

# Disparities in survival improvement for metastatic colorectal cancer by race/ethnicity and age in the United States

Helmneh M. Sineshaw · Anthony S. Robbins ·  
Ahmedin Jemal

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## Abstract

**Purpose** Previous studies documented significant increase in overall survival for metastatic colorectal cancer (CRC) since the late 1990s coinciding with the introduction and dissemination of new treatments. We examined whether this survival increase differed across major racial/ethnic populations and age groups.

**Methods** We identified patients diagnosed with primary metastatic colorectal cancer during 1992–2009 from 13 population-based cancer registries of the National Cancer Institute's Surveillance, Epidemiology, and End Results Program, which cover about 14 % of the US population. The 5-year cause-specific survival rates were calculated using SEER\*Stat software.

**Results** From 1992–1997 to 2004–2009, 5-year cause-specific survival rates increased significantly from 9.8 % (95 % CI 9.2–10.4) to 15.7 % (95 % CI 14.7–16.6) in non-Hispanic whites and from 11.4 % (95 % CI 9.4–13.6) to 17.7 % (95 % CI 15.1–20.5) in non-Hispanic Asians, but not in non-Hispanic blacks [from 8.6 % (95 % CI 7.2–10.1) to 9.8 % (95 % CI 8.1–11.8)] or Hispanics [from 14.0 % (95 % CI 11.8–16.3) to 16.4 % (95 % CI 14.0–19.0)]. By age group, survival rates increased significantly for the 20–64-year age group and 65 years or older age group in non-Hispanic whites, although the improvement in the older non-Hispanic whites was substantially smaller. Rates also increased in non-Hispanic Asians for the 20–64-year age group although marginally nonsignificant. In contrast, survival rates did not

show significant increases in both younger and older age groups in non-Hispanic blacks and Hispanics.

**Conclusion** Non-Hispanic blacks, Hispanics, and older patients diagnosed with metastatic CRC have not equally benefitted from the introduction and dissemination of new treatments.

**Keywords** Metastatic colorectal cancer · SEER · Survival · Race/ethnicity · Age · Chemotherapy

## Introduction

Previous reports indicated survival improvement for metastatic colorectal cancer (CRC) [1–4]. For instance, Kopetz et al. [4] documented that overall survival rates for metastatic CRC significantly increased beginning in 1998, followed by another increase starting in 2004 based on retrospective medical review of 2,470 metastatic CRC patients treated at two large academic centers [MD Anderson Cancer Center (Houston, TX) and the Mayo Clinic (Rochester, MN)] from 1990 through 2006. The authors also showed similar improvements in overall survival rates for metastatic CRC in population-based cancer registries participating in the National Cancer Institute's Surveillance, Epidemiology, and End Results (SEER) Program [4]. These improvements in survival beginning in 1998 and 2004, respectively, are thought to reflect rapid increases in resection of liver metastases and the introduction of new drugs, specifically bevacizumab and cetuximab [4–12]. In this paper, we examined survival improvement for metastatic CRC in the general U.S. population across major racial/ethnic groups and broad age groups (20–64 and  $\geq 65$  years) in view of a number of prior examples of significant disparities in dissemination of new treatments by race/ethnicity and age [13–17].

H. M. Sineshaw (✉) · A. S. Robbins · A. Jemal  
Surveillance and Health Services Research, American Cancer Society, Inc., 250 Williams Street NW, Atlanta, GA 30303, USA  
e-mail: helmneh.sineshaw@cancer.org

**Table 1** Trends in 5-year cause-specific survival for metastatic colorectal cancer, diagnosis age  $\geq 20$ , by race/ethnicity, 13 SEER regions, 1992–2009<sup>a</sup>

