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ORIGINAL REPORT

Survival for Patients With Invasive Cutaneous Melanoma Among Ethnic Groups: The Effects of Socioeconomic Status and Treatment

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The ideas and opinions expressed herein are those of the authors, and endorsement by the State of California, Department of Health Services, the National Cancer Institute, the Centers for Disease Control and Prevention, and/or the Genetic Epidemiology Research Institute of the University of California, Irvine is not intended, nor should it be inferred.

Authors' disclosures of potential conflicts of interest and author contributions are found at the end of this article.

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ABSTRACT

Purpose
Although uncommon, melanoma is associated with poor survival characteristics among African Americans and Hispanics compared with non-Hispanic whites (NHWs). Low socioeconomic status (SES) is also associated with poor survival among patients with melanoma, but it is not known whether this is because of SES itself or because of treatment disparities. We set out to determine this by using the large, population-based California Cancer Registry (CCR) database as a model.

Patients and Methods
We conducted a case-only analysis of CCR data (1993 to 2003), including a descriptive analysis of relevant clinical variables and SES. The SES variable used has been derived from principle component analysis of census block-level CCR data that was linked to census data to address seven indicators of SES. Univariate analyses of overall survival (OS) were conducted using the Kaplan-Meier method. Multivariate survival analyses were performed using Cox proportional hazard ratios (HRs).

Results
A total of 39,049 incident patient cases of cutaneous melanoma, including 36,694 in NHWs; 127 in African Americans; 1,996 in Hispanics; and 262 in Asian-Americans, were analyzed. Higher SES was associated with an early stage at presentation ($P < .0001$), with treatment with surgery ($P = .0005$), and with prolonged survival ($P < .0001$). After adjustments for age, sex, histology, American Joint Committee on Cancer stage, anatomic site, treatment, and SES, a statistically significant increased risk of death was observed for African Americans compared with NHWs (HR, 1.60; 95% CI, 1.17 to 2.18); no survival differences were noted for Asians or Hispanics compared with NHWs in the adjusted analysis.

Conclusion
Low SES independently predicts poor outcome among patients with cutaneous melanoma. However, the poor OS observed for African American patients with melanoma is not explained by differences in treatment or SES.

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INTRODUCTION

Non-Hispanic whites (NHWs) are at an increased risk for developing melanoma.[1] Melanomas in ethnic minority populations generally occur in different anatomic sites than in NHWs and are associated with different histologies, thicker lesions, and poorer survival.[2-10] Poor survival characteristics have been observed in African Americans with cutaneous melanoma. This finding is not explained by differences in stage at presentation when using the 2002 edition of the American Joint Committee on Cancer staging system, which incorporates factors such as Breslow depth and presence of ulceration.[10] Reasons for the observed poor survival characteristics among African American patients with cutaneous melanoma are currently unknown.

Differences in socioeconomic status (SES) may explain the observed survival differences among ethnic minority populations in the United States. Although melanoma incidence is generally associated with high SES,[11-13] low SES has been associated with an advanced stage at presentation[9,14-16] and with decreased survival.[9,17,18] However, the role of SES on treatment and survival among ethnic minority patients with melanoma in the United States has not been determined. We investigated if the differences in SES explain the differences in treatment rendered or in survival among ethnic minority patients with

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melanoma by using the large, population-based California Cancer Registry (CCR) as a model.

PATIENTS AND METHODS

Study Population

We performed a retrospective, case-only analysis of invasive cutaneous melanoma patient cases in the CCR database. The CCR is part of the National Cancer Institute's Surveillance, Epidemiology, and End Results (SEER) program and is the largest contiguous-area, population-based cancer registry in the world[19]; standardized data collection and quality control procedures have been in place since 1988.[20-23] Case reporting is estimated at 99% for the entire state of California,[24] and follow-up completion rates are more than 95%. Data were abstracted from medical and laboratory records by trained tumor registrars.[22] Tumor site and histology were coded according to the WHO criteria in International Classification of Diseases for Oncology (ICD-O; 3rd edition).[25] Patient cases were extracted based on histologic types for cutaneous melanomas (SEER code = 25010) according to ICD-O-3: superficial spreading melanoma (SSM; 8743), lentigo maligna melanoma (LMM; 8742), nodular melanoma (NM; 8721), acral lentiginous melanoma (ALM; 8744), melanoma not otherwise specified (NOS; 8720), and all other morphologies (other; 8722, 8723, 8730, 8740, 8745, 8761, 8770-8773, and 8780). Patient cases with melanoma in situ and patient cases with the following unknown or missing variables were excluded: missing information on the number of positive regional nodes (n = 1,661; 3.08%), unknown tumor thickness (n = 6,803; 12.6%), nonspecific or unknown SEER extent-of-disease classification (n = 1,018; 1.89%), and number of patients whose diagnosis dates and follow-up dates were inconsistent (n = 18; 0.03%).

SEER extent-of-disease and surgical-staging variables were used to derive TNM data in accordance with the 2002 AJCC staging system, as performed previously.[26-28] Patient cases of melanoma with tumor sizes less than 1.0 mm were coded as stage IA (without ulceration) or IB (with ulceration). Tumors between 1.0 and 2.0 mm were coded as stage IB (without ulceration) or IIA (with ulceration). Stage IIA patient cases also included nonulcerated tumors between 2.0 and 4.0 mm. Ulcerated tumors between 2.0 and 4.0 mm were coded as stage IIB along with nonulcerated tumors of greater than 4.0 mm. Stage IIC included ulcerated tumors greater than 4.0 mm. According to AJCC 2002, stage III classification requires inclusion of microscopic versus macroscopic nodal involvement. Because these variables were not available in the CCR, we could not assess nodal stage N1a through N3a. However, the CCR's variable for regional positive node status was used to classify the number of positive macroscopic lymph nodes. Stage IIIB patient cases included nonulcerated tumors with 1 to 3 positive regional nodes. Stage IIIC included ulcerated tumors with 1 to 3 positive regional nodes, or tumors with at least four positive regional nodes regardless of ulceration. Tumors of any size with metastatic involvement were coded as stage IV.

Data were obtained on 39,049 incident patient cases of cutaneous melanoma during 1993 to 2003 in the CCR. Type of reporting source was available for each case: no cases were identified through death certificate only, and only two cases were identified through autopsy alone. The remaining cases were identified through high-quality reporting sources (ie, hospital inpatient/outpatient centers, oncology treatment centers, laboratories, private practitioners, or nursing home/convalescent home/hospice facilities). Recorded data included demographic information, stage at presentation, histology, treatment during the first course of therapy, SES, and vital status. SES is denoted as a single-index variable in the CCR by using statewide measures of education, income, and occupation from census data, as described previously.[29] The SES variable used is a composite index that is based on the principle component analysis of census block-level CCR data linked to census data that assesses education level, median household income, proportion below 200% poverty level, median house value, median rent, percent employed, and percent with blue-collar employment, as previously described.[19,29-33] Quintiles for the SES score were analyzed.

