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# A Population-Based Retrospective Cohort Study on Colorectal Cancer Survival in Kentucky

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## ABSTRACT

Colorectal cancer (CRC) mortality in Kentucky exceeds the national average, with recent studies reporting up to a 29.6% increase. Non-Hispanic Blacks (NHBs) and rural residents face higher CRC incidence and worse survival rates. This study investigates factors driving Kentucky's elevated CRC mortality. This retrospective cohort study analyzed Surveillance, Epidemiology, and End Results (SEER) data from 2000 to 2021, including 42,963 eligible CRC patients from Kentucky. Demographic characteristics, diagnostic outcomes, and treatment modalities were examined. Kaplan-Meier and Cox regression model were used. The highest proportion of distant CRC diagnoses was in NHBs (17.8%), while the lowest was in Non-Hispanic Others (NHOs) (11.9%) (P-value =0.0001). NHBs also had the highest CRC mortality rate (42.7%) compared to NHOs (22.9%) (P-value < 0.0001). Unadjusted survival time was shortest for NHBs (70.6 months) and longest for NHOs (81.3 months) (P-value < 0.0006). Cox regression analysis (P-values < 0.0001) showed counties not adjacent to metropolitan areas had a 13% higher mortality risk than large metro areas. NHBs had an 18% higher CRC mortality risk than Non-Hispanic Whites (NHWs). Patients with regional or distant-stage diagnoses had 165% and 853% higher mortality risks, respectively. Also, those who were not recommended or refused surgery had a 233% higher risk. This study identifies key factors influencing CRC mortality in Kentucky, such as being NHB, rural residency, late-stage diagnosis, and lack of surgical options. These findings highlight the need for targeted public health strategies, access to care, and policy changes to address CRC-related health disparities in Kentucky.

KEYWORDS: CRC, Mortality, Survival Outcomes, Health disparities, Kaplan-Meier, Cox regression

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## Background

Colorectal cancer (CRC) remains a major public health concern in the United States, with disparities in both incidence and mortality rates. This is especially true in Kentucky, a state with some of the highest CRC rates in the nation. CRC mortality in Kentucky exceeds the national average, with recent studies indicating an increase of up to 29.6% (Hudson-Rose et al., 2023). Various factors contribute to these disparities, including race/ethnicity, geographic location, diagnosis, and treatment types, all of which play a crucial role in determining outcomes for CRC patients in Kentucky (Akinyemiju et al., 2016; American Cancer Society, 2020; Jackson et al., 2016; Shively et al., 2022).

In recent decades, both the incidence and mortality rates of colorectal cancer (CRC) in the United States have declined (Siegel et al., 2020). This reduction is largely due to increased CRC screening and colonoscopic polypectomy in individuals over the age of 50 (Edwards et al., 2014), as well as changes in risk factors, such as a reduction in smoking prevalence (Brenner & Chen, 2018).

Despite these trends, CRC incidence and mortality rates in Kentucky remain higher than the national average, with notably greater rates in Appalachian Kentucky compared to non-Appalachian regions (O'Shaughnessy et al., 2025). The Kentucky Cancer Needs Assessment and research by Yao et al. (2017) emphasize significantly elevated cancer rates in Appalachian Kentucky populations compared to non-Appalachian areas. Specifically, age-adjusted colorectal cancer rates were 12.2% higher, and mortality rates were 14.1% higher in Appalachian Kentucky compared to the rest of the state (2021 Kentucky Cancer Needs Assessment, 2021).

O'Shaughnessy et al. (2025) also highlighted persistent disparities in CRC rates and mortality between Appalachian and non-Appalachian Kentucky, with incidence rates of 51.8 vs. 44.1 per 100,000 and mortality rates of 19.0 vs. `15.1 per 100,000, reflecting respective increases of 17.5% and 25.8% (p-value < 0.0001). Historically, Appalachian Kentucky has faced barriers such as low educational attainment and high cancer rates, with a lack of high school education correlating with elevated CRC rates and mortality (Robertson et al., 2023). The region's rural and economically disadvantaged condition further hinders access to preventive healthcare, exacerbating these disparities.