Diagnosis years	5-Year cause-specific survival (% , 95 % CI), by race/ethnicity			
	NH white ( <i>n</i> = 34,642)	NH Asian/Pacific Islander ( <i>n</i> = 4,413)	NH black ( <i>n</i> = 6,369)	Hispanic (any race) ( <i>n</i> = 4,469)
1992–1997	9.8 (9.2–10.4)	11.4 (9.4–13.6)	8.6 (7.2–10.1)	14.0 (11.8–16.3)
1998–2000	11.4 (10.5–12.4)	13.3 (10.6–16.2)	8.9 (7.0–11.0)	13.2 (10.5–16.2)
2001–2003	13.0 (12.1–14.0)	14.4 (11.9–17.1)	10.4 (8.5–12.6)	15.1 (12.5–18.0)
2004–2009	15.7 (14.7–16.6)	17.7 (15.1–20.5)	9.8 (8.1–11.8)	16.4 (14.0–19.0)

NH non-Hispanic

<sup>a</sup> Cases were diagnosed between 1992 and 2009 and followed through 2010

## Materials and methods

We used cancer incidence data collected by the 13 population-based cancer registries of the National Cancer Institute's Surveillance, Epidemiology, and End Results (SEER) Program, which covers about 14 % of the US population [18]. Our analyses included patients who were diagnosed with primary metastatic CRC (historic stage = distant) between 1992 and 2009, aged 20 years or older, and actively followed for vital status. We excluded patients who were reported through death certificate or autopsy report only, alive with no survival time, missing or unknown cause of death, and with missing diagnosis dates. We further restricted our analyses to the four major US racial/ethnic groups (non-Hispanic whites, non-Hispanic blacks, non-Hispanic Asians, and Hispanics); data for American Indians/Alaska Natives were sparse. Age at diagnosis was grouped into two categories (20–64 years,  $\geq 65$  years) for each of the four major racial/ethnic groups. To evaluate temporal changes in survival rates, diagnosis years were grouped into four periods (1992–1997, 1998–2000, 2001–2003, 2004–2009). Using SEER\*Stat statistical software (version 8.0.4; National Cancer Institute), we then calculated 5-year cause-specific survival rates for the four major racial/ethnic groups by age and calendar periods. Cause-specific survival rate was calculated using the actuarial method, and the SEER cause-specific death classification variable was used as the endpoint [19, 20]. Cause-specific survival rate differences between groups were considered significant if their 95 % confidence intervals did not overlap.

## Results

There were a total of 49,893 selected patients with metastatic CRC in the SEER-13 database during 1992–2009. Of these patients, 69.4 % were non-Hispanic whites, 12.8 % non-Hispanic blacks, 8.8 % non-Hispanic Asians, and 9.0 %

Hispanics; 41.0 % of patients were 20–64 years old and 59.0 % were 65 years or older.

As Table 1 shows, from 1992–1997 to 2004–2009, 5-year cause-specific survival rate significantly increased from 9.8 % (95 % CI 9.2–10.4) to 15.7 % (95 % CI 14.7–16.6) in non-Hispanic whites and from 11.4 % (95 % CI 9.4–13.6) to 17.7 % (95 % CI 15.1–20.5) in non-Hispanic Asians, but not in non-Hispanic blacks [from 8.6 % (95 % CI 7.2–10.1) to 9.8 % (95 % CI 8.1–11.8)] or Hispanics [from 14.0 % (95 % CI 11.8–16.3) to 16.4 % (95 % CI 14.0–19.0)]. Notably, there was no significant difference in 5-year cause-specific survival between non-Hispanic whites, non-Hispanic blacks, and non-Hispanic Asians during 1992–1997, 1998–2000, and 2001–2003. However, during 2004–2009 period, non-Hispanic blacks had significantly lower 5-year cause-specific survival rate than did the other racial/ethnic groups.