Cause of death was recorded according to ICD criteria in effect at the time of death.[25] Hospital registrars contacted cases annually, and CCR staff annually reviewed state death certificates to identify deceased registry patient cases. The last date of follow-up was either the date of death or the last date of contact.

Statistical Analysis

The clinical characteristics, including age, sex, race/ethnicity, AJCC stage, histologic subtype, anatomic tumor site, tumor ulceration, SES quintile, and treatment were analyzed with Pearson's χ^2 test or Fisher's exact test for categoric and dichotomous variables and with the nonparametric Kruskall-Wallis test for the comparison of continuous variables for more than two groups. Life tables and Kaplan-Meier curves were generated for race/ethnicity and SES categories, and curves were compared with the log-rank test. Multivariate survival analysis was utilized to calculate overall survival and melanoma-specific survival (MSS) with Cox proportional hazard ratios (HRs). All statistical analyses were conducted using SAS 9.1 statistical software (SAS Institute, Inc, Cary, NC). Statistical significance was assumed for a two-tailed $P < .05$.

Ethical Considerations

This study involved analysis of existing data from CCR database with no patient intervention. No identities were linked to patients. This study was approved by the University of California, Irvine institutional review board (IRB) under the category of exempt status (IRB#2005-4524).

RESULTS

Demographic Data

Demographic and clinical data for the entire study population are presented in Table 1. Identified patient cases included 36,694 NHWs (94.0%); 127 African Americans (0.3%); 262 Asians (0.7%); and 1,966 Hispanics (5.0%; $P < .0001$). Additionally, 13 Native Americans and 2,953 patient cases reporting other race/ethnicity were identified and excluded, thereby restricting the primary analyses to the four major ethnic groups noted above. Median age at diagnosis was statistically different by race/ethnicity: 58 years for NHWs, 61 years for African Americans, 55 years for Asians, and 49 years for Hispanics ($P < .0001$). The distribution by sex also varied among the different races/ethnicities: NHW men account for 58.0%, African American men for 42.5%, Asian men for 51.5%, and Hispanic men for 39.0% ($P < .0001$).

Clinicopathologic Characteristics

Among NHWs, 35.0% had SSM, 5.7% had LMM, 8.7% had NM, and only 0.8% had ALM. Among African Americans, the distribution was 13.4% with ALM, 11.0% with NM, and 24.4% with SSM. Asians and Hispanics had higher NM rates of 14.1% and 11.4%, respectively. The proportion of cases with stage I, stage II, stage III, and stage IV disease at presentation was as follows: 80.3%, 14.4%, 4.6%, and 0.7%, respectively, in NHWs; 62.2%, 33.8%, 4.0%, and 0.0%, respectively, in African Americans; 59.5%, 28.2%, 11.1%, and 1.2%, respectively, in Asians; and 71.1%, 18.7%, 8.4%, and 1.8%, respectively, in Hispanics. Although 34.6% of melanomas in NHW patient cases occurred in the trunk, melanomas in the African American, Asian/Pacific Islander, and Hispanic patient cases occurred in the lower extremity (54.3%, 47.3%, and 31.6%, respectively). African American and Asian/Pacific Islander patient cases had significantly higher incidences of ulcerated tumors (11.9% and 15.0%, respectively) compared with NHW and Hispanic patient cases (5.9% and 9.6%, respectively).

Among the NHW, African American, Asian/Pacific Islander, and Hispanic patient cases that received surgery, the majority received wide excision (77.7%, 69.3%, 75.8%, and 73.6%, respectively), followed by local tumor excision (11.2%, 14.5%, 9.2%, and 13.0%,

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Table 1. Demographic Characteristics for Patient Cases of Invasive Melanoma by Major Race/Ethnicity Groups

Characteristic	Non-Hispanic White (n = 36,694)		African American (n = 127)		Hispanic (n = 1,966)		Asian/Pacific Islander (n = 262)		Total (N = 39,049)	
	No.	%	No.	%	No.	%	No.	%	No.	%
Median age at diagnosis, years	58.0		61.0		49.0		54.5		58.0	
95% CI	30.0 to 84.0		33.0 to 86.0		26.0 to 81.0		26.0 to 83.0		29.0 to 84.0	
Sex										
Female	15,423	42.0	73	57.5	1,196	61.0	127	48.5	16,819	43.1
Male	21,262	58.0	54	42.5	766	39.0	135	51.5	22,217	56.9
Stage										
IA	21,777	59.3	46	36.2	984	50.0	113	43.1	22,920	58.7
IB	7,706	21.0	33	26.0	414	21.1	43	16.4	8,196	21.0
IIA	3,109	8.5	16	12.6	200	10.2	40	15.3	3,365	8.6
IIB	1,757	4.8	21	16.5	133	6.8	26	9.9	1,937	5.0
IIC	408	1.1	6	4.7	34	1.7	8	3.0	456	1.2
IIIB	1,116	3.0	2.	1.6	87	4.4	13	5.0	1,218	13.1
IIIC	569	1.6	3	2.4	79	4.0	16	6.1	667	1.7
IV	252	0.7	0	0.0	35	1.8	3.	1.2	290	0.7
Histologic subtype										
SSM	12,852	35.0	31	24.4	652	33.2	81	30.9	13,616	34.9
LMM	2,091	5.7	3	2.4	59	3.0	7	2.7	2,160	5.5
NM	3,190	8.7	14	11.0	25	11.4	37	14.1	3,466	8.9
ALM	299	0.8	17	13.4	90	4.6	27	10.3	433	1.1
NOS	16,147	44.0	55	43.3	848	43.1	98	37.4	17,148	43.9
Other	2,115	5.8	7	5.5	92	4.7	12	4.6	2,226	5.7
Tumor ulceration										
Ulcerated	2,115	5.0	14	11.9	180	9.6	37	15.0	2,346	6.1
Not ulcerated	33,847	94.1	104	88.1	1,699	90.4	210	85.0	35,860	93.9
Anatomic site										
Head and neck	7,487	20.4	9	7.1	349	17.8	32	12.2	7,877	20.2
Trunk	12,708	34.6	25	19.7	555	28.2	69	26.3	13,357	34.2
Upper extremity	9,403	25.6	24	18.9	431	21.9	33	12.6	9,891	25.3
Lower extremity	6,957	19.0	69	54.3	621	31.6	124	47.3	7,771	19.9
Overlap	49	0.1	0	0.0	4	0.2	1	0.4	54	0.1
NOS	90	0.3	0	0.0	6	0.3	3	1.2	99	0.3
Surgery										
None	455	1.2	3	2.4	38	1.9	2	0.8	498	1.3
Any	36,236	98.9	124	97.6	1,928	98.1	260	99.2	38,548	98.7
Unknown	3	0.0	0	0.0	0	0.0	0	0.0	3	0.0
Type of surgery										
Local tumor destruction	10	0.0	0	0.0	1	0.0	0	0.0	11	0.0
Local tumor excision	4,060	11.2	18	14.5	250	13.0	24	9.2	4,352	11.3
Biopsy + gross excision	2,776	7.7	5	4.0	140	7.3	19	7.3	2,940	7.6
Wide excision	28,155	77.7	86	69.3	1,419	73.6	197	75.8	29,857	77.5
Major amputation	120	0.3	13	10.5	40	2.1	10	3.9	183	0.5
NOS	1,115	3.1	2	1.6	78	4.1	10	3.9	1,205	3.1
Chemotherapy										
None	36,211	98.7	118	92.9	1,913	97.3	250	95.4	38,492	98.6
Any	356	1.0	8	6.3	41	2.1	8	3.1	413	1.1
Unknown	127	0.3	1	0.8	12	0.6	4	1.5	144	0.4
Radiation therapy										
None	36,373	99.1	125	98.4	1,941	98.7	259	98.9	38,698	99.1
Any	321	0.9	2	1.6	25	1.3	3	1.2	351	0.9
Immunotherapy										
None	35,412	96.5	123	96.9	1,850	94.1	241	92.0	37,626	96.4
Any	1,233	3.4	4	3.1	112	5.7	20	7.6	1,369	3.5
Unknown	49	0.1	0	0.0	4	0.2	1	0.4	54	0.1
SES										
Lowest	2,170	5.9	29	22.8	402	20.5	29	11.1	2,630	6.7
Second-lowest	4,730	12.9	26	20.5	448	22.7	37	14.1	5,241	13.4
Middle	7,277	19.8	31	24.4	426	21.7	39	14.9	7,773	19.9
High	9.701	26.4	26	20.5	353	18.0	67	25.6	10,147	26.0
Highest	12,816	34.9	15	11.8	337	17.1	90	34.3	13,258	34.0

