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Racial and Ethnic Disparities in Early-Onset Colorectal Cancer Survival

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Abstract

BACKGROUND: Young adults diagnosed with colorectal cancer (CRC) comprise a growing, yet understudied, patient population. We estimated 5-year relative survival of early-onset CRC and examined disparities in survival by race-ethnicity in a population-based sample.

METHODS: We used the National Cancer Institute's Surveillance, Epidemiology, and End Results program of cancer registries to identify patients diagnosed with early-onset CRC (20–49 years of age) between January 1, 1992, and December 31, 2013. For each racial-ethnic group, we estimated 5-year relative survival, overall and by sex, tumor site, and stage at diagnosis. To illustrate temporal trends, we compared 5-year relative survival in 1992–2002 vs 2003–2013. We also used Cox proportional hazards regression models to examine the association of race-ethnicity and all-cause mortality, adjusting for age at diagnosis, sex, county type (urban vs rural), county-level median household income, tumor site, and stage at diagnosis.

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Conflicts of Interest

These authors disclose the following: Caitlin C. Murphy reports consulting for Freenome. Folasade P. May reports consulting for Freenome, Medtronic, and Takeda. Peter S. Liang reports research support from Epigenomics and Freenome and consulting for Guardant Health. The remaining author discloses no conflicts.

CRediT Authorship Contributions

Timothy Andrew Zaki, MD (Conceptualization: Equal; Data curation: Lead; Formal analysis: Equal; Methodology: Equal; Writing – original draft: Lead; Writing – review & editing: Supporting)
Peter S. Liang, MD, MPH (Formal analysis: Supporting; Writing – review & editing: Supporting)
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Caitlin C. Murphy, PhD, MPH (Conceptualization: Equal; Data curation: Supporting; Formal analysis: Equal; Methodology: Equal; Supervision: Lead; Writing – original draft: Supporting; Writing – review & editing: Supporting)

Supplementary Material

Note: To access the supplementary material accompanying this article, visit the online version of *Clinical Gastroenterology and Hepatology* at www.cghjournal.org, and at https://doi.org/10.1016/j.cgh.2022.05.035.

RESULTS: We identified 33,777 patients diagnosed with early-onset CRC (58.5% White, 14.0% Black, 13.0% Asian, 14.5% Hispanic). Five-year relative survival ranged from 57.6% (Black patients) to 69.1% (White patients). Relative survival improved from 1992–2002 to 2003–2013 for White patients only; there was no improvement for Black, Asian, or Hispanic patients. This pattern was similar by sex, tumor site, and stage at diagnosis. In adjusted analysis, Black (adjusted hazard ratio [aHR], 1.42; 95% confidence interval [CI], 1.36–1.49), Asian (aHR, 1.06; 95% CI, 1.01–1.12), and Hispanic (aHR, 1.16; 95% CI, 1.10–1.21) race-ethnicity were associated with all-cause mortality.

CONCLUSION: Our study adds to the well-documented disparities in CRC in older adults by demonstrating persistent racial-ethnic disparities in relative survival and all-cause mortality in patients with early-onset CRC.

Keywords

Colorectal Cancer; Survival; Disparities; Race-Ethnicity; Population-Based

Young adults diagnosed with colorectal cancer (CRC) comprise a growing, yet understudied, patient population.[1,2] Incidence rates of early-onset CRC (<50 years of age) have increased in the United States since the early 1990s; mortality rates have improved little during the same time period.[3]

Early-onset CRC disproportionately affects racial and ethnic minorities. We previously reported in this journal differences in incidence rates of early-onset CRC by race and ethnicity, noting consistently higher rates in Black compared with White persons and large, relative increases in young (20–29 years of age) Hispanic persons.[4] The extent to which these differences in incidence rates translate into differences in cancer survival remains less clear. Differences in cancer survival may reveal the influence of both upstream determinants and downstream factors across the cancer care continuum, ranging from social and environmental conditions to cancer treatment to biological response.[5] A growing literature suggests Black patients diagnosed with early-onset CRC have experienced smaller gains in survival over time compared with White patients,[6-8] but few studies have examined disparities in cancer survival in other patient populations with early-onset CRC, particularly Asian and Hispanic patients. To address this gap and extend the findings of our prior work, we estimated 5-year relative survival and examined disparities in survival by race and ethnicity in a diverse, population-based sample of patients diagnosed with early-onset CRC.