In addition to geographic disparities, racial disparities in early-onset colorectal cancer (EO-CRC) have been noted. Black patients, for example, report lower overall survival (OS) rates (Holowatyj et al., 2016). Meester et al. (2015) found that while EO-CRC incidence has increased across all racial groups, the most significant rise has been observed among non-Hispanic White individuals. Despite this, Black Americans continue to have the highest overall incidence of EO-CRC in the United States. Tsai et al. (2024) found that White patients in regions of Georgia with persistent poverty and Black patients in areas with low education levels faced an elevated risk of CRC mortality. Afshar et al. (2021) referenced two studies in the U.S. that suggested poorer overall survival rates among disadvantaged individuals with CRC, which may be partly attributed to factors such as disease stage, tumor grade, and differential access to treatment (Hines et al., 2014; Kim et al., 2011, as cited in Swati et al., 2022).

Timely diagnosis of CRC is crucial for improving survival outcomes. Delays in diagnosis are linked to higher rates of advanced-stage CRC, which are associated with poorer prognoses and higher mortality rates. Additionally, delays in colorectal cancer treatment have been shown to contribute to advanced-stage diagnoses and increased mortality. Chow et al. (2021) examined a 14-day treatment

delay from a positive colorectal screening via colonoscopy to the first specialist visit in Kentucky. They found that delays were more common among patients with Medicaid insurance (OR 3.1, P-value < 0.0001), low and moderate education levels (high school completion rate less than 67.9% and high school completion rate between 67.9% to 79.2%, respectively) (OR 1.4 and 1.3, respectively, P-value = 0.0127), and those diagnosed with stage I colorectal cancer (OR 1.5, P-value < 0.0001).

Swati et al. (2022) highlights substantial evidence supporting the U.S. Multi-Society Task Force (MSTF) recommendation to initiate average-risk CRC screening at age 45, addressing the rising disease burden in individuals under 50. Modeling studies suggest that the benefits of screening for individuals aged 45-49 outweigh the potential harms and costs. For individuals aged 76 to 85, the decision to start or continue screening should be tailored based on factors such as prior screening history, life expectancy, CRC risk, and personal preference. Screening is not recommended for individuals over age 85 (Swati et al., 2022).

While many studies have examined CRC health disparities based on geography, particularly between Appalachian and non-Appalachian regions of Kentucky, research on racial and ethnic disparities within the state remains limited. This study aims to address this gap by examining CRC disparities in Kentucky, considering both race/ethnicity and geographic location, with a focus on proximity to metropolitan areas. By investigating CRC survival rates in relation to demographic characteristics and exploring differences in diagnosis and treatment types, this research aims to provide a comprehensive understanding of the factors contributing to CRC disparities in Kentucky. Such insights are crucial for developing culturally tailored interventions that address contributing factors and improve CRC outcomes.

# Methods

## Study Design

This is a retrospective cohort study utilizing population-based data from the Surveillance, Epidemiology, and End Results (SEER) Program, covering the period from 2000 to 2021. The follow-up time is defined as the duration from diagnosis to death from colorectal cancer (CRC) or censoring. Censoring may occur due to loss to follow-up, death from causes other than CRC, or the end of the study period (November 2021).

## Data Source and Study Population

The SEER program provides one of the most comprehensive and reliable sources of cancer data in the United States, making it superior to many other publicly available secondary data sources. Managed by the National Cancer Institute, SEER offers high-quality, population-based data that covers a broad and diverse segment of the U.S. population, including detailed demographic, clinical, and survival information. Its rigorous data collection protocols ensure consistency, completeness, and accuracy across cancer registries. Unlike many other datasets, SEER includes longitudinal follow-up and geographic and racial/ethnic breakdowns, which are critical for examining disparities in cancer incidence, mortality, and survival outcomes. This makes SEER uniquely suited for robust epidemiological analyses and policy-relevant cancer research.

The data for this study were obtained from SEER. Specifically, the SEER Research Plus Data, 17 Registries, Nov 2023 Submission [2000–2021] dataset was used, which was downloaded on November 25, 2024. The selected variables included demographic characteristics, tumor characteristics (diagnosis), treatment modalities, and outcome variables. Data for patients diagnosed with colorectal cancer (CRC) were extracted using

the International Classification of Diseases for Oncology, 3rd edition (ICD-O-3/WHO 2008) codes: C180–C189, C199, and C209.

A total of 805,023 CRC patients were identified from the SEER data spanning years 2000 to 2021. When the data were limited to Kentucky, the sample size decreased to 55,845 patients. Cases with missing survival months (n = 395) were excluded. To ensure adequate follow-up time (at least 5 years), only data from diagnoses made between 2000 and 2016 were included in the analysis, resulting in a final sample size of 42,963 patients.

