Effects of Socioeconomic Status and Treatment Disparities in Colorectal Cancer Survival

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Abstract

Background: **Poor survival among colorectal cancer (CRC) cases has been associated with African-American race and low socioeconomic status (SES). However, it is not known whether the observed poor survival of African-American CRC cases is due to SES itself and/or treatment disparities. We set out to determine this using data from the large, population-based California Cancer Registry database.**

Methods: **A case-only analysis of CRC was conducted including all age groups using California Cancer Registry data from 1994 to 2003, including descriptive analysis of relevant clinical variables, race, and SES. CRC-specific survival univariate analyses were conducted using the Kaplan-Meier method. Multivariate survival analyses were done using Cox proportional hazards ratios (HR).**

Results: **Incident cases of colon (90,273) and rectal (37,532) cancer were analyzed, including 91,739 (71.8%) non-Hispanic Whites, 8,535 (6.7%) African-Americans, 14,943 (11.7%) Hispanics, 3,564 (2.8%) Chinese, and 7,950 (6.2%) non-Chinese Asians. African-Americans had a greater proportion of metastatic stage at presentation ($P < 0.0001$) and decreased CRC-specific survival ($P < 0.0001$ for colon and rectal cancer). After adjustment for age, sex, histology, site within the colon, and stage, African-Americans [colon: HR, 1.19; 95% confidence interval (95% CI), 1.14-1.25; rectum: HR, 1.27; 95% CI, 1.17-1.38] had an increased risk of death compared with Caucasians. However, after further adjustment for SES and treatment, the risk of death for African-Americans compared with Caucasians was substantially diminished (colon: HR, 1.08; 95% CI, 1.03-1.13; rectum: HR, 1.11; 95% CI, 1.02-1.20).**

Conclusion: **Among CRC cases, disparities in treatment and SES largely explain the observed decreased survival of African-Americans, underscoring the importance of health disparity research in this disease.** (Cancer Epidemiol Biomarkers Prev 2008;17(8):1950–62)

Introduction

During 2007, an estimated 112,340 new cases of colon cancer and 41,420 cases of rectal cancer were diagnosed in the United States. Colorectal cancer (CRC) is the third most common cancer among U.S. males and females (1). There are recent data supporting a decline in overall mortality for CRC (2). This is likely due, in part, to the increasing use of screening procedures such as colonoscopy, which can reduce the risk of CRC mortality by 50% (3). Unfortunately, screening procedures are only routinely used by 50% of Americans age 50 years or older (4). Despite overall mortality decreasing over time (2), there continues to be a widening disparity in CRC incidence and survival between African-Americans and Caucasians (5, 6). From 2000 to 2004, the age-adjusted incidence per 100,000 in males was 70.2 in African-Americans compared with 62.2 in Caucasians and 46.9 in Asian/Pacific Islanders (2). Similarly, in females, the incidence rate was 52.9 in African-Americans compared with 44.9 in Caucasians and 33.7 in Asian/Pacific Islanders. In the same period and similarly age adjusted, the death rate in males was 32.7 in African-Americans compared with 22.9 in Caucasians and 15 in Asian/Pacific Islanders (2). In females, the death rate was 22.9 in African-Americans compared with 15.9 in Caucasians and 10.3 in Asian/Pacific Islanders.

Using Surveillance, Epidemiology and End Results (SEER) data, the 5-year relative CRC-specific survival for Caucasians and African-Americans in a period between 1995 and 2001 was reported to be 65% and 55%, respectively (6). Differences in CRC survival across the major U.S. ethnicities have been suggested to be related to differences in stage at diagnosis (7), tumor grade (8), screening use (9), posttherapy follow-up (10, 11), patient beliefs (12, 13), and provider characteristics (14). The 2000 National Health Interview Survey revealed that self-reported screening rates were 42.5% in Caucasians compared with 40.3% in African-Americans (9, 15). The importance of proper screening practices becomes apparent when considering African-Americans more

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often present with metastatic disease (24%) compared with Caucasians (18%) using SEER data (6).

Despite the body of literature that exists, few studies have adequately accounted for treatment and socioeconomic status (SES) in addressing racial disparities in CRC survival. A recent meta-analysis by Du et al. (16) revealed that studies taking into account SES and survival in colon cancer have been relatively small and inconsistent. Larger population-based studies are limited to older populations and those with regional-staged disease (17). We set out to determine how differences in SES and treatment affect racial disparities in survival of colon and rectal cancer patients through a case-only analysis of data from the large, population-based California Cancer Registry (CCR).

Materials and Methods

Study Population. We did a retrospective, case-only analysis of colorectal cases in the CCR database. CCR is part of the National Cancer Institute's SEER program and is the largest contiguous-area population-based cancer registry in the world (18); standardized data collection and quality control procedures have been in place since 1988 (19-22). Case reporting is estimated at 99% for the entire state of California (23), with follow-up completion rates exceeding 95%. Data were abstracted from medical and laboratory records by trained tumor registrars (19). Tumor site and histology were coded according to WHO criteria in International Classification of Diseases (ICD) for Oncology (24). Cases were identified using CRC SEER primary site code 21041, 21043-21049, 21051, and 21052 and ICD-O-3 histology codes as follows: adenocarcinoma (8010, 8020-8022, 8140-8145, 8210, 8211, 8220, 8221, 8230, 8231, and 8260-8263) and mucinous adenocarcinoma (8470, 8480, and 8481). All histologies not in either of these two groups were categorized as ''other.''

SEER extent of disease and surgical staging variables were used to derive tumor-node-metastasis data in accordance with the 2002 American Joint Committee on Cancer staging system. Carcinoma *in situ* tumors were coded as stage 0. Stage I included tumors that invaded the submucosa or muscularis propria without lymph node involvement. Stage IIA included tumors with invasion into the subserosa or adjacent connective (nonperitoneal) tissues without lymph node involvement. Stage IIB were tumors that invaded adjacent organs and/or through to the peritoneum without lymph node involvement. Stage IIIA included invasion to the submucosa or muscularis propria with coding based on regional and pathologically confirmed three or less positive lymph nodes. Stage IIIB shared the same lymph node coding but the tumors invaded into the subserosa or visceral peritoneum. Stage IIIC was any degree of nonmetastatic tumor invasiveness with lymph node status coded as four or more regional lymph nodes. Stage IV included any distant metastases or distant lymph nodes, which included superior mesenteric lymph nodes.

Data were obtained on 90,273 incident colon and 37,532 incident rectal cancer cases during January 1994 through December 2003 in CCR with follow-up until December 2006. Recorded data included demographic information (age, gender, and ethnicity), stage at presentation, histology, treatment during the first course of therapy, SES, and vital status. All age groups were included in the analysis. SES is denoted as a single index variable in CCR using statewide measures of education, income, and occupation from census data, as described previously (25). The SES variable used is a composite index based on principle component analysis of census block level CCR data linked to census data assessing: 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 (18, 25-30). This variable has been used in population-based analyses of cancers of the colon, breast, pancreas, ovary, and nasopharynx (18, 25-30). Quintiles for the SES score were analyzed.

Treatment during the first course of therapy was ascertained using available data from CCR to determine whether cases underwent surgical resection, radiation therapy, or chemotherapy. Standard therapy was defined according to the National Comprehensive Cancer Network practice guidelines as follows: resection alone for stage I disease in both colon and rectal cancer, surgical resection alone or with adjuvant chemotherapy for stage II colon cancers, and surgical resection followed by adjuvant chemotherapy for all stage III colon cancers. Stage II and III rectal cancers typically require treatment with neoadjuvant (i.e., up-front) chemoradiation followed by surgery and additional chemotherapy, whereas stage IV colon and rectal cancers are treated with systemic chemotherapy (31). Limited comorbidity information was available for cases not receiving surgery and recorded as ''contraindicated due to other conditions.'' Cause of death was recorded according to ICD criteria in effect at the time of death. Hospital registrars contacted cases, and CCR staff reviewed state death certificates to identify deceased registry cases. The last date of follow-up was either the date of death or the last date of contact. In the text, overall survival (OS) is defined as all-cause mortality, whereas CRC-specific survival is defined as mortality from CRC itself.