Materials and Methods

We identified patients newly diagnosed with incident, invasive CRC at 20–49 years of age using population-based data from the National Cancer Institute's Surveillance, Epidemiology, and End Results (SEER) program of cancer registries. We combined concepts of race and ethnicity as race-ethnicity to include patients who were non-Hispanic White ("White"), non-Hispanic Black ("Black"), non-Hispanic Asian or Pacific Islander ("Asian"), or Hispanic (of any race, "Hispanic"). For each racial-ethnic group, we estimated 5-year relative survival, overall and by sex, tumor site, and stage at diagnosis. To illustrate temporal trends, we plotted estimates of 5-year relative survival in 2 time periods: January

1, 1992, to December 31, 2002, and January 1, 2003, to December 31, 2013. We used Cox proportional hazards regression models to examine the association of race-ethnicity and all-cause mortality, adjusting for age at diagnosis, sex, county type (urban vs rural), county-level median household income (≤$49,999 vs $50,000–$74,999 vs ≥$75,000), tumor site, and stage at diagnosis. See the Supplementary Methods for details.

Results

We identified 33,777 patients diagnosed with early-onset CRC, of whom 19,759 (58.5%) were White, 4728 (14.0%) were Black, 4388 (13.0%) were Asian, and 4902 (14.5%) were Hispanic. Table 1 summarizes characteristics of the study population by race-ethnicity.

As shown in Table 2, 5-year relative survival ranged from 57.6% (Black patients) to 69.1% (White patients). Relative survival increased from 1992–2002 to 2003–2013 for White patients only, and there was no improvement in survival for the other racial-ethnic groups over time (Figure 1, Supplementary Table 1). Survival for Black patients diagnosed in 2003–2013 (59.3%; 95% confidence interval [CI], 57.3%–61.3%) remained lower compared with survival for White (66.6%; 95% CI, 65.6%–67.6%) and Asian (65.0%; 95% CI, 62.7%–67.1%) patients diagnosed in 1992–2002, as well as compared with Hispanic patients diagnosed in 2003–2013 (64.0%; 95% CI, 62.3%–65.7%).

Racial-ethnic disparities in relative survival by sex

Relative survival was generally higher for women compared with men across all racial-ethnic groups (Table 2). Specifically, survival was lowest for Black men (56.5%; 95% CI, 54.4%–58.6%) and highest for White women (70.6%; 95% CI, 69.6%–71.5%). This pattern persisted over time (Figure 2). Survival increased from 1992–2002 to 2003–2013 for White men and women and Black women but not for other groups (Supplementary Table 1).

Racial-ethnic disparities in relative survival by tumor site

Relative survival differed by race-ethnicity and tumor site (Table 2), and was lowest for Black patients with proximal colon tumors (55.3%; 95% CI, 52.8%–57.7%) and highest for White patients with rectal tumors (72.2%; 95% CI, 71.2%–73.2%). Asian patients with rectal tumors (69.3%; 95% CI, 67.1%–71.3%) had better survival than Hispanic (63.5%; 95% CI, 61.2%–65.7%) and Black (61.3%; 95% CI, 58.8%–63.8%) patients with rectal tumors but similar to White patients (72.2%; 95% CI, 71.2%–73.2%). Survival differed by tumor site for White (proximal colon < distal colon < rectum) and Black (proximal colon < rectum) patients but was similar across tumor sites (ranging from 63.9% to 69.3%) for Asian and Hispanic patients. Improvements in survival from 1992–2002 to 2003–2013 (Figure 3) were limited to White patients with proximal colon (from 62.8% [95% CI, 61.0%–64.6%] to 69.1% [95% CI, 67.4%–70.8%]) and rectal (from 69.2% [95% CI, 67.6%–70.8%] to 74.6% [95% CI, 73.2%–75.9%]) tumors and Hispanic patients with distal colon tumors (from 58.2% [95% CI, 53.7%–62.5%] to 66.4% [95% CI, 63.2%–69.3%]) (Supplementary Table 1).

Racial-ethnic disparities in relative survival by stage at diagnosis

Across all racial-ethnic groups, 5-year relative survival was lowest for distant-stage disease, ranging from 13.1% (95% CI, 11.4%–15.0%) for Black patients to 19.7% (95% CI, 18.5%–20.8%) for White patients (Table 2). As shown in Figure 4, relative survival of distant-stage disease increased from 1992–2002 to 2003–2013 for all racial-ethnic groups except Black patients (from 10.5% [95% CI, 8.2%–13.2%] to 15.1% (95% CI, 12.7%–17.8%]). There was no improvement in survival over time for local-stage disease, although survival was generally high (Supplementary Table 1).