NOTE. Incidence cases, 1993 to 2003.
Abbreviations: SSM, superficial spreading melanoma; LMM, lentigo maligna melanoma; NM, nodular melanoma; ALM, acral lentiginous melanoma; NOS, not otherwise specified; SES, socioeconomic status.
*$P < .0001$ for comparisons of each variable listed across the four race/ethnicity groups.

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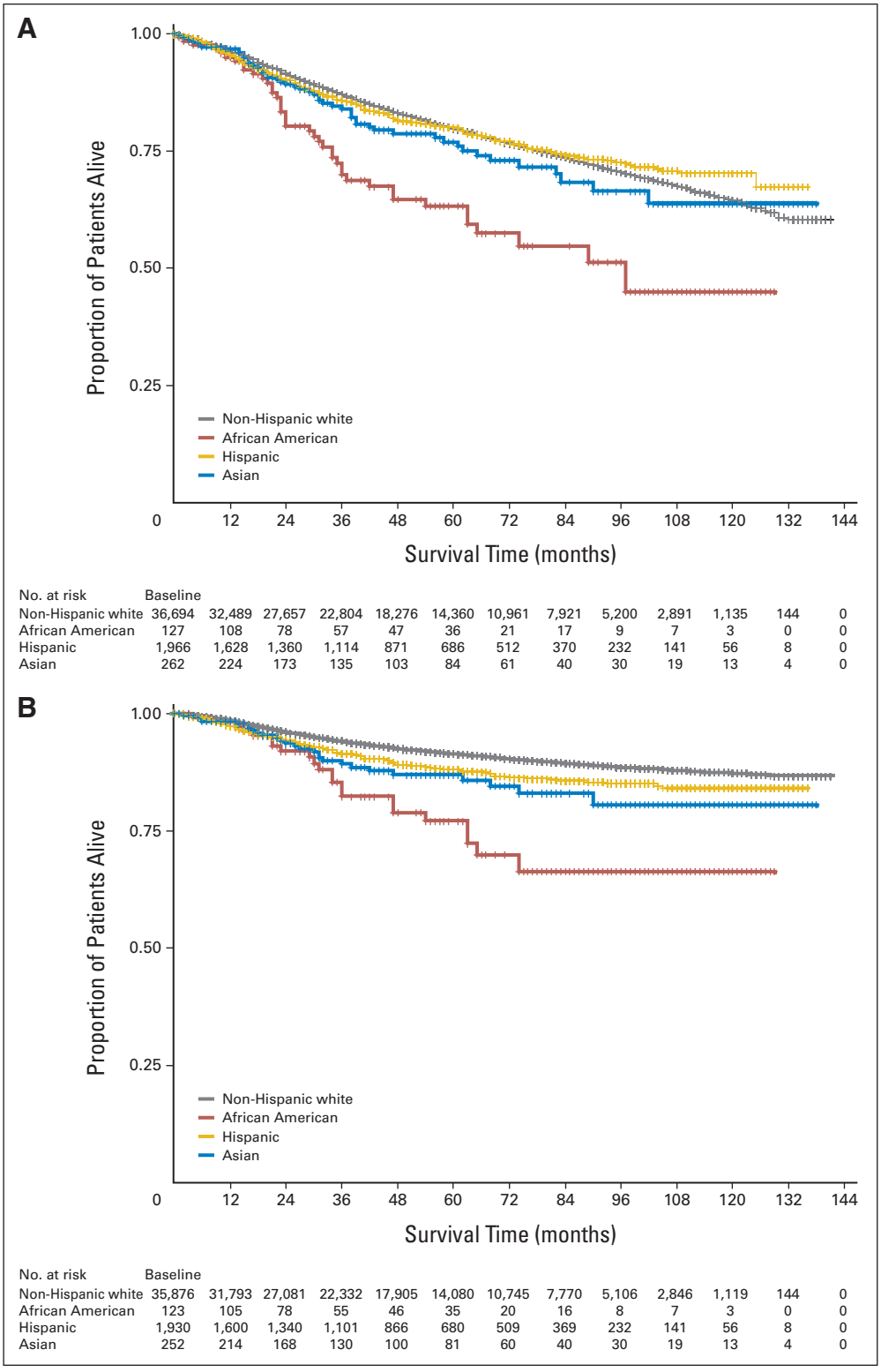

Fig 1. (A) Overall survival by race/ethnicity for invasive cutaneous melanoma, 1993 to 2003 ($P < .0001$). Censoring marks are indicated with small vertical lines. (B) Melanoma-specific survival by race/ethnicity for invasive cutaneous melanoma, 1993 to 2003 ($P < .0001$).

respectively). Although statistically significant differences were noted across the various ethnic groups by treatment variables (ie, surgery, chemotherapy, radiation therapy, and immunotherapy), these differences were small (Table 1).