### Data Analysis

For summary statistics, the Chi-Square test is used for categorical variables, the Mantel-Haenszel Chi-Square test for ordinal variables, and ANOVA for continuous variables to assess differences by race/ethnicity. Race/ethnicity is categorized into four groups: Non-Hispanic Blacks (NHB), Non-Hispanic Whites (NHW), Hispanic (all races), and Non-Hispanic Others (NHO). Kaplan-Meier (KM) five year survival curves were generated to compare the unadjusted survival distributions between different groups, with log-rank tests used to assess statistical differences. A multiple Cox regression model was constructed using a stepwise variable selection method, with a two-sided p-value threshold of 0.05.

The data analyses were conducted using SAS software, Version 9.4 of the SAS System for Windows (SAS Institute Inc., Cary, NC, USA). Kaplan-Meier survival curves were generated using R Foundation for Statistical Computing, version 4.3.3 for Windows.

## Results

### Demographic Characteristics

A statistically significant difference was observed when comparing the four race/ethnicity groups based on each demographic characteristic considered (Table 1). The lowest average age (58 years, SD = 14.06) was in the NHO group, while the highest average age (67.3 years, SD = 13.42) was observed in the NHW group (P-value < 0.0001). The proportion of women was lower than that of men in all race/ethnicity groups except for NHB, where women comprised 50.7%. The lowest proportion of women was found among Hispanic patients at 44% (P-value = 0.0043). The largest proportion of NHB resided in counties within metropolitan areas with populations over a million (52.4%), while the smallest proportion lived in counties not adjacent to metropolitan areas (10.3%). Similar trends were observed for Hispanic and NHO patients. For NHW, the highest proportion was found in counties not adjacent to metropolitan areas (29.8%), while the lowest was in counties within metropolitan areas with populations below 250,000 (8.6%) (P-value < 0.0001). The highest proportion of married individuals was observed among NHW and Hispanics at 54%, while the lowest proportion was found among NHB patients at 35% (P-value < 0.0001). The majority of individuals across all race/ethnicity groups had a median household income between $40,000 and $69,999. The highest proportion of individuals with the lowest median household income (< $40,000) was among NHW patients, at 13.7% (P-value = 0.0034).

Table 1. Patient Demographic Characteristics at Diagnosis by Race/Ethnicity.

| Characteristics | Non-Hispanic Black | Non-Hispanic White | Hispanic All Races | Non-Hispanic Others | P-Value [2] |
|---|---|---|---|---|---|

| | (N = 2843) [1] | (N = 39549) [1] | (N = 300) [1] | (N = 271) [1] | |
|---|---|---|---|---|---|
| Age | 65.4 (13.61), 65.0 (56.0, 76.0) | 67.3 (13.42), 68.0 (58.0, 78.0) | 61.9 (16.20), 64.5 (50.0, 74.0) | 58.1 (14.06), 58.0 (50.0, 68.0) | <.0001 |
| Sex | | | | | |
| Female | 1442 (50.7) | 18759 (47.4) | 132 (44.0) | 127 (46.9) | 0.0043 |
| Male | 1401 (49.3) | 20790 (52.6) | 168 (56.0) | 144 (53.1) | |
| Geographic Location | | | | | |
| Populations over one million [3] | 1490 (52.4) | 11768 (29.8) | 97 (32.3) | 116 (42.8) | |
| Populations between 250,000 and one million [3] | 511 (18.0) | 4996 (12.6) | 64 (21.3) | 66 (24.4) | <.0001 |
| Populations under 250,000 [3] | 250 (8.8) | 3412 (8.6) | 39 (13.0) | 36 (13.3) | |
| Adjacent to metropolitan areas [4] | 298 (10.5) | 7573 (19.1) | 42 (14.0) | 18 (6.6) | |
| Not adjacent to metropolitan areas [4] | 294 (10.3) | 11800 (29.8) | 58 (19.3) | 35 (12.9) | |
| Marital status at diagnosis | | | | | |
| Divorced or Separated | 384 (13.5) | 4086 (10.3) | 28 (9.3) | 16 (5.9) | |
| Married | 995 (35.0) | 21359 (54.0) | 162 (54.0) | 146 (53.9) | <.0001 |
| Single (never married) | 694 (24.4) | 3267 (8.3) | 40 (13.3) | 17 (6.3) | |
| Unmarried/Domestic Partner/Unknown | 256 (9.0) | 2923 (7.4) | 30 (10.0) | 71 (26.2) | |
| Widowed | 514 (18.1) | 7914 (20.0) | 40 (13.3) | 21 (7.7) | |
| Median Household Income | | | | | |
| < $40,000 | 55 (1.9) | 5423 (13.7) | 24 (8.0) | 15 (5.5) | |
| $40,000 - $69,999 | 2630 (92.5) | 29827 (75.4) | 249 (83.0) | 224 (82.7) | 0.0034 |
| $70,000 - $99,999 | 147 (5.2) | 3885 (9.8) | 24 (8.0) | 30 (11.1) | |
| > $99,000 | 11 (0.4) | 414 (1.0) | 3 (1.0) | 2 (0.7) | |

[1] Frequency (percent) for a categorical variable, Mean (Standard Deviation), Median (First Quartile, Third Quartile) for a continous variable.