Adjusted models of all-cause mortality

Supplementary Table 2 shows crude and adjusted hazard ratios (aHRs) demonstrating the association of race-ethnicity and all-cause mortality, adjusted for age at diagnosis, sex, county type, county-level household median income, tumor site, and stage at diagnosis. In adjusted analysis, Black (aHR, 1.40; 95% CI, 1.33–1.47), Asian (aHR, 1.07; 95% CI, 1.02–1.13), and Hispanic (aHR, 1.14; 95% CI, 1.08–1.19) race-ethnicity were associated with higher all-cause mortality.

Discussion

Our study demonstrates striking racial-ethnic disparities in relative survival and all-cause mortality in patients with early-onset CRC. Specifically, we observed lower 5-year relative survival of Hispanic and Asian patients diagnosed with early-onset CRC compared with White patients, and this difference persisted across sex, tumor site, and stage at diagnosis. Black patients also had worse survival than White patients. Disparities remained in models adjusted for other clinical and sociodemographic factors.

Relative survival was consistently worse for Hispanic and Asian compared with White patients, and Black patients recently diagnosed with early-onset CRC in our study had worse survival than White patients diagnosed a decade earlier. Notably, Hispanic and Asian patients had worse survival than White patients, despite the comparatively lower incidence rates of early-onset CRC in these 2 groups.[4] Although racial-ethnic disparities in survival may be, in part, due to late stage diagnoses, differences remained in adjusted models accounting for clinical and sociodemographic factors. It is likely that these disparities reflect unequal access to, receipt of, and timeliness of cancer treatment; limited access to information,[9] treatment,[10,11] and high-quality care facilities[12] impacts cancer survival in medically underserved and minority populations. For example, studies show Black, Asian, and Hispanic patients are less likely to receive adjuvant chemotherapy for colon cancer[13,14] or radiation therapy for advanced rectal cancer[15] compared with White patients. Health insurance coverage and pre-existing chronic conditions, such as obesity and diabetes,[16-18] may also contribute to differences in survival, particularly the stark disparities among patients with distant disease.[19]

A limited number of population-based studies have examined CRC survival (across all ages) among Hispanic and Asian patients. We observed lower relative survival of Asian and Hispanic patients diagnosed with early-onset CRC compared with White patients. By

contrast, Liang et al[20] observed higher relative survival of Asian compared with White patients, although this study was conducted only among patients diagnosed at ≥65 years of age. Others report Asian and Hispanic patients have equivalent or better survival compared with White patients at comparable levels of income, education, and insurance, regardless of age at diagnosis.[21] Hispanic and Asian populations are heterogeneous,[22] and there may be differences in survival within these groups that have not yet been examined in the setting of early-onset CRC.

Some have suggested genetic and biological differences also drive disparities in early-onset CRC,[23,24] based on the observation that epigenetic aging of the normal colon and immune response profiles of colon tumors[25,26] differ between Black and White patients. Although differences in biological response may contribute to the disparities in early-onset CRC survival that we and others[20,27] have observed, these factors are likely downstream consequences of upstream determinants—a broad set of social and environmental conditions that influence health.[28] Upstream determinants are increasingly recognized as important influences across the cancer care continuum.[29] For example, emerging research in epigenetics suggests that neighborhood characteristics (eg, poverty, safety, social cohesion)[30] influence DNA methylation and may drive differences in cancer survival.[31,32] Similarly, unequal access to and receipt of treatment may be related to interpersonal and structural racism.[10,33] Mistrust of the healthcare system,[34,35] language barriers,[36] and cultural factors may also play a role.[34,37,38]

Relative survival was lowest among Black men and remained stagnant over time, and we observed a similar pattern for Hispanic men, albeit to a lesser degree. Relative survival was generally higher for women compared with men across all racial-ethnic groups. Reasons for these differences are not well understood but may be driven by both sex-related biologic factors (eg, endogenous sex hormones, immune response)[39] and gender-related factors (eg, cultural belief systems, health-seeking behavior).[34,38] Literature on sex and gender differences in early-onset CRC is limited: few studies have examined gender-related factors, and no studies have examined the intersection of gender and race.[40] Instead, most studies report sex-related differences in survival, and survival is generally higher or similar in women vs men. For example, in a study conducted in the United Kingdom, men and women with early-onset CRC had similar survival,[41] but a German study reported lower 5-year relative survival in men vs women with early-onset CRC.[42] U.S. studies have also shown differences in survival between men and women.[7]