SES Analysis

Statistically significant differences in SES were observed across the four major ethnic groups analyzed ($P < .0001$). Although a large proportion of NHW and Asian/Pacific Islander patient cases belonged

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to the highest SES category (34.9% and 34.3%, respectively), significantly fewer African American and Hispanic cases belonged to this SES category (11.8% and 17.1%, respectively). An incremental increase in the number of patient cases with stage I disease was observed with increasing SES quintile: 71.5%, 75.1%, 78.9%, 81.1%, and 82.5%, respectively ($P < .0001$). The vast majority (98.7%) of all patient cases received surgery regardless of SES. There were no significant associations with radiation therapy and SES ($P = .62$); however significant associations with high SES and treatment with chemotherapy and immunotherapy were observed ($P = .0002$ and .0092, respectively).

Univariate Survival Analysis

Median follow-up duration for the entire cohort was 47 months; median follow-up duration for NHWs, African Americans, Hispanics, and Asians was 47, 34, 42, and 38 months, respectively. Among those alive, a median of 11 months (95% CI, 5 to 31) elapsed between the date of last follow-up and the date of data extraction. Overall survival (OS) rates were statistically different across the four major ethnic categories ($P < .0001$). Figure 1A shows the OS curves for all races/ethnicities. One year, 5-year, and 10-year OS rates were 96.4%, 79.8%, and 64.4%, respectively, for NHWs; 95.0%, 63.2%, and 44.9%, respectively, for African Americans; 96.8%, 76.9%, and 63.7%, respectively, for Asians; and 95.5%, 80.0%, and 70.0%, respectively, for Hispanics. Because of the observed poor survival for African Americans, subset-stage–specific univariate survival analyses were performed. Stage-specific survival differences were noted for African American versus NHW patient cases with melanoma within stage I (5-year OS, 83% *v* 86%; $P = .035$), and stage II (5-year OS, 34% *v* 56%; $P = .018$); comparisons for advanced-stage melanoma were not done because of inadequate sample size.

One year, 5-year, and 10-year melanoma-specific survival rates were 98.6%, 91.4%, and 87.3%, respectively, for NHWs; 98.2%, 77.1%, and 66.4%, respectively, for African Americans; 98.3%, 86.9%, and 80.6%, respectively, for Asians; and 97.3%, 88.1%, and 84.1%, respectively, for Hispanics ($P < .0001$; Fig 1B).

Cause of Death Analysis

A total of 6,706 (17.2%) of the 39,049 patient cases with melanoma died. Of these, 2, 842 (42.4%) were because of melanoma itself. The second major cause of death (18.9%) was heart disease. Cause of death was unknown in 868 (12.9%) of the 6,706 patient cases.

Multivariate Survival Analysis

The variables of age, sex, histologic subtype, 2002 AJCC stage, race/ethnicity, melanoma site, surgery status, radiation therapy, chemotherapy, immunotherapy, and SES were included in the multivariate Cox regression model for OS and for MSS (Table 2). Age was included as a continuous variable. A high proportion (41%) of patient cases who reported other race/ethnicity had SSM histology, early stage at diagnosis (95% were stage I), and improved OS compared with other ethnicities (data not shown). However, inclusion of these cases into the multivariate survival models did not significantly affect the risk estimates for any race/ethnicity or SES quintile; thus, they were not included in the final multivariate models. After adjustment for the aforementioned factors, African Americans had a significantly increased risk of death compared with NHWs (OS: HR, 1.60; 95% CI, 1.17 to 2.18; $P = .0030$; MSS: HR, 2.00; 95% CI, 1.30 to 3.06; $P = .0015$; Table 2). Multivariate analysis of OS by histologic subtype also revealed an increased risk of death for African Americans with NM (HR, 2.52; 95% CI, 1.34 to 4.75) and NOS (HR, 1.70; 95% CI, 1.09 to 2.66; Table 3).

Multivariate survival analysis for treatment types after adjustment for age, sex, histologic subtype, 2002 AJCC stage, race/ethnicity, melanoma site, and SES revealed a significantly decreased risk of death for patient cases who received surgery (OS: HR, 0.53; 95% CI, 0.45 to 0.63; MSS: HR, 0.56; 95% CI, 0.41 to 0.75; Table 2). For OS and MSS, patient cases who received chemotherapy, radiation therapy, or immunotherapy had a significantly increased risk of death. This trend likely reflects the fact that such treatments were reserved for cases with poor prognostic features, advanced stage, or incompletely resected tumors.

In the unadjusted (Fig 2) and adjusted survival analyses, there was an incremental increase in the risk of death for each decrease in SES quintile. For OS, the HRs for the highest to the lowest SES quintiles were as follows: 0.63 (95% CI, 0.58 to 0.69), 0.76 (95% CI, 0.70 to 0.83), 0.83 (95% CI, 0.76 to 0.91), 0.92 (95% CI, 0.83 to 1.00), and 1.00 (reference). A similar trend was noted for MSS (Table 2).

DISCUSSION

Our data show that, among invasive cutaneous melanoma patient cases, African Americans have poorer survival rates than NHWs, even after adjustment for age, sex, histologic subtype, 2002 AJCC stage (which includes Breslow depth), anatomic site, treatment with surgery, radiation therapy, chemotherapy, immunotherapy, and SES. Thus, treatment differences and differences in SES do not explain the poor survival for patient cases of melanoma in African Americans. Our epidemiologic analysis of 39,049 patient cases, including 127 African Americans and 1,966 Hispanics, represents one of the largest reported clinical outcomes studies to assess the role of SES on outcomes in cutaneous melanoma occurring in ethnic minority populations.

African American race/ethnicity has been associated with poor survival for various malignancies, such as pancreatic cancer[33] and breast cancer[34]; yet, in these cancer types, the observed survival differences were related to treatment disparities or to disparities in SES. Although we are the first to report the independent increase in hazard of death for African Americans with melanoma after accounting for the effects of treatment and SES differences, others have reported ethnic differences in clinical outcomes for melanoma. A recent study of US SEER data during 1992 to 2002 involved 48,143 NHWs, 251 African Americans, 932 Hispanics, and 394 Asians; NHWs had improved OS compared with African Americans.[10] In the multivariate analysis, these investigators showed that, after adjustment for age, sex, and SEER region, there was an increased risk of mortality in other races/ethnicities compared with NHWs. When their analysis was adjusted for stage and for other factors, such as tumor size, anatomic site, and histologic subtypes, only the African Americans showed a greater mortality risk compared with NHWs.[10] Although our study of melanoma using the CCR data has fewer African Americans (127 patient cases) than this SEER study (251 patient cases), the CCR contains information on SES and on additional treatment variables not recorded in SEER, which allowed us to account for the potential confounding effects of these factors on survival.