[2] Chi-square test for a categorical variable, CMH for an ordinal variable and ANOVA for a continuous variable.

[3] Counties in metropolitan areas.

[4] Nonmetropolitan counties.

## Tumor Characteristics-Diagnosis

Regarding cancer grades, the highest proportion of Grade III and IV diagnoses was observed among NHW patients at 15.8%, while the lowest was seen among NHO patients at 11.4 (P-value = 0.4286). In terms of cancer stage at diagnosis, the highest proportion of distant diagnoses was found among NHB patients at 17.8%, while the lowest was among NHO patients at 11.87% (P-value = 0.0001). For the total number of malignant cancers reported at diagnosis, Hispanic patients had the highest proportion of individuals with four or more malignant cancers at 2.7%, while NHO patients had the lowest, with none having more than three malignant cancers (P-value < 0.0007) (Table 2).

## Treatment Regimen and Outcomes

When comparing time from diagnosis to treatment by race/ethnicity, NHB had the longest average time (15.7 days), while NHO had the shortest (11.2 days) (P-value = 0.0481). Regarding chemotherapy treatment, the proportion of NHB patients receiving chemotherapy was the lowest (32.3%), while Hispanic patients had the highest proportion (37.7%) (P-value = 0.0014). A similar trend was observed for radiation treatment, with only 10.1% of NHB patients receiving radiation, compared to 13.3% of Hispanic patients (P-value < 0.0001). For surgery, NHB patients undergoing surgery was the lowest at 81.4%, while NHW patients had the highest proportion at 85.3% (P-value < 0.0001). The highest proportion of deaths due to colorectal cancer (CRC) occurred in NHB patients (42.7%), while the lowest was observed in NHO patients (22.9%) (P-value < 0.0001). When comparing unadjusted survival times, the median survival time was shortest for NHB patients (52 months) and longest for NHO patients (76 months) (P-value = 0.0006) (Table 2). In essence, NHB are at the bottom of the rung for prospects of treatment, mortality and longevity following diagnoses – all representing. remarkable evidence of health disparities.

Table 2. Patient Diagnoses, Treatments, and Outcomes by Race/Ethnicity.

| Characteristics | Non-Hispanic Black (N = 2843) [1] | Non-Hispanic White (N = 39549) [1] | Hispanic All Races (N = 300) [1] | Non-Hispanic Others (N = 271) [1] | P-Value [2] |
|---|---|---|---|---|---|
| Year of Diagnosis | | | | | |
| 2000- 2005 | 1011 (35.6) | 14065 (35.6) | 86 (28.7) | 52 (19.2) | |
| 2006- 2010 | 822 (28.9) | 11573 (29.3) | 92 (30.7) | 75 (27.7) | <.0001 |
| 2011- 2016 | 1010 (35.5) | 13911 (35.2) | 122 (40.7) | 144 (53.1) | |
| Cancer Grade | | | | | |
| Grade I | 235 (8.3) | 2451 (6.2) | 18 (6.0) | 37 (13.7) | |
| Grade II | 1705 (60.0) | 24435 (61.8) | 174 (58.0) | 146 (53.9) | 0.4286 |
| Grade III | 236 (8.3) | 4518 (11.4) | 34 (11.3) | 21 (7.7) | |
| Grade IV | 105 (3.7) | 1747 (4.4) | 12 (4.0) | 10 (3.7) | |
| Unknown | 562 (19.8) | 6398 (16.2) | 62 (20.7) | 57 (21.0) | |