Our study adds to the well-documented disparities in survival of Black and White patients diagnosed with CRC.[20,43-45] We previously reported smaller improvements in relative survival of proximal colon cancer but larger improvements in rectal cancer survival over time for younger Black compared with White patients.[6] In the current study, we observed a similar pattern for proximal colon cancer but persistent Black-White disparities for rectal cancer, consistent with results from Acuna-Villaorduna et al.[27] Elsewhere, Holowatyj et al[7] observed lower cancer-specific survival in Black vs White patients with early-onset CRC but no difference in survival between Hispanic and White patients. Similar findings were noted by others.[8,46] The differences in findings between these studies may be related to differences in time periods or populations examined.

An important strength of our study is the large and diverse (41% Black, Asian, or Hispanic) population-based sample. The diversity of our study population allowed us to examine relative survival of Asian and Hispanic patients diagnosed with early-onset CRC, groups that are underrepresented in research on this disease. There were some limitations. We used information on race and ethnicity collected by cancer registries as an imperfect proxy for social constructs; similarly, we used county-level measures of income and urban vs rural as proxies for socioeconomic status. The field will benefit from improved collection and use of individual-level information that more accurately capture social determinants of health. We did not include American Indian or Alaska Native patients due to small sample size, and this group generally has lower survival compared with White patients.[47] Cancer registry data may not be uniformly accurate for some population groups, including racial-ethnic minorities; however, studies assessing the validity of SEER data show no racial-ethnic differences in case ascertainment (98%)[48,49] and high agreement between SEER and self-reported race.[50] We also could not examine the contribution of access to and receipt of treatment to disparities in relative survival because population-based cancer registries do not systematically collect this information. Further, information on tumor markers (eg, microsatellite instability) is often incomplete, and missingness differs by race-ethnicity.

In summary, our findings contribute to the growing literature on racial-ethnic disparities in early-onset CRC and extend knowledge by demonstrating lower relative survival and higher all-cause mortality of Asian and Hispanic compared with White patients. These findings serve as a forewarning for worsening disparities as 2 critical events continue to unfold in the United States. First, our study included patients diagnosed with early-onset CRC before the COVID-19 pandemic, and the social and economic impact of the pandemic will likely exacerbate existing cancer health disparities.[51] Second, the U.S. Preventive Services Task Force recommended in May 2021 that CRC screening begin at 45 (vs 50) years of age.[52] Although differences in the uptake of screening are unlikely to explain the disparities in our study conducted among patients diagnosed prior to new guidelines, implementation of these guidelines may disproportionately benefit the worried well.[53] Future research and interventions should address disparities in this growing patient population by targeting both upstream determinants and downstream factors that contribute to inequities in CRC outcomes.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Abbreviations used in this paper:

aHR	adjusted hazard ratio
CI	confidence interval
CRC	colorectal cancer
SEER	Surveillance, Epidemiology, and End Results

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What You Need to Know

Background

Early-onset colorectal cancer (CRC) is rising and disproportionately affects racial-ethnic minorities. We estimated 5-year relative survival of early-onset CRC and examined disparities by race-ethnicity in a diverse population-based sample.

Findings

Relative survival improved over time for White individuals only, and there was no improvement for Black, Asian, or Hispanic individuals. Black, Asian, and Hispanic race-ethnicity were associated with all-cause mortality.

Implications for patient care

Future research and interventions should address disparities in this growing patient population by targeting both upstream determinants and downstream factors that contribute to inequities in CRC outcomes.