The major observed difference in survival for African Americans compared with NHWs in our study resulted from differences in

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Table 2. Cox Multivariate Analysis of Overall and Melanoma-Specific Survival in Patient Cases with Invasive Melanoma

Characteristic	Overall Survival			Melanoma-Specific Survival		
	HR	95% CI	*P*	HR	95% CI	*P*
Age, years	1.05	1.051 to 1.054	< .0001	1.02	1.017 to 1.022	< .0001
Sex						
Male		1.00*	—		1.00*	—
Female	0.75	0.71 to 0.79	< .0001	0.74	0.68 to 0.81	< .0001
Race/ethnicity						
Non-Hispanic white		1.00*	—		1.00*	—
African American	1.60	1.17 to 2.18	.003	2.00	1.30 to 3.06	.0015
Hispanic	1.03	0.92 to 1.15	.577	1.09	0.93 to 1.27	.296
Asian/Pacific Islander	1.02	0.77 to 1.34	.901	1.07	0.73 to 1.56	.745
Stage						
I		1.00*	—		1.00*	—
II	2.26	2.14 to 2.39	< .0001	4.96	4.51 to 5.56	< .0001
III	4.27	3.90 to 4.67	< .0001	9.99	8.84 to 11.29	< .0001
IV	10.39	8.96 to 12.0	< .0001	27.1	22.4 to 32.8	< .0001
Histologic subtype						
SSM		1.00*	—		1.00*	—
LMM	1.07	0.97 to 1.19	.160	0.67	0.52 to 0.87	.002
NM	1.51	1.40 to 1.63	< .0001	1.87	1.66 to 2.11	< .0001
ALM	1.11	0.92 to 1.34	.292	1.29	0.98 to 1.70	.070
NOS	1.18	1.11 to 1.25	< .0001	1.30	1.17 to 1.44	< .0001
Other	1.05	0.95 to 1.15	.385	1.05	0.89 to 1.24	.533
Anatomic site						
Head and neck		1.00*	—		1.00*	—
Trunk	0.89	0.84 to 0.95	.0002	0.93	0.84 to 1.03	.170
Upper extremity	0.80	0.75 to 0.85	< .0001	0.71	0.63 to 0.79	< .0001
Lower extremity	0.83	0.76 to 0.89	< .0001	0.91	0.81 to 1.03	.135
Overlap	0.94	0.56 to 1.59	.821	0.45	0.11 to 1.79	.254
NOS	1.00	0.68 to 1.47	.997	1.10	0.60 to 2.00	.761
Surgery†						
None		1.00*	—		1.00*	—
Any	0.53	0.45 to 0.63	< .0001	0.56	0.41 to 0.75	.0001
SES						
Lowest		1.00*	—		1.00*	—
Second-lowest	0.92	0.83 to 1.00	.068	0.91	0.79 to 1.06	.239
Middle	0.83	0.76 to 0.91	< .0001	0.85	0.74 to 0.98	.025
High	0.76	0.70 to 0.83	< .0001	0.72	0.63 to 0.84	< .0001
Highest	0.63	0.58 to 0.69	< .0001	0.68	0.59 to 0.78	< .0001

NOTE: Number of melanoma-specific patient case survivals = 38,129; deaths = 2,841 (8%); and censored = 35,288 (92%). Number of overall survivals = 38,996; deaths = 7,571 (19%); and censored = 31,425 (81%). The model includes adjustment for radiation therapy, chemotherapy, and immunotherapy.

Abbreviations: HR, hazard ratio; SSM, superficial spreading melanoma; LMM, lentigo maligna melanoma; NM, nodular melanoma; ALM, acral lentiginous melanoma; NOS, not otherwise specified; SES, socioeconomic status.

*Reference group.

†Three patient cases with unknown surgery status were included in the analysis but were not included in the table.

stage-specific survival, particularly within stage II melanoma. Rates of treatment (Table 1) were similar, and rates of treatment refusal were similarly low in both groups (data not shown). A greater proportion of African Americans (and also of Asians) had ulcerative lesions compared with NHWs, including those diagnosed as stage IIC (T4bN0M0)—a stage grouping that exhibits particularly poor survival when compared with stage IIA, IIB, or even stage III disease.[28] The major survival differences become apparent after approximately 2 years (Fig 1A, B), and the reason for this is unknown. Two possible explanations are proposed. African Americans with melanoma may be inadequately staged compared with NHWs (because of factors unaccounted for in this study, such as access to subspecialty care), which results in inadequate treatment and long-term survival differences. Alternatively, melanoma in African Americans may represent a biologically different cancer, and certain individuals may have a particularly aggressive biology.

Our study demonstrates significant differences in the distribution of melanoma histologic subtypes among various US races/ethnicities. A consideration might be that survival in African Americans is poorer because of a higher incidence of ALM and because of deeper lesions, but we have adjusted for these factors. ALM histology was associated with poor OS and MSS on unadjusted analysis in our study (data not shown)—a finding that did not persist in the adjusted analysis (Table 2). Melanoma NOS was the most common histologic subtype in all races/ethnicities, as has been shown in other population-based studies.[2,6,9] A high percentage of melanoma-NOS exists in any large epidemiologic study[2,35] and is a known limitation of such studies. It is possible that a high percentage of melanoma NOS

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Table 3. Cox Multivariate Analysis of Overall Survival for Patient Cases of Invasive Melanoma by Histologic Subtype