Statistical Analysis. The clinical characteristics, including age, gender, race, American Joint Committee on Cancer 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 categorical variables and the nonparametric Kruskal-Wallis test for comparison of continuous variables for more than two groups. Life tables and Kaplan-Meier curves were generated for race and SES categories, and curves were compared with the log-rank test. Multivariate survival analysis was used to calculate OS and CRC-specific survival using Cox proportional hazards ratios (HR). Proportionality assumptions for the Cox regression models were tested. First, univariate log [−log(survival)] versus log of survival curves by race were plotted and found to be nonintersecting. Next, proportionality tests were done for each of the ethnic categories within Cox models adjusting for known differences in age and stage at presentation. Dummy variables were created for each variable multiplied by the log of the survival time. For colon and then rectum analyses, the proportionality test for race was not violated (P = 0.15 and 0.25, respectively). Thus, Cox proportional hazards regression models were used for

Table 1. Demographic characteristics for CRC by colon versus rectum; incident cases, January 1994 to December 2003 (all $P < 0.0001$; except gender for colon $P < 0.01$)

	Colon (n = 90,273), n (%)	Rectum (n = 37,532), n (%)	Total (N = 127,805), n (%)
Gender			
Male	44,753 (49.6)	21,198 (56.5)	65,951 (51.6)
Female	45,520 (50.4)	16,334 (43.5)	61,854 (48.4)
Stage			
I	21,280 (23.6)	13,606 (36.3)	34,886 (27.3)
IIA	22,812 (25.3)	6,880 (18.3)	29,692 (23.2)
IIB	5,278 (5.9)	1,761 (4.7)	7,039 (5.5)
IIIA	1,769 (2.0)	1,121 (3.0)	2,890 (2.3)
IIIB	11,949 (13.2)	3,582 (9.5)	15,531 (12.2)
IIIC	6,665 (7.4)	2,585 (6.9)	9,250 (7.2)
IV	15,509 (17.2)	5,576 (14.9)	21,085 (16.5)
Histologic subtype			
Adenocarcinoma	78,275 (86.7)	32,592 (86.8)	110,867 (86.7)
Mucinous adenocarcinoma	9,922 (11.0)	2,304 (6.1)	12,226 (10.0)
Other	2,076 (2.3)	2,636 (7.0)	4,712 (3.7)
Colon site			
Proximal and transverse	53,907 (59.7)		53,907 (42.2)
Descending	5,855 (6.5)		5,855 (4.6)
Sigmoid	30,511 (33.8)		30,511 (23.9)
Rectosigmoid		12,263 (32.7)	12,263 (9.6)
Rectum		25,269 (67.3)	25,269 (19.8)
Age category			
0-39	1,709 (1.9)	1,147 (3.0)	2,856 (2.2)
40-49	4,624 (5.1)	3,138 (8.4)	7,762 (6.1)
50-59	11,193 (12.4)	6,688 (17.8)	17,881 (14.0)
60-69	19,978 (22.1)	9,345 (24.9)	29,323 (22.9)
70+	52,769 (58.5)	17,214 (45.9)	69,983 (54.8)
Histologic grade			
Well differentiated	8,505 (10.9)	3,299 (10.9)	11,804 (9.2)
Moderately differentiated	52,377 (66.8)	21,581 (71.1)	73,958 (57.9)
Poorly differentiated	16,836 (21.5)	5,250 (17.3)	22,086 (17.3)
Undifferentiated/anaplastic	666 (0.9)	219 (0.7)	885 (0.69)
Race			
White	65,558 (72.6)	26,181 (69.8)	91,739 (71.8)
Black	6,479 (7.2)	2,056 (5.5)	8,535 (6.7)
Hispanic	9,945 (11.0)	4,998 (13.3)	14,943 (11.7)
Chinese	2,504 (2.8)	1,060 (2.8)	3,564 (2.8)
Non-Chinese Asian	5,099 (5.7)	2,851 (7.6)	7,950 (6.2)
Other	688 (0.8)	386 (1.0)	1,074 (0.84)
SES			
Lowest	11,943 (13.2)	5,297 (14.1)	17,240 (13.5)
Second lowest	17,040 (18.9)	7,288 (19.4)	24,328 (19.0)
Middle	19,809 (21.9)	8,188 (21.8)	27,997 (21.9)
High	20,376 (22.6)	8,338 (22.2)	28,714 (22.5)
Highest	21,105 (23.4)	8,421 (22.4)	29,526 (23.1)

the multivariate survival analyses. All statistical analyses were conducted using Statistical Analysis System 9.1 statistical software (SAS Institute, Inc.). Statistical significance was assumed for a two-tailed $P < 0.05$.

Ethical Considerations. This study involved analysis of existing data from CCR database with no subject intervention. No identifiers were linked to subjects. This study was approved by the University of California at Irvine Institutional Review Board under the category ''exempt status'' (Institutional Review Board 2007-5842).

Results

Demographic Characteristics. Table 1 shows the demographic and clinical data for the entire study population, which included 91,739 (71.8%) non-Hispanic Whites, 8,535 (6.7%) African-Americans, 14,943 (11.7%) Hispanics, 3,564 (2.8%) Chinese, 7,950 (6.2%) non-Chinese Asian, and 1,074 (0.84%) others (not listed). Rectal cancer patients were predominantly male (56.5%; $P < 0.0001$). Rectal cancer was more often stage I (36.3%; $P < 0.0001$) compared with colon cancer (23.6%), which was more often stage IIA (25.3%; $P < 0.0001$). The age distribution for colon cancer was older (58.5% 70+ age; $P < 0.0001$) compared with rectal cancer (45.9% 70+ age; $P < 0.0001$).

Demographic Characteristics by Ethnicity. African-Americans and Hispanics among colon (Table 2A) and rectal cancer cases (Table 2B) were more likely to have metastatic disease compared with Caucasians and Asians. There was a female predominance among African-Americans with colon cancer (53.3%; $P < 0.0001$) compared with a more even distribution across the other groups. In rectal cancer, African-Americans (14.5%) tended to have histology other than adenocarcinoma or mucinous adenocarcinoma more often than Caucasians (5.3%; $P < 0.0001$). Regarding anatomic site,

Table 2. Demographic information for CRC by race; incident cases, January 1994 to December 2003 (all $P < 0.0001$)

A. Colon cancer

	White (n = 65,558), n (%)	Black (n = 6,479), n (%)	Hispanic (n = 9,945), n (%)	Chinese (n = 2,504), n (%)	Non-Chinese Asian (n = 5,099), n (%)	Other (n = 688), n (%)	Total (N = 90,273), n (%)
Gender							
Male	32,536 (49.6)	3,029 (46.8)	4,992 (50.2)	1,293 (51.6)	2,519 (49.4)	384 (55.8)	44,753 (49.6)
Female	33,022 (50.4)	3,450 (53.3)	4,953 (49.8)	1,211 (48.4)	2,580 (50.6)	304 (44.2)	45,520 (50.4)
Stage							
I	15,701 (24.0)	1,438 (22.2)	2,131 (21.4)	609 (24.3)	1,119 (22.0)	282 (41)	21,280 (23.6)
IIA	17,080 (26.1)	1,337 (20.6)	2,450 (24.6)	636 (25.4)	1,197 (23.5)	112 (16.3)	22,812 (25.3)
IIB	3,893 (5.9)	376 (5.8)	613 (6.2)	109 (4.4)	271 (5.3)	16 (2.3)	5,278 (5.9)
IIIA	1,285 (2.0)	120 (1.9)	193 (1.9)	63 (2.5)	100 (2.0)	8 (1.2)	1,769 (2.0)
IIIB	8,549 (13.0)	852 (13.2)	1,369 (13.8)	362 (14.5)	768 (15.1)	49 (7.1)	11,949 (13.2)
IIIC	4,715 (7.2)	454 (7.0)	787 (7.9)	189 (7.6)	488 (9.6)	32 (4.7)	6,665 (7.4)
IV	10,888 (16.6)	1,432 (22.1)	1,861 (18.7)	392 (15.7)	896 (17.6)	40 (5.8)	15,509 (17.2)
Histologic subtype							
Adenocarcinoma	56,758 (86.6)	5,552 (85.7)	8,605 (86.5)	2,223 (88.8)	4,510 (88.5)	627 (91.1)	78,275 (86.7)
Mucinous adenocarcinoma	7,291 (11.1)	769 (11.9)	1,091 (11.0)	248 (9.9)	481 (9.4)	42 (6.1)	9,922 (11.0)
Other	1,509 (2.3)	158 (2.4)	249 (2.5)	33 (1.3)	108 (2.1)	19 (2.8)	2,076 (2.3)
Colon site							
Proximal and transverse	40,376 (61.9)	4,078 (62.9)	5,616 (56.5)	1,220 (48.7)	2,356 (46.2)	261 (37.9)	53,907 (59.7)
Descending	4,108 (6.3)	495 (7.6)	587 (5.9)	213 (8.5)	394 (7.7)	58 (8.4)	5,855 (6.5)
Sigmoid	21,074 (32.2)	1,906 (29.4)	3,742 (37.6)	1,071 (42.8)	2,349 (46.1)	369 (53.6)	30,511 (33.8)
Age category							
0-39	786 (1.2)	151 (2.3)	522 (5.3)	48 (1.9)	180 (3.5)	22 (3.2)	1,709 (1.9)
40-49	2,679 (4.1)	467 (7.2)	834 (8.4)	160 (6.4)	422 (8.3)	62 (9.0)	4,624 (5.1)
50-59	7,076 (10.8)	1,162 (17.9)	1,639 (16.5)	306 (12.2)	892 (17.5)	118 (17.2)	11,193 (12.4)
60-69	13,503 (20.6)	1,781 (27.5)	2,620 (26.3)	578 (23.1)	1,311 (25.7)	185 (26.9)	19,978 (22.1)
70+	41,514 (63.3)	2,918 (45.0)	4,330 (43.5)	1,412 (56.4)	2,294 (45.0)	301 (43.8)	52,769 (58.5)
Histologic grade							
Well differentiated	6,201 (10.8)	644 (11.9)	1,008 (11.7)	148 (6.8)	428 (9.6)	76 (17.6)	8,505 (10.9)
Moderately differentiated	37,961 (66.3)	3,752 (69.5)	5,783 (67)	1,566 (71.6)	3,034 (67.7)	281 (64.9)	52,377 (66.8)
Poorly differentiated	12,580 (22.0)	966 (17.9)	1,767 (20.5)	454 (20.8)	999 (22.3)	70 (16.2)	16,836 (21.5)
Undifferentiated/anaplastic	512 (0.9)	36 (0.7)	72 (0.8)	19 (0.9)	21 (0.5)	6 (1.4)	666 (0.9)
SES							
Lowest	5,712 (8.7)	2,237 (34.5)	2,905 (29.2)	310 (12.4)	689 (13.5)	90 (13.1)	11,943 (13.2)
Second lowest	11,363 (17.3)	1,633 (25.2)	2,544 (25.6)	387 (15.5)	980 (19.2)	133 (19.3)	17,040 (18.9)
Middle	14,947 (22.8)	1,271 (19.6)	1,989 (20)	390 (15.6)	1,062 (20.8)	150 (21.8)	19,809 (21.9)
High	16,048 (24.5)	894 (13.8)	1,480 (14.9)	590 (23.6)	1,222 (24)	142 (20.6)	20,376 (22.6)
Highest	17,488 (26.7)	444 (6.9)	1,027 (10.3)	827 (33)	1,146 (22.5)	173 (25.2)	21,105 (23.4)
Surgery							
No	3,679 (5.6)	580 (9.0)	619 (6.2)	132 (5.3)	264 (5.2)	77 (11.2)	5,351 (5.9)
Yes	61,868 (94.4)	5,897 (91.1)	9,325 (93.8)	2,371 (94.7)	4,834 (94.8)	610 (88.8)	84,905 (94.1)
Chemotherapy as first line							
No	47,740 (75.3)	4,509 (71.9)	6,511 (68.2)	1,735 (71.9)	3,258 (66.9)	590 (88.2)	64,343 (73.8)
Yes	15,705 (24.8)	1,761 (28.1)	3,037 (31.8)	679 (28.1)	1,615 (33.1)	79 (11.8)	22,876 (26.2)
Radiation							
No	64,332 (98.1)	6,369 (98.3)	9,682 (97.4)	2,445 (97.6)	4,958 (97.2)	684 (99.4)	88,470 (98)
Yes	1,225 (1.9)	110 (1.7)	263 (2.6)	59 (2.4)	141 (2.8)	4 (0.6)	1,802 (2.0)