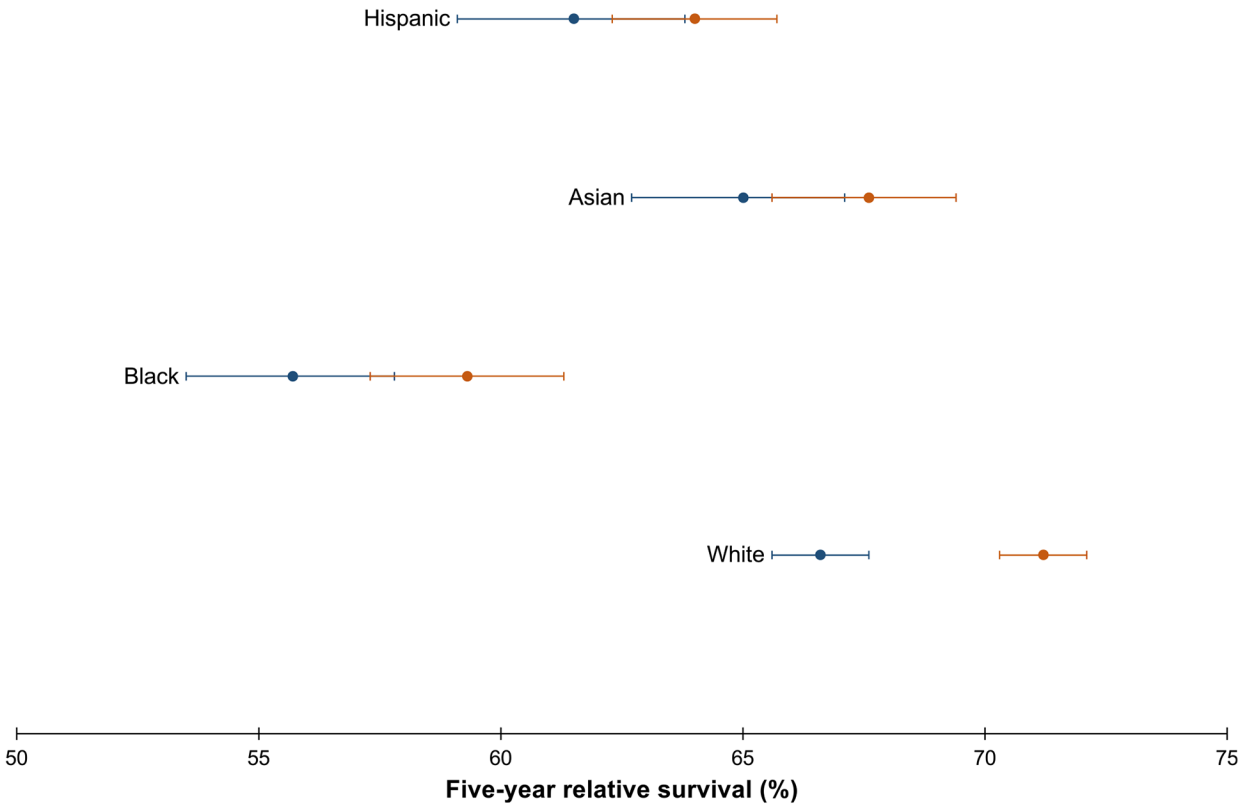

Figure 1.

Five-year relative survival of CRC (20–49 years of age) with corresponding 95% CIs, by race-ethnicity, shown over the period 1992–2002 (blue dot) vs 2003–2013 (orange dot). Source: SEER 13.