	Histologic Subtype								
	SSM (n = 13,616)			LMM (n = 2,160)			NM (n = 3,466)		
Characteristic	No.	HR	95% CI	No.	HR	95% CI	No.	HR	95% CI
Age	13,608	1.06	1.06 to 1.07	2,155	1.09	1.08 to 1.10	3,464	1.03	1.03 to 1.04
Sex									
Male	6,307	1.00*		739	1.00*		1,327	1.00*	
Female	7,301	0.71	0.64 to 0.78	1,421	0.74	0.61 to 0.89	2,138	0.75	0.67 to 0.85
Race/ethnicity									
White	12,964	1.00*		2,091	1.00*		3,190	1.00*	
African American	31	0.96	0.40 to 2.31	3	0.00		14	2.52	1.34 to 4.75
Hispanic	652	1.13	0.87 to 1.45	59	0.64	0.35 to 1.17	225	0.97	0.76 to 1.23
Asian	81	0.85	0.48 to 1.51	7	1.21	0.30 to 4.87	37	1.19	0.71 to 2.0
Stage									
I	12,270	1.00*		2,018	1.00*		1,167	1.00*	
II	908	2.61	2.30 to 2.97	131	2.02	1.54 to 2.65	1,707	1.66	1.46 to 1.90
III	403	4.44	3.56 to 5.52	8	5.85	1.73 to 19.77	518	3.04	2.53 to 3.65
IV	35	8.39	5.49 to 12.81	3	0.95	0.13 to 6.81	74	6.69	4.90 to 9.13
Anatomic site									
Head and neck	1,814	1.00*		1,329	1.00*		790	1.00*	
Trunk	5,293	0.89	0.78 to 1.01	318	0.70	0.53 to 0.92	1,081	0.89	0.77 to 1.03
Upper extremity	3,456	0.80	0.69 to 0.91	421	0.88	0.70 to 1.10	947	0.78	0.67 to 0.90
Lower extremity	3,012	0.73	0.63 to 0.86	82	0.82	0.50 to 1.37	641	0.89	0.75 to 1.06
Overlap	21	0.84	0.31 to 2.25	5	2.06	0.51 to 8.35	2	0.00	
NOS	20	1.13	0.36 to 3.51	6	1.0	0.25 to 4.01	5	0.19	0.03 to 1.37
Surgery†									
None	131	1.00*		34	1.00*		33	1.00*	
Any	13,485	0.50	0.33 to 0.76	2,124	0.80	0.38 to 1.70	3,433	0.33	0.21 to 0.53
Chemotherapy‡									
None	13,514	1.00*		2,146	1.00*		3,327	1.00*	
Any	68	2.29	1.58 to 3.32	3	1.70	0.18 to 16.23	118	2.07	1.62 to 2.6
Radiation therapy									
None	13,564	1.00*		2,150	1.00*		3,394	1.00*	
Any	52	2.97	2.05 to 4.30	10	1.13	0.36 to 3.55	72	2.16	1.61 to 2.89
Immunotherapy§									
None	13,328	1.00*		2,150	1.00*		3,048	1.00*	
Any	273	1.47	1.14 to 1.90	9	0.82	0.21 to 3.21	405	0.96	0.80 to 1.14
SES									
Lowest	819	1.00*		137	1.00*		323	1.00*	
Second-lowest	1,675	1.01	0.82 to 1.25	274	0.75	0.50 to 1.11	586	0.95	0.78 to 1.17
Middle	2,644	0.90	0.74 to 1.10	389	0.75	0.52 to 1.09	746	0.83	0.68 to 1.01
High	3,661	0.87	0.71 to 1.05	520	0.93	0.66 to 1.32	825	0.78	0.64 to 0.96
Highest	4,817	0.68	0.56 to 0.83	840	0.72	0.51 to 1.01	986	0.60	0.50 to 0.74

(continued on following page)

histology among the African Americans is in fact misdiagnosed ALM; however, 99.96% of all our patient cases and 99.97% of the melanoma NOS patient cases were confirmed microscopically. Nonetheless, these specimens were not all reviewed by the same pathologists or by pathologists with the same background (a limitation of population-based analyses). The CCR data does not include comorbidity information, insurance status, or date of relapse; nor does it contain specific melanoma sites, like subungal melanoma or plantar melanoma. Thus, we are unable to account for the effect of these additional variables on survival.

Gene-environment interactions may explain the observed survival differences in our study (ie, differential mutation spectra in *BRAF* or *NRAS*).[36,37] Recently, gene alterations were shown to vary with melanoma site and also with sun exposure levels.[38] Skin melanomas without signs of chronic sun-induced damage (CSD) frequently harbor mutations in *BRAF* or *NRAS*.[38] However, CSD skin melanomas and melanomas of mucosal and acral sites often have wild-type *BRAF* or *NRAS* and are associated with increased copy numbers of downstream *RAS-BRAF* pathway components, including cyclin-dependent kinase 4 and cyclin D1.[38] Gene amplification and mutations in *KIT* have also been discovered among these mucosal, acral, and CSD melanomas, thus implicating a potential role for targeted therapy with the cyclin-dependent kinase 4–inhibitor imatinib.[39] Melanocortin-1 receptor (*MC1R*) gene variants are associated with *BRAF* mutations in non-CSD melanomas among NHW populations.[40] However, potential differences in *NRAS* or *KRAS* mutational spectra across the major ethnicities represented in the United States are not yet determined. Alternatively, different DNA/gene ultraviolet (UV) repair

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Table 3. Cox Multivariate Analysis of Overall Survival for Patient Cases of Invasive Melanoma by Histologic Subtype (continued)

Characteristic	Histologic Subtype								
	ALM (n = 433)			NOS (n = 17,148)			Other (n = 2,226)		
	No.	HR	95% CI	No.	HR	95% CI	No.	HR	95% CI
Age	433	1.02	1.01 to 1.04	17,122	1.05	1.05 to 1.06	2,226	1.06	1.05 to 1.06
Sex									
Male	219	1.00*		7,399	1.00*		828	1.00*	
Female	214	0.89	0.62 to 1.28	9,746	0.76	0.70 to 0.82	1,397	0.85	0.70 to 1.03
Race/ethnicity									
White	299	1.00*		16,147	1.00*		2115	1.00*	
African American	17	1.24	0.49 to 3.19	55	1.70	1.09 to 2.66	7	2.02	0.28 to 14.70
Hispanic	90	0.80	0.46 to 1.38	848	1.05	0.89 to 1.24	92	1.61	1.02 to 2.54
Asian	27	1.01	0.45 to 2.27	98	0.98	0.59 to 1.63	12	0.24	0.03 to 1.74
Stage									
I	222	1.00*		14,072	1.00*		1,367	1.00*	
II	142	2.36	1.53 to 3.64	2,165	2.48	2.28 to 2.70	705	1.77	1.46 to 2.13
III	64	6.43	3.68 to 11.22	767	4.74	4.14 to 5.42	125	3.32	2.31 to 4.77
IV	5	10.56	2.67 to 41.80	144	11.65	9.39 to 14.45	29	9.18	5.58 to 15.08
Anatomic site									
Head and neck	7	1.00*		3,249	1.00*		688	1.00*	
Trunk	7	0.92	0.06 to 14.92	5,954	0.90	0.82 to 0.99	704	0.89	0.70 to 1.12
Upper extremity	79	0.96	0.12 to 7.39	4,459	0.80	0.72 to 0.88	529	0.81	0.64 to 1.02
Lower extremity	338	1.14	0.15 to 8.47	3,399	0.83	0.74 to 0.93	299	0.96	0.72 to 1.28
Overlap	0	—		26	1.15	0.57 to 2.30	1	0.00	
NOS	2	0.00		61	1.32	0.83 to 2.12	5	0.60	0.08 to 4.28
Surgery†									
None	6	1.00*		256	1.00*		28	1.00*	
Any	427	2.28	0.52 to 9.93	16,891	0.50	0.39 to 0.64	2,188	0.69	0.41 to 1.17
Chemotherapy‡									
None	412	1.00*		16,919	1.00*		2,174	1.00*	
Any	15	0.80	0.35 to 1.85	165	2.62	2.11 to 3.24	44	1.71	1.10 to 2.65
Radiation therapy									
None	423	1.00*		17,007	1.00*		2,160	1.00*	
Any	10	5.95	1.9 to 18.56	141	1.45	1.15 to 1.83	66	1.42	0.98 to 2.06
Immunotherapy§									
None	395	1.00*		16,618	1.00*		2,087	1.00*	
Any	38	0.61	0.32 to 1.15	510	1.33	1.14 to 1.56	134	0.96	0.68 to 1.35
SES									
Lowest	55	1.00*		1,160	1.00*		136	1.00*	
Second-lowest	63	0.83	0.44 to 1.56	2,351	0.88	0.76 to 1.01	292	1.16	0.77 to 1.74
Middle	78	0.53	0.28 to 0.98	3,475	0.83	0.72 to 0.95	441	1.00	0.68 to 1.49
High	99	0.81	0.46 to 1.42	4,472	0.69	0.60 to 0.79	570	0.93	0.63 to 1.37
Highest	138	0.43	0.23 to 0.77	5,690	0.62	0.54 to 0.70	787	0.93	0.64 to 1.36