(*Continued on the following page*)

Table 2. Demographic information for CRC cases by race; incident cases, January 1994 to December 2003 (all $P < 0.0001$; except gender $P = 0.0005$) (Cont'd)

B. Rectal cancer

	White (n = 26,181), n (%)	Black (n = 2,056), n (%)	Hispanic (n = 4,998), n (%)	Chinese (n = 1,060), n (%)	Non-Chinese Asian (n = 2,851), n (%)	Other (n = 386), n (%)	Total (N = 37,532), n (%)
Gender							
Male	14,697 (56.1)	1,103 (53.7)	2,947 (59)	612 (57.7)	1,628 (57.1)	211 (54.7)	21,198 (56.5)
Female	11,484 (43.9)	953 (46.4)	2,051 (41)	448 (42.3)	1,223 (42.9)	175 (45.3)	16,334 (43.5)
Stage							
I	9,574 (36.6)	722 (35.1)	1,671 (33.4)	393 (37.1)	1,020 (35.8)	226 (58.6)	13,606 (36.3)
IIA	4,920 (18.8)	360 (17.5)	899 (18)	190 (17.9)	490 (17.2)	21 (5.4)	6,880 (18.3)
IIB	1,205 (4.6)	99 (4.8)	290 (5.8)	42 (4.0)	120 (4.2)	5 (1.3)	1,761 (4.7)
IIIA	811 (3.1)	54 (2.6)	125 (2.5)	30 (2.8)	97 (3.4)	4 (1.0)	1,121 (3.0)
IIIB	2,447 (9.4)	194 (9.4)	507 (10.1)	119 (11.2)	305 (10.7)	10 (2.6)	3,582 (9.5)
IIIC	1,710 (6.5)	141 (6.9)	400 (8.0)	82 (7.7)	240 (8.4)	12 (3.1)	2,585 (6.9)
IV	3,804 (14.5)	350 (17)	820 (16.4)	145 (13.7)	434 (15.2)	23 (6.0)	5,576 (14.9)
Histologic subtype							
Adenocarcinoma	23,223 (88.7)	1,603 (78)	4,176 (83.6)	910 (85.9)	2,394 (84)	286 (74.1)	32,592 (86.8)
Mucinous adenocarcinoma	1,561 (6.0)	155 (7.5)	352 (7.0)	64 (6.0)	163 (5.7)	9 (2.3)	2,304 (6.1)
Other	1,397 (5.3)	298 (14.5)	470 (9.4)	86 (8.1)	294 (10.3)	91 (23.6)	2,636 (7.0)
Colon site							
Rectosigmoid	8,628 (33)	676 (32.9)	1,628 (32.6)	352 (33.2)	899 (31.5)	80 (20.7)	12,263 (32.7)
Rectum	17,553 (67)	1,380 (67.1)	3,370 (67.4)	708 (66.8)	1,952 (68.5)	306 (79.3)	25,269 (67.3)
Age category							
0-39	554 (2.1)	67 (3.3)	336 (6.7)	28 (2.7)	152 (5.3)	10 (2.6)	1,147 (3.0)
40-49	1,825 (7)	249 (12.1)	577 (11.5)	123 (11.6)	320 (11.2)	44 (11.4)	3,138 (8.4)
50-59	4,244 (16.2)	442 (21.5)	1,044 (20.9)	219 (20.7)	644 (22.6)	95 (24.6)	6,688 (17.8)
60-69	6,363 (24.3)	581 (28.3)	1,334 (26.7)	229 (21.6)	735 (25.8)	103 (26.7)	9,345 (24.9)
70+	13,195 (50.4)	717 (34.9)	1,707 (34.2)	461 (43.5)	1,000 (35.1)	134 (34.7)	17,214 (45.9)
Histologic grade							
Well differentiated	2,402 (11.2)	146 (9.5)	470 (11.7)	56 (6.6)	189 (8.3)	36 (21.6)	3,299 (10.9)
Moderately differentiated	15,306 (71.2)	1,098 (71.4)	2,828 (70.5)	617 (72.8)	1,624 (71.3)	108 (64.7)	21,581 (71.1)
Poorly differentiated	3,645 (17)	275 (17.9)	687 (17.1)	169 (19.9)	452 (19.9)	22 (13.2)	5,250 (17.3)
Undifferentiated/anaplastic	153 (0.7)	19 (1.2)	28 (0.7)	6 (0.7)	12 (0.5)	1 (0.6)	219 (0.7)
SES							
Lowest	2,506 (9.6)	698 (34)	1,544 (30.9)	112 (10.6)	386 (13.5)	51 (13.2)	5,297 (14.1)
Second lowest	4,706 (18)	530 (25.8)	1,285 (25.7)	154 (14.5)	547 (19.2)	66 (17.1)	7,288 (19.4)
Middle	5,915 (22.6)	411 (20)	989 (19.8)	174 (16.4)	605 (21.2)	94 (24.4)	8,188 (21.8)
High	6,340 (24.2)	265 (12.9)	714 (14.3)	278 (26.2)	645 (22.6)	96 (24.9)	8,338 (22.2)
Highest	6,714 (25.6)	152 (7.4)	466 (9.3)	342 (32.3)	668 (23.4)	79 (20.5)	8,421 (22.4)
Surgery							
No	2,938 (11.2)	314 (15.3)	661 (13.2)	95 (9)	319 (11.2)	69 (17.9)	4,396 (11.7)
Yes	23,232 (88.8)	1,741 (84.7)	4,337 (86.8)	964 (91)	2,531 (88.8)	316 (82.1)	33,121 (88.3)
Chemotherapy as first line							
No	16,341 (64.2)	1,296 (64.7)	2,770 (57.4)	644 (63)	1,576 (57.3)	331 (88.5)	22,958 (63)
Yes	9,131 (35.9)	706 (35.3)	2,059 (42.6)	378 (37)	1,177 (42.8)	43 (11.5)	13,494 (37)
Radiation							
No	18,411 (70.3)	1,476 (71.8)	3,300 (66)	758 (71.5)	1,898 (66.6)	353 (91.5)	26,196 (69.8)
Yes	7,769 (29.7)	580 (28.2)	1,698 (34)	302 (28.5)	953 (33.4)	33 (8.6)	11,335 (30.2)

Table 3. Therapy for CRC by race, controlling for stage; incident cases, January 1994 to December 2003