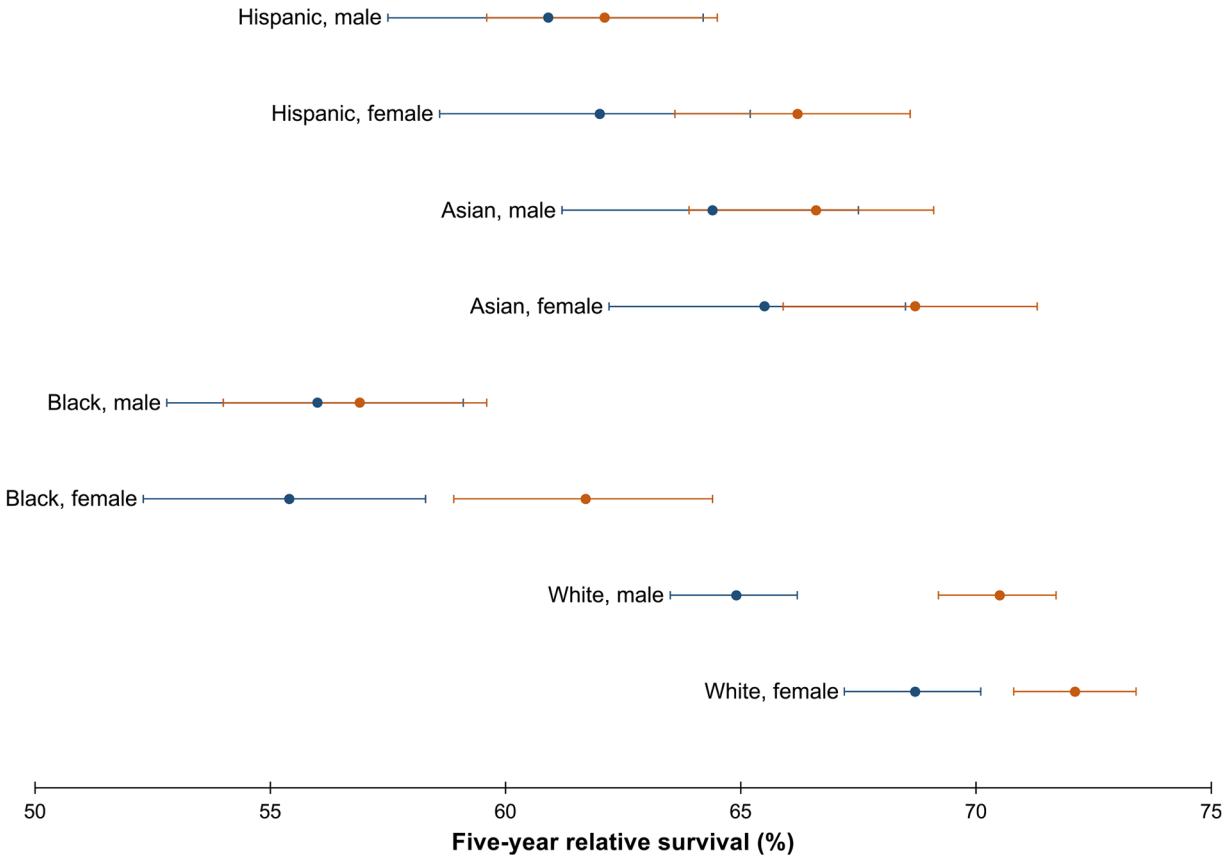

Figure 2.

Five-year relative survival of CRC (20–49 years of age) with corresponding 95% CIs, by race-ethnicity and sex, shown over the period 1992–2002 (blue dot) vs 2003–2013 (orange dot). Source: SEER 13.

