Furthermore, the follow-up period was not the same for all 3 decades. Finally, this study did not account for all factors that might have an impact on survival such as treatment regimens, prognostic factors (such as Breslow thickness, Clark level, mitoses, ulceration,

and serum lactate dehydrogenase), and demographic factors (such as socioeconomic status, education, and insurance status).

When taking cause-specific mortality into consideration and after controlling for stage and site at diagnosis, gender, and age and decade of diagnosis, non-Hispanic Black patients had a lower HR compared to non-Hispanic White patients. However, this difference disappeared when examining all-cause mortality. Further research is needed to explore this finding and to determine what factors may be associated with late-stage melanoma diagnosis.

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