Table 2 shows 5-year cause-specific survival rates for racial/ethnic groups by age group. From 1992–1997 to 2004–2009, survival rates increased in age 20–64 years and  $\geq 65$  years for both non-Hispanic whites and non-Hispanic Asians, although the increase was statistically significant in non-Hispanic whites only. In contrast, survival rates remained unchanged for non-Hispanic blacks and Hispanics, especially in the older age group. Although survival rates in non-Hispanic whites aged 65 years or older significantly increased from 1992–1997 to 2004–2009, the magnitude of increase was smaller and survival rates were significantly lower compared with their counterparts in the 20–64 years age group. The widening of the gap in cause-specific survival rates over the study period between non-Hispanic whites and non-Hispanic blacks, especially in the younger age group, is further illustrated in the Fig. 1.

## Discussion

We found that the improvement in survival rates for metastatic CRC from 1992 to 2009, presumably due to the

**Table 2** Trends in 5-year cause-specific survival for metastatic colorectal cancer, diagnosis age  $\geq 20$ , by age at diagnosis and race/ethnicity, 13 SEER regions, 1992–2009<sup>a</sup>

Diagnosis years	5-Year cause-specific survival (%; 95 % CI), by age at diagnosis (years) and race/ethnicity							
	$\geq 65$							
	$20-64$							
	NH white (n = 12,718)	NH Asian/Pacific Islander (n = 2,077)	NH black (n = 3,264)	Hispanic (any race) (n = 2,385)	NH white (n = 21,924)	NH Asian/Pacific Islander (n = 2,336)	NH black (n = 3,105)	Hispanic (any race) (n = 2,084)
1992–1997	12.5 (11.4–13.6)	14.0 (10.9–17.6)	9.8 (7.8–12.1)	15.9 (12.8–19.4)	8.5 (7.8–9.2)	9.2 (6.8–12.1)	7.5 (5.7–9.6)	12.1 (9.2–15.3)
1998–2000	15.3 (13.7–17.0)	15.1 (11.1–19.8)	10.4 (7.7–13.5)	12.6 (9.1–16.8)	9.2 (8.2–10.3)	11.7 (8.4–15.7)	7.3 (4.9–10.4)	14.4 (10.3–19.1)
2001–2003	17.9 (16.2–19.7)	15.3 (11.6–19.5)	11.9 (9.3–14.9)	19.0 (15.2–23.1)	9.7 (8.6–10.9)	13.7 (10.4–17.5)	8.5 (5.9–11.6)	10.0 (6.8–14.0)
2004–2009	20.8 (19.2–22.4)	21.0 (17.2–25.1)	11.9 (9.4–14.6)	18.8 (15.5–22.4)	11.6 (10.5–12.7)	13.9 (10.6–17.6)	7.2 (5.0–9.9)	13.1 (9.8–16.8)

NH non-Hispanic

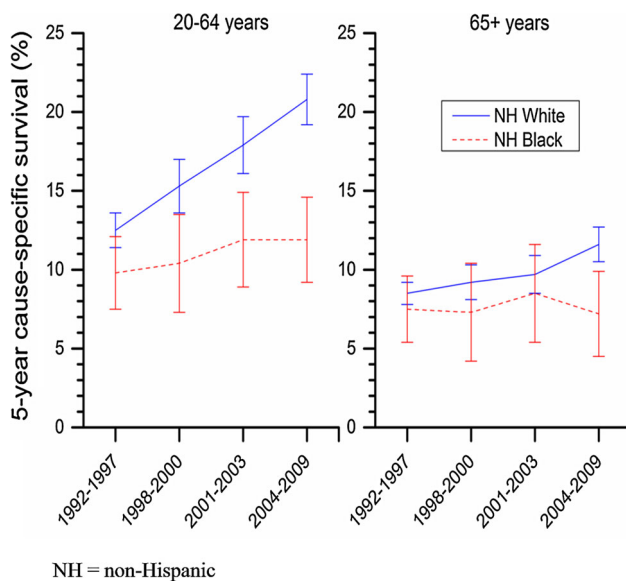
<sup>a</sup> Cases were diagnosed between 1992 and 2009 and followed through 2010

introduction and dissemination of new treatments, was largely confined to the younger non-Hispanic whites and non-Hispanic Asians. There were no statistically significant increases in survival rates for non-Hispanic blacks and Hispanics.