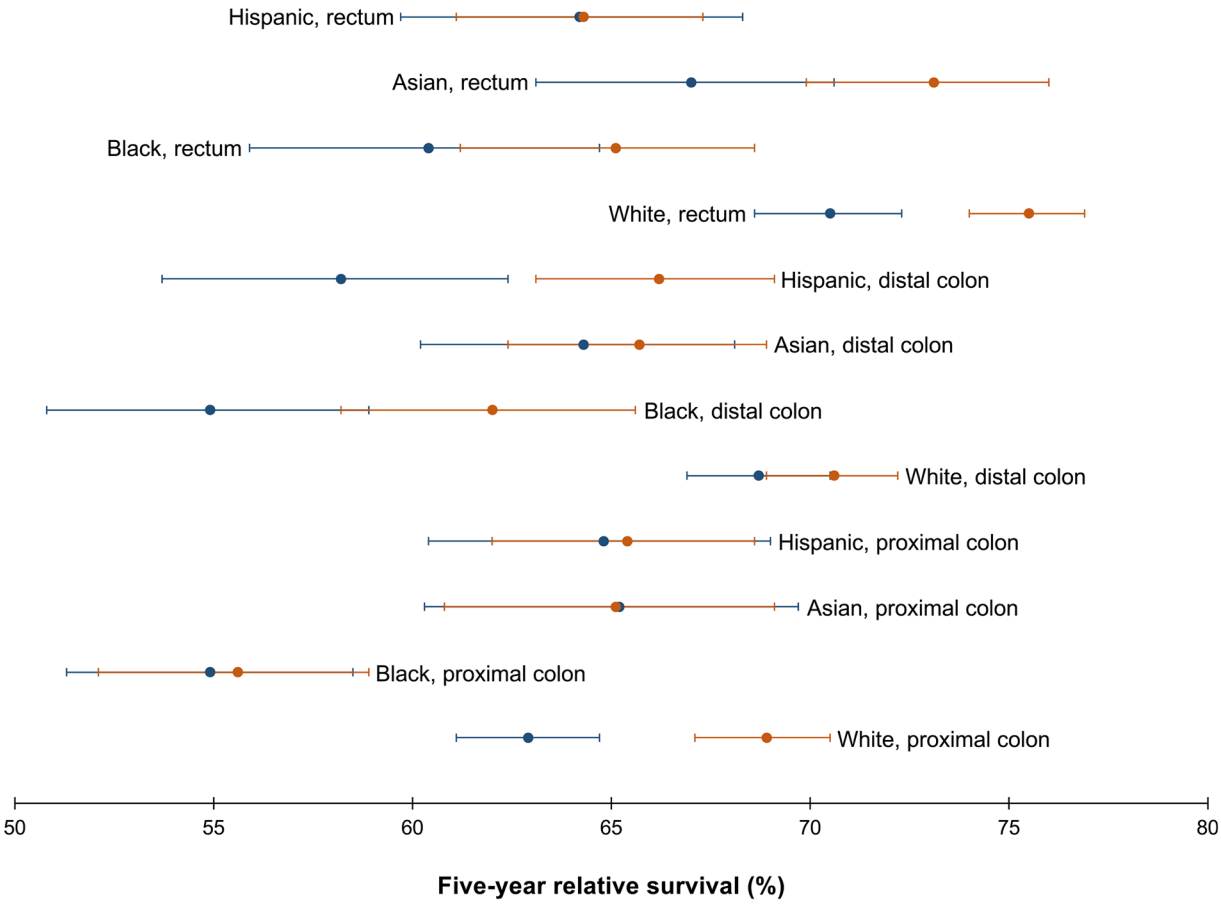

Figure 3.

Five-year relative survival of CRC (20–49 years of age) with corresponding 95% CIs, by race-ethnicity and tumor site, shown over the period 1992–2002 (blue dot) vs 2003–2013 (orange dot). Source: SEER 13.

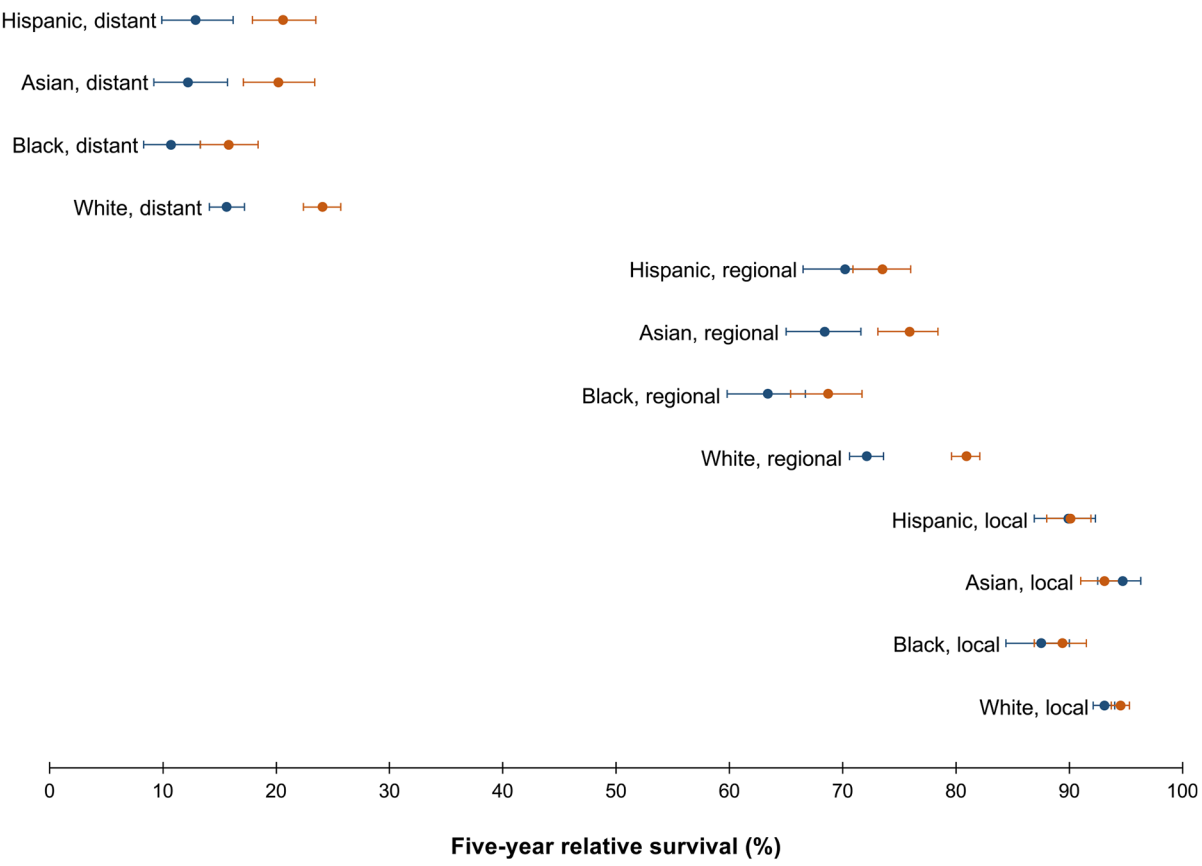

Figure 4.