A. Colon cancer

	White	Black	Hispanic	Chinese	Non-Chinese Asian
Stage I (n = 21,277)					
Surgery (P < 0.0001)					
No	587 (3.7)	78 (5.4)	78 (3.7)	24 (3.9)	35 (3.1)
Yes	15,108 (96.3)	1,358 (94.6)	2,052 (96.3)	585 (96.1)	1,084 (96.9)
Chemotherapy as first line (P = 0.0002)					
No	15,386 (98.5)	1,406 (98.5)	2,079 (98.1)	584 (96.7)	1,080 (97.2)
Yes	231 (1.5)	21 (1.5)	40 (1.9)	20 (3.3)	31 (2.8)
Radiation (P = 0.16)					
No	15,663 (99.8)	1,436 (99.9)	2,123 (99.7)	605 (99.3)	1,117 (99.8)
Yes	36 (0.2)	1 (0.07)	7 (0.3)	4 (0.7)	2 (0.2)
Stage II (n = 28,034)					
Surgery (P = 0.58)					
No	356 (1.7)	35 (2)	60 (2)	9 (1.2)	23 (1.6)
Yes	20,574 (98.3)	1,676 (98)	2,993 (98)	735 (98.8)	1,444 (98.4)
Chemotherapy as first line (P < 0.0001)					
No	16,672 (82)	1,302 (78.8)	2,169 (74)	549 (75.6)	1,033 (73.3)
Yes	3,650 (18)	351 (21.2)	760 (26)	177 (24.4)	377 (26.7)
Radiation (P < 0.0001)					
No	20,481 (97.9)	1,677 (98)	2,944 (96.4)	727 (97.7)	1,422 (96.9)
Yes	449 (2.1)	35 (2)	109 (3.6)	17 (2.3)	45 (3.1)
Stage III (n = 20,383)					
Surgery (P = 0.097)					
No	28 (0.2)	7 (0.5)	10 (0.4)	1 (0.2)	5 (0.4)
Yes	14,521 (99.8)	1,419 (99.5)	2,339 (99.6)	613 (99.8)	1,351 (99.6)
Chemotherapy as first line (P < 0.0001)					
No	6,727 (49)	614 (45.4)	891 (40.5)	269 (47.5)	501 (40.2)
Yes	6,979 (51)	740 (54.6)	1,308 (59.5)	297 (52.5)	744 (59.8)
Radiation (P = 0.008)					
No	14,163 (97.4)	1,400 (98.2)	2,272 (96.7)	594 (96.7)	1,302 (96)
Yes	386 (2.6)	26 (1.8)	77 (3.3)	20 (3.3)	54 (4)
Stage IV (n = 15,509)					
Surgery (P < 0.0001)					
No	2,538 (23.3)	434 (30.3)	444 (23.9)	84 (21.5)	189 (21.1)
Yes	8,346 (76.7)	998 (69.7)	1,416 (76.1)	307 (78.5)	706 (78.9)
Chemotherapy as first line (P < 0.0001)					
No	5,497 (53.3)	715 (52.4)	823 (47)	188 (50.4)	385 (45.5)
Yes	4,821 (46.7)	649 (47.6)	926 (53)	185 (49.6)	462 (54.5)
Radiation (P = 0.14)					
No	10,541 (96.8)	1,385 (96.7)	1,792 (96.3)	374 (95.4)	856 (95.5)
Yes	347 (3.2)	47 (3.3)	69 (3.7)	18 (4.6)	40 (4.5)

B. Rectal cancer

Stage I (n = 13,601)					
Surgery (P < 0.0001)					
No	618 (6.5)	74 (10.2)	121 (7.2)	20 (5.1)	69 (6.8)
Yes	8,948 (93.5)	648 (89.8)	1,550 (92.8)	372 (94.9)	950 (93.2)
Chemotherapy as first line (P < 0.0001)					
No	8,209 (86.5)	643 (89.8)	1,410 (85)	349 (89.7)	882 (87.8)
Yes	1,278 (13.5)	73 (10.2)	248 (15)	40 (10.3)	123 (12.2)
Radiation (P < 0.0001)					
No	7,987 (83.5)	626 (86.7)	1,383 (82.8)	342 (87)	875 (85.9)
Yes	1,582 (16.5)	96 (13.3)	288 (17.2)	51 (13)	144 (14.1)
Stage II (n = 8,607)					
Surgery (P = 0.07)					
No	571 (9.4)	47 (10.3)	141 (11.9)	16 (6.9)	63 (10.4)
Yes	5,534 (90.6)	409 (89.7)	1,040 (88.1)	216 (93.1)	544 (89.6)
Chemotherapy as first line (P < 0.0001)					
No	3,170 (53.5)	242 (53.9)	496 (43.6)	114 (51.4)	248 (42.9)
Yes	2,752 (46.5)	207 (46.1)	642 (56.4)	108 (48.6)	330 (57.1)
Radiation (P < 0.0001)					
No	3,397 (55.6)	251 (55)	579 (49)	129 (55.6)	291 (47.9)
Yes	2,708 (44.4)	205 (45)	602 (51)	103 (44.4)	316 (52.1)
Stage III (n = 7,288)					
Surgery (P = 0.56)					
No	12 (0.2)	0	4 (0.4)	1 (0.4)	0
Yes	4,956 (99.8)	389 (100)	1,028 (99.6)	230 (99.6)	642 (100)

(*Continued on the following page*)

Table 3. Therapy for CRC by race, controlling for stage; incident cases, January 1994 to December 2003 (Cont'd)

Chemotherapy as first line ($P < 0.0001$)					
No	1,631 (34.6)	127 (34.5)	261 (27)	65 (30.1)	151 (25)
Yes	3,089 (65.4)	241 (65.5)	705 (73)	151 (69.9)	452 (75)
Radiation ($P = 0.005$)					
No	2,536 (51.1)	206 (53)	479 (46.4)	125 (54.1)	290 (45.2)
Yes	2,432 (48.9)	183 (47)	553 (53.6)	106 (45.9)	352 (54.8)
Stage IV ($n = 5,576$)					
Surgery ($P = 0.005$)					
No	1,624 (42.8)	181 (51.9)	373 (45.5)	56 (38.6)	173 (40)
Yes	2,175 (57.2)	168 (48.1)	447 (54.5)	89 (61.4)	260 (60)
Chemotherapy as first line ($P = 0.012$)					
No	1,628 (45.1)	148 (44.8)	317 (41)	58 (42.6)	152 (36.3)
Yes	1,983 (54.9)	182 (55.2)	456 (59)	78 (57.4)	267 (63.7)
Radiation ($P = 0.20$)					
No	2,788 (73.3)	258 (73.7)	573 (69.9)	103 (71)	299 (68.9)
Yes	1,016 (26.7)	92 (26.3)	247 (30.1)	42 (29)	135 (31.1)

African-Americans more often presented with disease in the proximal and transverse colon ($P < 0.0001$). Caucasians were consistently older (70+ age) in colon and rectal cancer than the other ethnicities, whereas African-Americans tended to be younger with a higher proportion in the 60 to 69 age range ($P < 0.0001$). African-Americans and Hispanics were more often in the lowest SES compared with Caucasians and Asians who were more often in the highest SES ($P < 0.0001$). African-Americans were less likely than Caucasians to have surgery in both colon (91.1% versus 94.4%) and rectal cancer (84.7% versus 88.8%; $P < 0.0001$). Among those who had a contraindication to surgery, a higher proportion of African-Americans (1.25%) were unable to have surgery compared with Caucasians (0.85%; $P < 0.0001$). The most apparent discrepancy when comparing standard treatment and ethnicity by stage (Table 3A and B) was African-Americans receiving less surgery in stage I (colon: 94.6% versus 96.3%; rectum: 89.8% versus 93.5%) and stage IV (colon: 69.7% versus 76.7%; rectum: 48.1% versus 57.2%) disease when compared with Caucasians ($P < 0.0001$). In colon cancer, African-Americans and Caucasians had similar rates of chemotherapy as first-line treatment in stage IV disease (47.6% versus 46.7%, respectively; $P < 0.0001$). In rectal cancer, in stage II disease, similar use of chemotherapy and radiation treatment was observed (stage II chemotherapy: African-American 46.1% versus Caucasian 46.5%; stage II radiation: African-American 45% versus Caucasian 44.4%; $P < 0.0001$). In stage III rectal cancer, chemotherapy use was similar by race (African-American 65.5% versus Caucasian 65.4%; $P < 0.0001$) but a modest discrepancy in the use of radiation was observed (African-American 47% versus Caucasian 48.9%; $P = 0.005$). In stage IV rectal cancer, African-Americans and Caucasians had similar rates of chemotherapy as first-line treatment (55.2% versus 54.9%, respectively; $P = 0.012$).

Cause of Death Analysis and CRC-Specific Survival Analysis. Of 127,805 CRC cases in this study, 63,309 (49.5%) died. Thirty-six thousand eight hundred thirty-eight of those died from CRC (58.2%). The majority of the other deaths were due to infection, unknown, or other causes (24.2%), heart disease (15.3%), and lung cancer (2.3%). The proportions of death due to CRC were 56.3% in Caucasians, 62.3% in African-Americans, 63.9% in Hispanics, 65.2% in Chinese, and 66.6% in non-Chinese Asian. In comparison, proportions of death due to heart disease were 16.1% in Caucasians, 14.6% in African-Americans, 12.3% in Hispanics, 12.1% in Chinese, and 11.3% in non-Chinese Asian ($P < 0.0001$).