NOTE. Deaths from SSM = 1,815 (13%); censored = 11,785 (87%). Deaths from LMM = 551 (26%); censored = 1604 (74%). Deaths from NM = 1,369 (40%); censored = 2,095 (60%). Deaths from ALM = 127 (29%); censored = 306 (71%). Deaths from melanoma NOS = 3,154 (18%); censored = 13,965 (82%). Other deaths = 555 (25%); censored = 1,670 (75%).

Abbreviations: HR, hazard ratio; SSM, superficial spreading melanoma; LMM, lentigo maligna melanoma; NM, nodular melanoma; NOS, not otherwise specified; ALM, acral lentiginous melanoma; SES, socioeconomic status.

*Reference group.

†Three patient cases with unknown surgery status were included in the analysis but were not included in the table.

‡One hundred forty-four patient cases with unknown chemotherapy status were included in the analysis but were not included in the table.

§Fifty-four patient cases with unknown immunotherapy status were included in the analysis but were not included in the table.

mechanisms may exist that explain the ethnic differences in survival observed in our study. For both Hispanics and African Americans, melanoma incidence is positively associated with the UV index.[5,6,41,42] However, another study showed that melanoma incidence was associated with increased UV index only in NHWs.[43] Possible ethnic differences may exist in the oxidation of melanin and in the release of reactive oxygen species secondary to melanosomal damage, DNA damage, and redox metabolism.[44-46]

The results from our study indicate that more awareness efforts are warranted for the prevention and control of melanoma in all races/ethnicities, even for those patients who are at a lower risk of developing the disease. Additional biologic and genetic studies are required to explain differential effects among race/ethnicities, specifically among African Americans. Such research efforts will help uncover reasons for the observed poor survival of African Americans with melanoma and may also lead to targeted therapeutic interventions.

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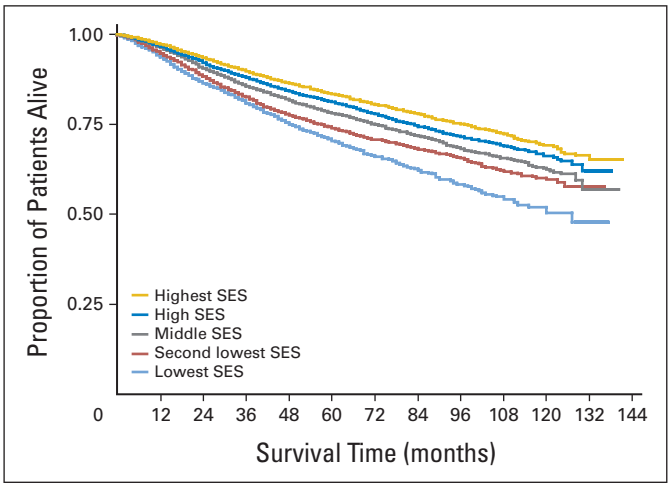

Fig 2. Overall survival by socioeconomic status (SES) quintile for invasive cutaneous melanoma, 1993 to 2003 (10-year overall survival for highest to lowest SES quintile = 69.2%, 66.1%, 62.5%, 59.6%, and 50.4%; $P < .0001$).

AUTHORS' DISCLOSURES OF POTENTIAL CONFLICTS OF INTEREST

The author(s) indicated no potential conflicts of interest.

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REFERENCES

1. Rhodes AR, Weinstock MA, Fitzpatrick TB, Mihm MC, Sober AJ: Risk-Factors for Cutaneous Melanoma—A Practical Method of Recognizing Predisposed Individuals. JAMA 258:3146-3154, 1987

2. Cress RD, Holly EA: Incidence of cutaneous melanoma among non-Hispanic whites, Hispanics, Asians, and blacks: An analysis of California Cancer Registry data, 1988-93. Cancer Causes Control 8:246-252, 1997

3. Bellows CF, Belafsky P, Fortgang IS, Beech DJ: Melanoma in African-Americans: Trends in biological behavior and clinical characteristics over two decades. J Surg Oncol 78:10-16, 2001

4. Crowley NJ, Dodge R, Vollmer RT, Seigler HF: Malignant-melanoma in black Americans: A Trend Toward Improved Survival. Arch Surg 126:1359-1365, 1991

5. Hu S, Parker DF, Thomas AG, Kirsner RS: Advanced presentation of melanoma in African Americans: The Miami-Dade County experience. J Am Acad Dermatol 51:1031-1032, 2004

6. Tsai T, Vu C, Henson DE: Cutaneous, ocular, and visceral melanoma in African Americans and Caucasians. Melanoma Res 15:213-217, 2005

7. Byrd KM, Wilson DC, Hoyler SS, Peck GL: Advanced presentation of melanoma in African Americans. J Am Acad Dermatol 50:21-24, 2004

8. Swan MC, Hudson DA: Malignant melanoma in South Africans of mixed ancestry: A retrospective analysis. Melanoma Res 13:415-419, 2003

9. Chang AE, Karnell LH, Menck HR: The National Cancer Data Base report on cutaneous and noncutaneous melanoma: A summary of 84,836 cases from the past decade. Cancer 83:1664-1678, 1998

10. Cormier JN, Xing Y, Ding MC, et al: Ethnic differences among patients with cutaneous melanoma. Arch Intern Med 166:1907-1914, 2006

11. Hemminki K, Li XJ: Level of education and the risk of cancer in Sweden. Cancer Epidemiol Biomarkers Prev 12:796-802, 2003