Five-year relative survival of CRC (20–49 years of age) with corresponding 95% CIs, by race-ethnicity and stage at diagnosis, shown over the period 1992–2002 (blue dot) vs 2003–2013 (orange dot). Source: SEER 13.

Table 1.

Characteristics of 33,777 Young Adults (20–49 Years of Age) Diagnosed With Colorectal Cancer by Race-Ethnicity (SEER 13, 1992–2013)

	Non-Hispanic White (n = 19,759 [58.5%])		Non-Hispanic Black (n = 4728 [14.0%])		Non-Hispanic Asian/Pacific Islander (n = 4388 [13.0%])		Hispanic (n = 4902 [14.5%])		All (N = 33,777 [100%])	
	n	%	n	%	n	%	n	%	n	%
Age										
20–29 y	864	4.4	194	4.1	217	4.9	350	7.1	1625	4.8
30–39 y	3969	20.1	967	20.5	1003	22.9	1266	25.8	7205	21.3
40–49 y	14,926	75.5	3567	75.4	3168	72.2	3286	67.0	24,947	73.9
Sex										
Male	10,671	54.0	2328	49.2	2271	51.8	2561	52.2	17,831	52.8
Female	9088	46.0	2400	50.8	2117	48.2	2341	47.8	15,946	47.2
Stage										
Local	6998	35.4	1493	31.6	1474	33.6	1593	32.5	11,558	34.2
Regional	7504	38.0	1656	35.0	1760	40.1	1829	37.3	12,749	37.7
Distant	4725	23.9	1372	29.0	1029	23.5	1293	26.4	8419	24.9
Missing	532	2.7	207	4.4	125	2.8	187	3.8	1051	3.1
Tumor site										
Proximal colon	5820	29.5	1650	34.9	916	20.9	1325	27.0	9711	28.8
Distal colon	5629	28.5	1317	27.9	1422	32.4	1504	30.7	9872	29.2
Rectum	7795	39.4	1577	33.4	1961	44.7	1906	38.9	13,239	39.2
Missing	515	2.6	184	3.9	89	2.0	167	3.4	955	2.8

SEER, Surveillance, Epidemiology, and End Results.

Table 2.

Five-Year Relative Survival of Colorectal Cancer (20–49 Years of Age) by Race-Ethnicity, Overall and by Sex, Tumor Site, and Stage at Diagnosis (SEER 13, 1992–2013)

	Non-Hispanic White (n = 19,759)	Non-Hispanic Black (n = 4728)	Non-Hispanic Asian/Pacific Islander (n = 4388)	Hispanic (n = 4902)
Overall	69.1 (68.4–69.7)	57.6 (56.2–59.1)	66.5 (65.0–67.9)	63.1 (61.7–64.5)
Sex				
Male	67.8 (66.9–68.7)	56.5 (54.4–58.6)	65.7 (63.6–67.6)	61.7 (59.7–63.7)
Female	70.6 (69.6–71.5)	58.8 (56.7–60.8)	67.3 (65.2–69.3)	64.7 (62.6–66.6)
Tumor site				
Proximal colon	66.1 (64.8–67.3)	55.3 (52.8–57.7)	65.2 (61.9–68.2)	65.4 (62.7–68.0)
Distal colon	69.8 (68.5–71.0)	59.0 (56.2–61.7)	65.1 (62.5–67.6)	63.6 (61.0–66.1)
Rectum	72.2 (71.2–73.2)	61.3 (58.8–63.8)	69.3 (67.1–71.3)	63.5 (61.2–65.7)
Stage at diagnosis				
Local	94.2 (93.6–94.8)	89.2 (87.3–90.9)	94.4 (93.0–95.6)	90.9 (89.2–92.3)
Regional	76.8 (75.8–77.8)	66.1 (63.7–68.4)	72.5 (70.3–74.6)	72.4 (70.2–74.5)
Distant	19.7 (18.5–20.8)	13.1 (11.4–15.0)	16.1 (13.9–18.5)	17.0 (14.9–19.2)

Values in parentheses are 95% confidence interval.

SEER, Surveillance, Epidemiology, and End Results.