The CRC-specific survival continued to be consistent with the all-cause data for colon and rectal cancer cases on univariate survival analysis. CRC-specific survival was better for Asians compared with African-Americans and Caucasians (Fig. 1A and B). African-Americans continued to have the poorest survival in both colon and rectal cancer. In CRC-specific analysis of colon cancer by race (Fig. 1A), 1-, 5-, and 10-year survival rates are as follows (all median OSs were not reached): African-American (82%, 64%, and 60%), Caucasians (85%, 70%, and 66%), Hispanic (86%, 70%, and 67%), Chinese (88%, 73%, and 70%), and non-Chinese Asian (88%, 72%, and 70%; $P < 0.0001$). In rectal cancer by race (Fig. 1B), 1-, 5-, and 10-year survival rates are as follows (all median OSs were not reached): African-American (86%, 65%, and 60%), Hispanic (89%, 69%, and 62%), Caucasians (88%, 71%, and 66%), Chinese (90%, 73%, and 66%), and non-Chinese Asian (90%, 73%, and 69%; $P < 0.0001$).

In CRC-specific analysis of colon cancer by SES (Fig. 2A), 1-, 5-, and 10-year survival rates are as follows (all median OSs were not reached): lowest (83%, 66%, and 63%), second lowest (84%, 68%, and 65%), middle (85%, 70%, and 66%), high (86%, 70%, and 67%), and highest (87%, 73%, and 69%; $P < 0.0001$). In rectal cancer by SES (Fig. 2B), 1-, 5-, and 10-year survival rates are as follows (all median OSs were not reached): lowest (85%, 64%, and 58%), second lowest (87%, 67%, and 62%), middle (88%, 70%, and 65%), high (89%, 73%, and 67%), and highest (91%, 76%, and 71%; $P < 0.0001$).

OS for Race and SES. Among colon and rectal cancer patients, OS was significantly better for Asians compared with Caucasians and African-Americans (Supplementary Fig. S1A and B). African-Americans consistently had the poorest survival in both colon and rectal cancer. On analysis of colon cancer by race, 1-, 5-, and 10-year survival rates and median OS are as follows: African-American (75%, 47%, 32%, and 51 months), Caucasians (78%, 50%, 32%, and 62 months), Hispanic (80%, 54%, 39%, and 73 months), Chinese (83%, 58%, 45%, and 92 months), and non-Chinese Asian (84%, 58%, 45%, and 95 months; $P < 0.0001$). In rectal cancer by race, 1-, 5-, and 10-year survival rates and median OS are as follows:

African-American (80%, 50%, 34%, and 58 months), Caucasians (82%, 54%, 37%, and 72 months), Hispanic (84%, 55%, 39%, and 73 months), Chinese (86%, 61%, 43%, and 102 months), and non-Chinese Asian (86%, 60%, 47%, and 106 months; $P < 0.0001$).

In colon cancer by SES (Supplementary Fig. S2A), 1-, 5-, and 10-year survival rates and median OS are as follows: lowest (74%, 46%, 29%, and 50 months), second lowest (77%, 49%, 31%, and 58 months), middle (78%, 50%, 32%, and 62 months), high (79%, 52%, 35%, and 67 months), and highest (82%, 56%, 40%, and 80 months; $P < 0.0001$). In rectal cancer by SES (Supplementary Fig. S2B), 1-, 5-, and 10-year survival rates and median OS are as follows: lowest (79%, 47%, 29%, and 53 months), second lowest (81%, 50%, 33%, and 61 months), middle (82%, 53%, 37%, and 68 months), high (84%, 58%, 40%, and 82 months), and highest (87%, 62%, 46%, and 104 months; $P < 0.0001$).

CRC-Specific Multivariate Survival Analysis with Confounding. Among colon cancer cases, compared with Caucasians, African-Americans had 1.32 times [95% confidence interval (95% CI), 1.26-1.38] and Hispanics had 1.04 times (95% CI, 0.99-1.08) the risk of death where Chinese had 10% less risk of death (HR, 0.90; 95% CI, 0.83-0.97) and non-Chinese Asians had 5% less risk of death (HR, 0.95; 95% CI, 0.90-1.01) after adjustment for age, gender, histology, and site in colon (Table 4A). This was also observed in rectal cancer

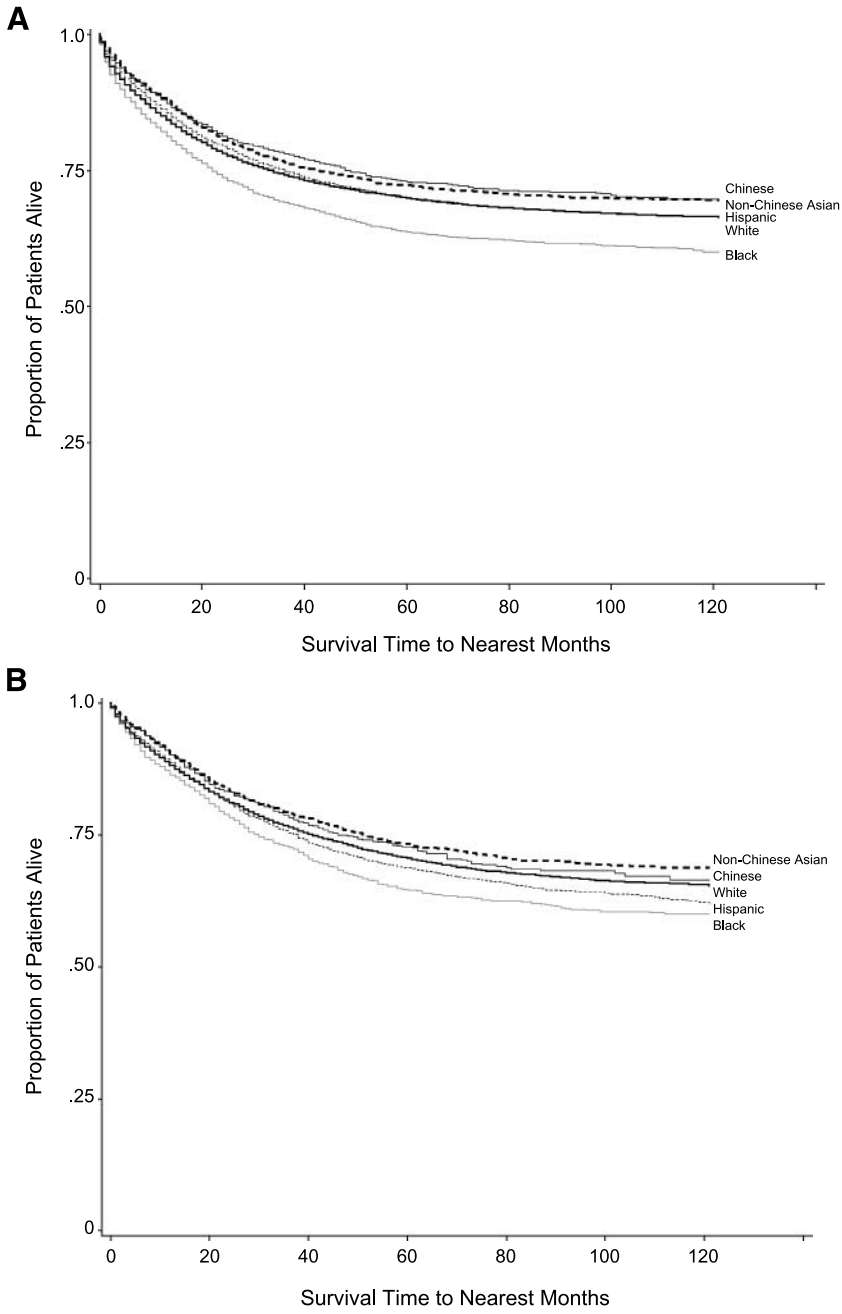

Figure 1. CRC-specific survival by race/ethnicity, CCR, January 1994 to December 2003. **A.** Colon cancer (n = 90,273; $P < 0.0001$). **B.** Rectal cancer (n = 37,532; $P < 0.0001$).