12. Hemminki K, Zhang H, Czene K: Socioeconomic factors in cancer in Sweden. Int J Cancer 105:692-700, 2003

13. Goodman KJ, Bible ML, London S, Mack TM: Proportional melanoma incidence and occupation among white males in Los-Angeles-County (California, United-States). Cancer Causes Control 6:451-459, 1995

14. Epstein DS, Lange JR, Gruber SB, Mofid M, Koch SE: Is physician detection associated with thinner melanomas? JAMA 281:640-643, 1999

15. Roetzheim RG, Pal N, Van Durme DJ, et al: Increasing supplies of dermatologists and family physicians are associated with earlier stage of melanoma detection. J Am Acad Dermatol 43:211-218, 2000

16. Roetzheim RG, Pal N, Tennant C, et al: Effects of health insurance and race on early detection of cancer. J Natl Cancer Inst 91:1409-1415, 1999

17. Luke CG, Coventry BJ, Foster-Smith EJ, Roder DM: A critical analysis of reasons for improved survival from invasive cutaneous melanoma. Cancer Causes Control 14:871-878, 2003

18. Coleman MP, Rachet B, Woods LM, et al: Trends and socioeconomic inequalities in cancer survival in England and Wales up to 2001. Br J Cancer 90:1367-1373, 2004

19. Parikh-Patel A, Bates JH, Campleman S: Colorectal cancer stage at diagnosis by socioeconomic and urban/rural status in California, 1988-2000. Cancer 107:1189-1195, 2006

20. Cancer Reporting in California: Standards for Automated Reporting, in California Cancer Reporting System Standards, Volume II. Sacramento, CA, California Department of Health Services, Cancer Surveillance Section, 1997

21. Cancer Reporting in California: Data Standards for Regional Registries and Calfornia Cancer Registry, in California Cancer Reproting Standards, Volume III. Sacramento, CA, California Department of Health Services, Cancer Surveillance Section, 1997

22. Cancer Reporting in California: Abstracting and Coding Procedures for Hospitals, in California Cancer Reporting System Standards, Volume I. Sacramento, CA, California Department of Health Services, Cancer Surveillance Section, 1997

23. Cancer Reporting in California: Reporting Procedures for Physicians, in California Cancer Reporting System Standards, Volume IV. Sacramento, CA, California Department of Health Services, Cancer Surveillance Section, 1998

24. California Cancer Registry: How complete are California Cancer Registry data? http://www.ccrcal.org/questions.html

25. Fritz A, Percy C, Jack A, et al: International Classification of Diseases for Oncology (ed 3). Geneva, Switzerland, World Health Organization, 2000

26. Balch CM, Soong SJ, Gershenwald JE, et al: Prognostic factors analysis of 17,600 patients with melanoma: Validation of the American Joint Committee on Cancer melanoma staging system. J Clin Oncol 19:3622-3634, 2001

27. Balch CM, Buzaid AC, Soong SJ, et al: Final version of the American Joint Committee on Cancer staging system for cutaneous melanoma. J Clin Oncol 19:3635-3648, 2001

28. Gimotty PA, Botbyl J, Soong SJ, Guerry D: A population-based validation of the American Joint Committee on Cancer melanoma staging system. J Clin Oncol 23:8065-8075, 2005

29. Yost K, Perkins C, Cohen R, Morris C, Wright W: Socioeconomic status and breast cancer incidence in California for different race/ethnic groups. Cancer Causes Control 12:703-711, 2001

30. Morris CR, Snipes KP, Schlag R, Wright WE: Sociodemographic factors associated with prostatectomy utilization and concordance with the physician data query for prostate cancer (United States). Cancer Causes Control 10:503-511, 1999

31. Cress RD, O'Malley CD, Leiserowitz GS, Campleman SL: Patterns of chemotherapy use for women with ovarian cancer: A population-based study. J Clin Oncol 21:1530-1535, 2003

32. Ou SI, Zell JA, Ziogas A, Anton-Culver H: Epidemiology of nasopharyngeal carcinoma (NPC) in California: Survival advantage of Chinese WHO Type 1 NPC patients resulted in Asian ethnicity as an independent and favorable prognostic factor of survival for NPC patients as a whole and for patients with the WHO histologic type 1. J Clin Oncol 24: 283S, 2006 (suppl; asbtr 5514)

33. Zell JA, Rhee JM, Ziogas A, Lipkin SM, Anton-Culver H: Race, socioeconomic status, treatment, and survival time among pancreatic cancer cases in California. Cancer Epidemiol Biomarkers Prev 16: 546-552, 2007

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34. Hirschman J, Whitman S, Ansell D: The black: white disparity in breast cancer mortality: The Example of Chicago. Cancer Causes Control 18:323-333, 2007

35. Howe HL, Wu XC, Ries LAG, et al: Annual report to the nation on the status of cancer, 1975-2003, featuring cancer among US Hispanic/Latino populations. Cancer 107:1711-1742, 2006

36. Albino AP, Nanus DM, Mentle IR, et al: Analysis of Ras Oncogenes in Malignant-Melanoma and Precursor Lesions: Correlation of Point Mutations with Differentiation Phenotype. Oncogene 4:1363-1374, 1989

37. Davies H, Bignell GR, Cox C, et al: Mutations of the BRAF gene in human cancer. Nature 417:949-954, 2002

38. Curtin JA, Fridlyand J, Kageshita T, et al: Distinct sets of genetic alterations in melanoma. N Engl J Med 353:2135-2147, 2005

39. Curtin JA, Busam K, Pinkel D, Bastian BC: Somatic activation of KIT in distinct subtypes of melanoma. J Clin Oncol 24:4340-4346, 2006

40. Landi MT, Bauer J, Pfeiffer RM, et al: MC1R germline variants confer risk for BRAF-mutant melanoma. Science 313:521-522, 2006

41. Green A, McCredie M, MacKie R, et al: A case-control study of melanomas of the soles and palms (Australia and Scotland). Cancer Causes Control 10:21-25, 1999

42. Hu S, Ma FC, Collado-Mesa F, Kirsner RS: UV radiation, latitude, and melanoma in US Hispanics and blacks. Arch Dermatol 140:819-824, 2004

43. Eide MJ, Weinstock MA: Association of UV index, latitude, and melanoma incidence in non-white populations: US surveillance, epidemiology, and end results (SEER) program, 1992 to 2001. Arch Dermatol 141:477-481, 2005

44. Meyskens FL, Farmer PJ, Anton-Culver H: Etiologic pathogenesis of melanoma: A unifying hypothesis for the missing attributable risk. Clinical Cancer Res 10:2581-2583, 2004

45. Meyskens FL, Farmer P, Fruehauf JP: Redox regulation in human melanocytes and melanoma. Pigment Cell Res 14:148-154, 2001

46. Meyskens FL, Farmer PJ, Anton-Culver H: Diet and melanoma in a case-control study. Cancer Epidemiol Biomarkers Prev 14:293, 2005

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