A number of studies have reported significant inequalities in dissemination of new treatments for CRC and other cancers between racial/ethnic groups [13, 21–24] despite accumulated evidence for equal treatment leading to equal outcome from randomized trials and from observational studies based on more equitable health care delivery systems [25–32]. For instance, Obeidat et al. [13] reported that African American patients were 37.9 % less likely to initially receive newer chemotherapy agents for metastatic CRC than white patients. Blacks also were less likely to receive surgical resection of colon cancer compared with whites (68 % blacks vs. 78 % whites) [33]. In addition, minorities have also been reported to be more likely to have a delayed initiation of treatment (especially adjuvant or neoadjuvant chemotherapy) and be less likely to be adherent to the treatment plan [13, 21]. Reasons for these treatment disparities may include difference in comorbidities, socioeconomic and psychosocial factors, quality of screening or diagnostic tests, affordability of new drugs, structural barriers such as lack of health insurance and limited transportation means to travel to treatment facilities, as well as within stage disease severity which may impact eligibility for certain treatments such as surgical resection of liver metastases [17, 23, 34–41].

Similarly, several studies documented that persons aged 65 years or older are less likely to receive aggressive treatment for CRC in part because of comorbidities, provider or patient preferences, and high Medicare co-payments for new drugs [14, 21, 27, 42, 43]. For example, McKibbin et al. [15] reported that 58 % of patients aged >65 years received chemotherapy for advanced CRC compared with 84 % of those aged  $\leq 65$  years. However, a recent study showed that first-line chemotherapy for metastatic CRC in older patients significantly improves survival rates with side effects comparable with those in younger patients [44].

The differences in survival improvement for metastatic CRC between racial/ethnic groups may also in part reflect changes in the distribution of disease severity over time because of differential uptake of screening [45, 46]. Compared with interval cancers, screen-detected cancers are more likely to be diagnosed at the earlier stage of the disease and have better prognosis [47], in view of significant heterogeneity in disease severity within stage [48]. CRC screening rates increased more for non-Hispanic whites than for other racial and ethnic groups. For example, according to the 2010 National Health Interview Survey, 62 % of non-Hispanic whites were current with their CRC



**Fig. 1** Trends in 5-year cause-specific survival among NH whites and NH blacks by age group: SEER 1992–2009

screening tests compared with 55 % of non-Hispanic blacks and 47 % of Hispanics [49]. Furthermore, non-Hispanic whites are more likely to receive high-quality screening tests and follow-up after abnormal tests [45, 46, 50, 51].

Our study has certain limitations. The 13 SEER cancer registries considered in our analysis cover approximately 14 % of the US population. However, SEER 13 is a reasonably representative of the entire US population [52]. For example, 11.8 % of the population in SEER 13 was below poverty level compared with 13.1 % in the total US population [52]. Misclassification of race and ethnicity on medical records and inaccuracy of cause of death in death certificates are also possible limitations of our study, especially for racial/ethnic groups other than non-Hispanic whites and non-Hispanic blacks [53, 54]. In addition, cause-specific survival in Hispanics and non-Hispanic Asians may be influenced by the return of foreign-born migrants back to their home country after cancer diagnosis [55]. The marginally nonsignificant survival increase in non-Hispanic Asians aged 20–64 years may indicate lack of statistical power.

In conclusion, the improvement in survival rates for metastatic CRC in the general population since 1998 largely reflects gains in younger non-Hispanic whites and non-Hispanic Asians. Survival has not significantly improved in non-Hispanic blacks, Hispanics, and the elderly, which suggests that these subpopulations have not equally benefited from new treatment advances for metastatic CRC. Our findings underscore the need for concerted efforts to increase access to new treatments for minority groups and the elderly, as well as additional research to

better understand factors associated with race/ethnicity- and age-related survival disparities for metastatic colorectal cancer.

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