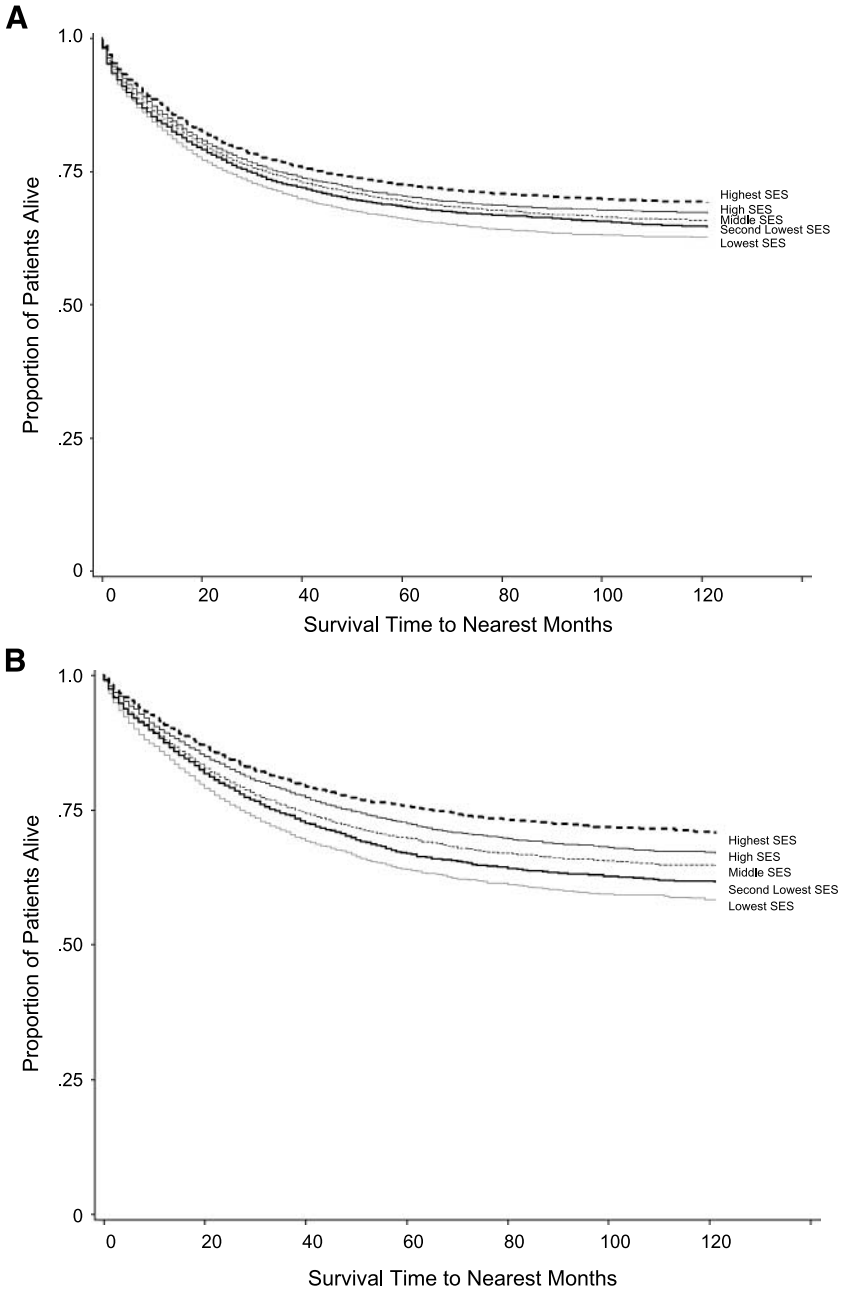

Figure 2. CRC-specific survival by SES quintile, CCR, January 1994 to December 2003. **A.** Colon cancer (n = 90,273; $P < 0.0001$). **B.** Rectal cancer (n = 37,532; $P < 0.0001$).

where, compared with Caucasians, African-Americans had 1.37 times (95% CI, 1.27-1.49) and Hispanics had 1.16 times (95% CI, 1.10-1.23) the risk of death after adjustment for age, gender, histology, and site in rectum (Table 4B). The survival benefit seen in Asians was no longer significant.

To determine the relevant confounders of risk (including treatment variables and SES) by ethnicity in this model, separate multivariate survival analyses were conducted among colon and rectal cancer cases (Table 4A and B). After further adjustment for stage at presentation, the increased risk of death in colon (HR, 1.19; 95% CI, 1.14-1.25) and rectal (HR, 1.27; 95% CI, 1.17-1.38) cancer remained for African-Americans compared with Caucasians. After additional adjustment for surgery, radiation, chemotherapy, and SES, the risk of death for colon (HR, 1.08; 95% CI, 1.03-1.13) and rectal (HR, 1.11; 95% CI, 1.02-1.20) cancer in African-Americans improved substantially compared with Caucasians. The improved survival seen in Chinese and non-Chinese Asians persisted after adjustment with the exception of Chinese in rectal cancer.

Discussion

Our population-based analysis of CRC cases in California reveals that the risk of death for colon and rectal cancer is greater for African-Americans when compared with

Caucasians but that this difference substantially diminishes after adjustment for stage, SES, and treatment. In our analysis for confounding, the greatest magnitude of change in HR was seen when adjusting specifically for stage followed equally by treatment and SES. These data suggest that these factors most strongly explain the observed survival differences.

We observed that African-Americans tended to be in the lowest SES more often than the other groups, a finding consistent with prior reports (16, 17). Indeed, race and ethnicity itself may not represent a higher risk of mortality as much as it is a proxy for SES (32), a theory in congruence with our observation that SES confounds the association between race and survival in CRC. Poorer

Table 4. CRC-specific multivariate survival analysis and analysis for confounding of CRC cases by ethnicity using Cox proportional hazards models (January 1994 to December 2003)

A. Colon cancer*	HR (95% CI)	HR (95% CI)	HR (95% CI)	HR (95% CI)	HR (95% CI)
Race					
Caucasian	1.00 (Reference)	1.00 (Reference)	1.00 (Reference)	1.00 (Reference)	1.00 (Reference)
African-American	1.32 (1.26-1.38)	1.19 (1.14-1.25)	1.14 (1.09-1.19)	1.15 (1.10-1.20)	1.08 (1.03-1.13)
Hispanic	1.04 (0.99-1.08)	0.98 (0.94-1.03)	0.97 (0.93-1.01)	0.97 (0.93-1.01)	0.92 (0.88-0.96)
Chinese	0.90 (0.83-0.97)	0.89 (0.82-0.97)	0.89 (0.82-0.96)	0.88 (0.81-0.96)	0.88 (0.81-0.96)
Non-Chinese Asian	0.95 (0.90-1.01)	0.88 (0.83-0.93)	0.88 (0.83-0.93)	0.89 (0.84-0.94)	0.88 (0.83-0.93)
Stage					
I		1.00 (Reference)	1.00 (Reference)	1.00 (Reference)	1.00 (Reference)
II		2.81 (2.64-2.98)	2.88 (2.71-3.06)	3.00 (2.82-3.18)	2.99 (2.81-3.17)
III		6.09 (5.74-6.45)	6.30 (5.94-6.68)	7.08 (6.67-7.53)	7.05 (6.63-7.49)
IV		35.26 (33.30-37.33)	30.89 (29.16-32.73)	34.65 (32.63-36.81)	34.53 (32.51-36.67)
Surgery					
None			1.00 (Reference)	1.00 (Reference)	1.00 (Reference)
Any			0.34 (0.33-0.36)	0.35 (0.34-0.37)	0.35 (0.34-0.37)
Radiation					
None				1.00 (Reference)	1.00 (Reference)
Any				1.41 (1.32-1.50)	1.40 (1.31-1.50)
Chemotherapy					
None				1.00 (Reference)	1.00 (Reference)
Any				0.80 (0.77-0.82)	0.80 (0.78-0.83)
SES					
Lowest					1.26 (1.20-1.32)
Second lowest					1.17 (1.12-1.22)
Middle					1.13 (1.08-1.17)
High					1.06 (1.02-1.10)
Highest					1.00 (Reference)
B. Rectal cancer†					
Race					
Caucasian	1.00 (Reference)	1.00 (Reference)	1.00 (Reference)	1.00 (Reference)	1.00 (Reference)
African-American	1.37 (1.27-1.49)	1.27 (1.17-1.38)	1.19 (1.10-1.29)	1.19 (1.09-1.29)	1.11 (1.02-1.20)
Hispanic	1.16 (1.10-1.23)	1.07 (1.01-1.13)	1.05 (0.99-1.11)	1.05 (0.99-1.11)	0.99 (0.93-1.05)
Chinese	0.96 (0.85-1.08)	0.98 (0.87-1.11)	1.00 (0.88-1.13)	0.98 (0.87-1.11)	0.98 (0.87-1.11)
Non-Chinese Asian	0.96 (0.89-1.03)	0.89 (0.82-0.96)	0.87 (0.81-0.94)	0.87 (0.80-0.94)	0.86 (0.80-0.93)
Stage					
I		1.00 (Reference)	1.00 (Reference)	1.00 (Reference)	1.00 (Reference)
II		2.99 (2.79-3.20)	2.85 (2.66-3.05)	3.14 (2.93-3.38)	3.11 (2.90-3.34)
III		4.15 (3.88-4.44)	4.29 (4.01-4.59)	4.99 (4.64-5.36)	4.93 (4.59-5.30)
IV		24.12 (22.63-25.71)	17.09 (15.97-18.28)	19.41 (18.06-20.87)	19.22 (17.87-20.66)
Surgery					
None			1.00 (Reference)	1.00 (Reference)	1.00 (Reference)
Any			0.34 (0.32-0.36)	0.33 (0.31-0.35)	0.33 (0.32-0.35)
Radiation					
None				1.00 (Reference)	1.00 (Reference)
Any				0.97 (0.92-1.02)	0.97 (0.92-1.02)
Chemotherapy					
None				1.00 (Reference)	1.00 (Reference)
Any				0.78 (0.74-0.82)	0.79 (0.75-0.83)
SES					
Lowest					1.33 (1.24-1.42)
Second lowest					1.20 (1.13-1.28)
Middle					1.17 (1.10-1.25)
High					1.11 (1.04-1.18)
Highest					1.00 (Reference)

*Each model includes adjustment for age at diagnosis, gender, histology, and site in colon.
† Each model includes adjustment for age at diagnosis, gender, histology, and site in rectum.

outcomes related to SES are most likely multifactorial. Issues such as unemployment certainly equate to a lack of health care coverage and in turn decrease the likelihood of a timely diagnosis, treatment, and optimal care. The result is a higher mortality rate related to poor health insurance status (33), and this has generated discussion about changes in health care coverage eligibility. In addition, lower SES has been associated with lack of knowledge regarding healthy living and behavior, living in poorer neighborhoods resulting in higher stress, and even the cumulative effect of interfering with activities of daily living (34, 35). A lack of awareness of test availability has been observed to correlate with lower usage of screening tests (12, 36, 37). The need for aggressive social policy is only highlighted further here.

Differences in receipt of treatment have been reported in many prior studies (38-44). A major finding of ours was that African-Americans received surgery less often than in the other groups. This has previously been reported by Cooper et al. (45) and Ball and Elixhauser (46). Again, the mortality reduction we observed when adjusting for surgery was substantial and had a stronger influence on survival than chemotherapy or radiation treatment. When comparing surgery by race and controlling for stage, African-Americans less often received surgery in stage I and IV disease (Table 3A and B). Interestingly, when comparing the CCR variable of reason for no surgery by race and separately by SES (data not shown), we observed that the reasons for not receiving surgery were that it was less often recommended and more often refused by African-Americans. In addition, data pertaining to surgical treatment and contraindication to surgery ''due to other conditions'' were available. Analysis of these data reveals that African-Americans more often did not receive surgery due to comorbid disease. This may be a reflection of worse baseline health in African-Americans (32). Nonacceptance of surgery is likely attributed to SES differences, as low SES was strongly associated with increased treatment refusal (data not shown). Reasons for this are unknown and must await further study. Questions have arisen regarding whether these disparities are specific to certain institutions or health care systems. Although some studies have suggested less disparity in single institution or system setting (47, 48), there has been suggestion that some disparities still exist in these models (44). Our multivariate analyses done with adjustment for insurance status did not reveal any substantial differences in risk (data not shown). Having a true measure of provider preferences is a difficult task but perhaps understanding patient preferences based on cultural knowledge would aid in bridging this gap. Indeed, there is a complex interplay between factors governing physician recommendations and patient decision making. Recommendations may be influenced by personal bias, stage of disease, prognostic indicators, and perception of patients' effort to comply with therapy. On the other hand, patients will make choices based on their personal beliefs, perception of therapy, and ability to comply with therapy and navigate the medical system. Jepson et al. (49) found that later diagnosis in African-Americans seemed to be partially due to beliefs that cancer is not a preventable disease.

Despite the discrepancies observed in surgery by stage, it is interesting to note the similarities in receiving standard of care for stage IV colon and rectal cancer (chemotherapy) and stage II and III rectal cancer (chemoradiation, typically given as neoadjuvant, or preoperative treatment; Table 3A and B). This suggests that stage at presentation, rather than SES and treatment, accounts for much of the observed discrepancy in survival. In our study, African-Americans presented with metastatic stage disease more often than the other ethnic groups. This is consistent with prior reports (7, 50). It is thought that this difference in stage at presentation explains much of the survival difference between Caucasians and African-Americans. Our results strengthen this finding. The reason for advanced stage at presentation has been suggested by lower screening rates (6, 50-52). The factors that explain this, however, have not been completely elucidated. Recently published data reveal an overall decline in cancer death rates, and particularly a decline in CRC mortality (2). This is believed to be due, in part, to improving trends in CRC screening (53, 54). Barriers to access have been shown to contribute to poorer screening rates (55-57). Confounding the screening process is the observation that African-Americans present more frequently with proximal tumors (47, 58, 59) and at a younger age (51), which we also observed. This underscores the importance of colorectal screening in this population and has been the impetus for proposing modified screening guidelines (60).

Our study is retrospective in nature and shares limitations of other population-based studies. Information on comorbidities is not coded for all CCR cases, although comorbidity data are available for those not undergoing surgery. We cannot account for cases with poor health that proceeded with surgical therapy, and it is presumed that the proportion of cases with known contraindications in our analysis are a small subset of the cases with comorbid conditions. Thus, differences in comorbidity among ethnic groups may explain some of the observed survival differences. Details of recurrence during follow-up were also not available. The existence of disparities found in follow-up, or surveillance, has been highlighted in prior studies (61-64). In addition, factors not so easily accounted for are institutional standards, physician preferences, and patient beliefs. There was no uniform standard protocol on how the CRC patients were staged; thus, all the cases were analyzed using ''best available stage'' based on combined clinical and pathologic staging data. There was no centralized review of pathologic specimens along with no uniform protocol on how treatment (surgery, radiation, or chemotherapy) was given. We omitted the race unknown/other group from our analyses as this population was not representative of the entire group as a whole given such a high proportion of censored data. Our primary findings remained consistent regardless of whether this race unknown/other group was included. Despite these limitations, to our knowledge, this study represents the largest analysis of colon and rectal cancer to date, accounting for the effects of SES and treatment (including chemotherapy) across all stage and age groups.

Our results show that stage at presentation, surgery, and SES contribute substantially to poorer outcomes in

CRC survival for African-Americans and Hispanics, and yet, this disparity almost normalizes after adjustment for SES. There is suggestion that African-Americans are younger at diagnosis and are more likely to present with proximal tumors than other ethnic groups, findings that suggest a role for investigating policy changes on current screening practices. Education is the key to rectifying any misconceptions that exist between patient and physician that become paramount for those of lower SES. Further investigation is necessary to clarify the reasons for this disparity and hopefully lead to policy changes in favor of community awareness and educational outreach.

Disclosure of Potential Conflicts of Interest

No potential conflicts of interest were disclosed.

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References

1. Jemal A, Siegel R, Ward E, Murray T, Xu J, Thun MJ. Cancer statistics, 2007. CA Cancer J Clin 2007;57:43–66.
2. Espey DK, Wu XC, Swan J, et al. Annual report to the nation on the status of cancer, 1975-2004, featuring cancer in American Indians and Alaska Natives. Cancer, 2007.
3. Walsh JM, Terdiman JP. Colorectal cancer screening: scientific review. JAMA 2003;289:1288–96.
4. Smith RA, Cokkinides V, Eyre HJ. American Cancer Society guidelines for the early detection of cancer, 2004. CA Cancer J Clin 2004;54:41–52.
5. Irby K, Anderson WF, Henson DE, Devesa SS. Emerging and widening colorectal carcinoma disparities between Blacks and Whites in the United States (1975-2002). Cancer Epidemiol Biomarkers Prev 2006;15:792–7.
6. Polite BN, Dignam JJ, Olopade OI. Colorectal cancer model of health disparities: understanding mortality differences in minority populations. J Clin Oncol 2006;24:2179–87.
7. Marcella S, Miller JE. Racial differences in colorectal cancer mortality. The importance of stage and socioeconomic status. J Clin Epidemiol 2001;54:359–66.
8. Alexander D, Jhala N, Chatla C, et al. High-grade tumor differentiation is an indicator of poor prognosis in African Americans with colonic adenocarcinomas. Cancer 2005;103:2163–70.
9. Swan J, Breen N, Coates RJ, Rimer BK, Lee NC. Progress in cancer screening practices in the United States: results from the 2000 National Health Interview Survey. Cancer 2003;97:1528–40.
10. Alexander D, Chatla C, Funkhouser E, Meleth S, Grizzle WE, Manne U. Postsurgical disparity in survival between African Americans and Caucasians with colonic adenocarcinoma. Cancer 2004;101:66–76.
11. Ellison GL, Warren JL, Knopf KB, Brown ML. Racial differences in the receipt of bowel surveillance following potentially curative colorectal cancer surgery. Health Serv Res 2003;38:1885–903.
12. Powe BD. Fatalism among elderly African Americans. Effects on colorectal cancer screening. Cancer Nurs 1995;18:385–92.
13. Advani AS, Atkeson B, Brown CL, et al. Barriers to the participation of African-American patients with cancer in clinical trials: a pilot study. Cancer 2003;97:1499–506.
14. Baldwin LM, Dobie SA, Billingsley K, et al. Explaining black-white differences in receipt of recommended colon cancer treatment. J Natl Cancer Inst 2005;97:1211–20.
15. Shokar NK, Carlson CA, Weller SC. Prevalence of colorectal cancer testing and screening in a multiethnic primary care population. J Community Health 2007;32:311–23.
16. Du XL, Meyer TE, Franzini L. Meta-analysis of racial disparities in survival in association with socioeconomic status among men and women with colon cancer. Cancer 2007;109:2161–70.
17. Du XL, Fang S, Vernon SW, et al. Racial disparities and socioeconomic status in association with survival in a large population-based cohort of elderly patients with colon cancer. Cancer 2007;110:660–9.
18. Parikh-Patel A, Bates JH, Campleman S. Colorectal cancer stage at diagnosis by socioeconomic and urban/rural status in California, 1988-2000. Cancer 2006;107:1189–95.
19. California Department of Health Services, Cancer Surveillance Section. Cancer reporting in California: abstracting and coding procedures for hospitals. California Cancer Reporting System standards. Volume I. Sacramento (CA): California Department of Health Services, Cancer Surveillance Section; 1997.
20. California Department of Health Services, Cancer Surveillance Section. Cancer reporting in California: standards for automated reporting. California Cancer Reporting System standards. Volume II. Sacramento (CA): California Department of Health Services, Cancer Surveillance Section; 1997.
21. California Department of Health Services, Cancer Surveillance Section. Cancer reporting in California: data standards for Regional Registries and California Cancer Registry. California Cancer Reporting System standards. Volume III. Sacramento (CA): California Department of Health Services, Cancer Surveillance Section; 1997.
22. California Department of Health Services, Cancer Surveillance Section. Cancer reporting in California: reporting procedures for physicians. California Cancer Reporting System standards. Volume IV. Sacramento (CA): California Department of Health Services, Cancer Surveillance Section; 1998.
23. How complete are California Cancer Registry data? Available from: http://www.ccrcal.org/questions.html [California Cancer Registry Web site (2007)].
24. Fritz A, Percy C, Jack A, et al. International classification of diseases for oncology. 3rd ed. Geneva: WHO; 2000.
25. 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 2001;12:703–11.
26. 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 1999;10:503–11.
27. 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 2003;21:1530–5.
28. 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 2007;16:546–52.
29. Ou SI, Zell J, 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 2006;24:283S.
30. Zell JA, Cinar P, Mobasher M, Ziogas A, Meyskens FL, Jr., Anton-Culver H. Survival for patients with invasive cutaneous melanoma among ethnic groups: the effects of socioeconomic status and treatment. J Clin Oncol 2008;26:66–75.
31. NCCN clinical practice guidelines in oncology, version 1.2008. 2007. Available from: http://www.nccn.org.
32. Sudano JJ, Baker DW. Explaining US racial/ethnic disparities in health declines and mortality in late middle age: the roles of socioeconomic status, health behaviors, and health insurance. Soc Sci Med 2006;62:909–22.
33. Roetzheim RG, Pal N, Gonzalez EC, Ferrante JM, Van Durme DJ, Krischer JP. Effects of health insurance and race on colorectal cancer treatments and outcomes. Am J Public Health 2000;90:1746–54.
34. Lynch JW, Kaplan GA, Salonen JT. Why do poor people behave poorly? Variation in adult health behaviours and psychosocial characteristics by stages of the socioeconomic lifecourse. Soc Sci Med 1997;44:809–19.
35. Lynch JW, Kaplan GA, Shema SJ. Cumulative impact of sustained economic hardship on physical, cognitive, psychological, and social functioning. N Engl J Med 1997;337:1889–95.
36. Chu KC, Tarone RE, Chow WH, Alexander GA. Colorectal cancer trends by race and anatomic subsites, 1975 to 1991. Arch Fam Med 1995;4:849–56.
37. Robinson RG, Kessler LG, Naughton MD. Cancer awareness among African Americans: a survey assessing race, social status, and occupation. J Natl Med Assoc 1991;83:491–7.
38. Schrag D, Cramer LD, Bach PB, Cohen AM, Warren JL, Begg CB. Influence of hospital procedure volume on outcomes following surgery for colon cancer. JAMA 2000;284:3028–35.
39. Schrag D, Gelfand SE, Bach PB, Guillem J, Minsky BD, Begg CB. Who gets adjuvant treatment for stage II and III rectal cancer? Insight from surveillance, epidemiology, and end results—Medicare. J Clin Oncol 2001;19:3712–8.

40. Schrag D, Rifas-Shiman S, Saltz L, Bach PB, Begg CB. Adjuvant chemotherapy use for Medicare beneficiaries with stage II colon cancer. J Clin Oncol 2002;20:3999–4005.
41. Potosky AL, Harlan LC, Kaplan RS, Johnson KA, Lynch CF. Age, sex, and racial differences in the use of standard adjuvant therapy for colorectal cancer. J Clin Oncol 2002;20:1192–202.
42. Ayanian JZ, Zaslavsky AM, Fuchs CS, et al. Use of adjuvant chemotherapy and radiation therapy for colorectal cancer in a population-based cohort. J Clin Oncol 2003;21:1293–300.
43. Tropman SE, Hatzell T, Paskett E, Ricketts T, Cooper MR, Aldrich T. Colon cancer treatment in rural North and South Carolina. Cancer Detect Prev 1999;23:428–34.
44. Govindarajan R, Shah RV, Erkman LG, Hutchins LF. Racial differences in the outcome of patients with colorectal carcinoma. Cancer 2003;97:493–8.
45. Cooper GS, Yuan Z, Landefeld CS, Rimm AA. Surgery for colorectal cancer: race-related differences in rates and survival among Medicare beneficiaries. Am J Public Health 1996;86:582–6.
46. Ball JK, Elixhauser A. Treatment differences between blacks and whites with colorectal cancer. Med Care 1996;34:970–84.
47. Dominitz JA, Samsa GP, Landsman P, Provenzale D. Race, treatment, and survival among colorectal carcinoma patients in an equal-access medical system. Cancer 1998;82:2312–20.
48. Wudel LJ, Jr., Chapman WC, Shyr Y, et al. Disparate outcomes in patients with colorectal cancer: effect of race on long-term survival. Arch Surg 2002;137:550–4; discussion 554–6.
49. Jepson C, Kessler LG, Portnoy B, Gibbs T. Black-white differences in cancer prevention knowledge and behavior. Am J Public Health 1991;81:501–4.
50. Mayberry RM, Coates RJ, Hill HA, et al. Determinants of black/white differences in colon cancer survival. J Natl Cancer Inst 1995; 87:1686–93.
51. Jessup JM, McGinnis LS, Steele GD, Jr., Menck HR, Winchester DP. The National Cancer Data Base. Report on colon cancer. Cancer 1996; 78:918–26.
52. Morris AM, Billingsley KG, Baxter NN, Baldwin LM. Racial disparities in rectal cancer treatment: a population-based analysis. Arch Surg 2004;139:151–5; discussion 156.
53. Robertson RH, Burkhardt JH, Powell MP, Eloubeidi MA, Pisu M, Weissman NW. Trends in colon cancer screening procedures in the US Medicare and Tricare populations: 1999-2001. Prev Med 2006;42: 460–2.
54. Phillips KA, Liang SY, Ladabaum U, et al. Trends in colonoscopy for colorectal cancer screening. Med Care 2007;45:160–7.
55. Guidry JJ, Aday LA, Zhang D, Winn RJ. Transportation as a barrier to cancer treatment. Cancer Pract 1997;5:361–6.
56. Guidry JJ, Aday LA, Zhang D, Winn RJ. Information sources and barriers to cancer treatment by racial/ethnic minority status of patients. J Cancer Educ 1998;13:43–8.
57. Holmes-Rovner M, Williams GA, Hoppough S, Quillan L, Butler R, Given CW. Colorectal cancer screening barriers in persons with low income. Cancer Pract 2002;10:240–7.
58. Dignam JJ, Colangelo L, Tian W, et al. Outcomes among African-Americans and Caucasians in colon cancer adjuvant therapy trials: findings from the National Surgical Adjuvant Breast and Bowel Project. J Natl Cancer Inst 1999;91:1933–40.
59. Doubeni CA, Field TS, Buist DS, et al. Racial differences in tumor stage and survival for colorectal cancer in an insured population. Cancer 2007;109:612–20.
60. Agrawal S, Bhupinderjit A, Bhutani MS, et al. Colorectal cancer in African Americans. Am J Gastroenterol 2005;100:515–23; discussion 514.
61. Rolnick S, Hensley Alford S, Kucera GP, et al. Racial and age differences in colon examination surveillance following a diagnosis of colorectal cancer. J Natl Cancer Inst Monogr 2005;35:96–101.
62. Rulyak SJ, Mandelson MT, Brentnall TA, Rutter CM, Wagner EH. Clinical and sociodemographic factors associated with colon surveillance among patients with a history of colorectal cancer. Gastrointest Endosc 2004;59:239–47.
63. Cooper GS, Yuan Z, Chak A, Rimm AA. Geographic and patient variation among Medicare beneficiaries in the use of follow-up testing after surgery for nonmetastatic colorectal carcinoma. Cancer 1999;85:2124–31.
64. Elston Lafata J, Cole Johnson C, Ben-Menachem T, Morlock RJ. Sociodemographic differences in the receipt of colorectal cancer surveillance care following treatment with curative intent. Med Care 2001;39:361–72.

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