| | | | | | |
|---|---|---|---|---|---|
| Cancer Stage at Diagnosis | | | | | |
| Localized | 916 (32.2) | 12667 (32.0) | 91 (30.3) | 132 (48.7) | |
| Regional | 647 (22.8) | 10241 (25.9) | 86 (28.7) | 59 (21.8) | 0.0001 |
| Distant | 505 (17.8) | 5804 (14.7) | 53 (17.7) | 32 (11.8) | |
| Clinical classification criteria not met or Unknown | 775 (27.3) | 10837 (27.4) | 70 (23.3) | 48 (17.7) | |
| Count of patient's total reported malignant cancers | | | | | |
| 1 | 1925 (67.7) | 26716 (67.6) | 201 (67.0) | 236 (87.1) | |
| 2 | 676 (23.8) | 9480 (24.0) | 73 (24.3) | 31 (11.4) | 0.0007 |
| 3 | 180 (6.3) | 2518 (6.4) | 18 (6.0) | 4 (1.5) | |
| 4 or more | 62 (2.2) | 835 (2.1) | 8 (2.7) | 0 (0.0) | |
| Time from Diagnosis to treatment in Days | 15.7 (26.63), 5.0 (0.0, 22.0) | 14.8 (25.03), 6.0 (0.0, 21.0) | 14.8 (29.54), 4.5 (0.0, 19.5) | 11.2 (20.75), 1.0 (0.0, 17.0) | 0.0481 |
| Chemotherapy | | | | | |
| Yes | 918 (32.3) | 14188 (35.9) | 113 (37.7) | 93 (34.3) | 0.0014 |
| No or Unknown | 1925 (67.7) | 25361 (64.1) | 187 (62.3) | 178 (65.7) | |
| Radiation | | | | | |
| Yes | 288 (10.1) | 5238 (13.2) | 40 (13.3) | 29 (10.7) | <.0001 |
| Refused, None or Unknown | 2555 (89.9) | 34311 (86.8) | 260 (86.7) | 242 (89.3) | |
| Surgery | | | | | |
| Yes | 2314 (81.4) | 33748 (85.3) | 252 (84.0) | 224 (82.7) | <.0001 |
| Not recommended, Refused or Unknown | 529 (18.6) | 5801 (14.7) | 48 (16.0) | 47 (17.3) | |
| Surgery Radiation Sequence | | | | | |
| Radiation prior to surgery | 120 (4.2) | 2396 (6.1) | 18 (6.0) | 17 (6.3) | |
| Radiation after surgery | 75 (2.6) | 1763 (4.5) | 10 (3.3) | 8 (3.0) | <.0001 |
| Radiation before and after surgery | 0 (0.0) | 55 (0.1) | 1 (0.3) | 0 (0.0) | |
| Surgery both before and after radiation | 4 (0.1) | 64 (0.2) | 1 (0.3) | 0 (0.0) | |
| No radiation and/or no surgery or Unknown | 2644 (93.0) | 35271 (89.2) | 270 (90.0) | 246 (90.8) | |
| Survival Time in Months | 70.6 (67.78), 52.0 (12.0, 112.0) | 75.6 (68.15), 62.0 (15.0, 120.0) | 71.8 (64.12), 62.0 (14.0, 110.5) | 81.3 (62.72), 76.0 (20.0, 125.0) | 0.0006 |

| | | | | | |
|---|---|---|---|---|---|
| Death Status | | | | | |
| Dead (attributable to CRC) | 1215 (42.7) | 15080 (38.1) | 108 (36.0) | 62 (22.9) | <.0001 |
| Alive or dead of other cause or missing COD | 1628 (57.3) | 24469 (61.9) | 192 (64.0) | 209 (77.1) | |

[1] Frequency (percent) for a categorical variable, Mean (Standard Deviation), Median (First Quartile, Third Quartile) for a continuous variable.

[2] Chi-square test for a categorical variable, CMH for an ordinal variable and ANOVA for a continuous variable.

## Unadjusted Comparison Using Kaplan-Meier Curve

When comparing five-year unadjusted survival rates due to colorectal cancer (CRC) using Kaplan-Meier curves by demographic characteristics, there was strong evidence of a statistically significant difference between the groups (Fig. 1). Geographic locations were categorized into five groups: Counties in metropolitan areas with populations over one million (PA1), Counties in metropolitan areas with populations between 250,000 and one million (PA2), Counties in metropolitan areas with populations under 250,000 (PA3), Counties adjacent to metropolitan areas (PA4), and Counties not adjacent to metropolitan areas (PA5). PA5 had the lowest survival rate, while PA1 had the highest (P-value < 0.0001). When comparing survival rates by race, NHB had the lowest survival rate, while NHO had the highest (P-value < 0.0001). Regarding marital status, widowed individuals had the lowest survival rate, while married individuals had the highest (P-value < 0.0001). When compared by median household income, those earning below $40,000 had the lowest survival rate, while those earning more than $99,000 had the highest (P-value = 0.0006).

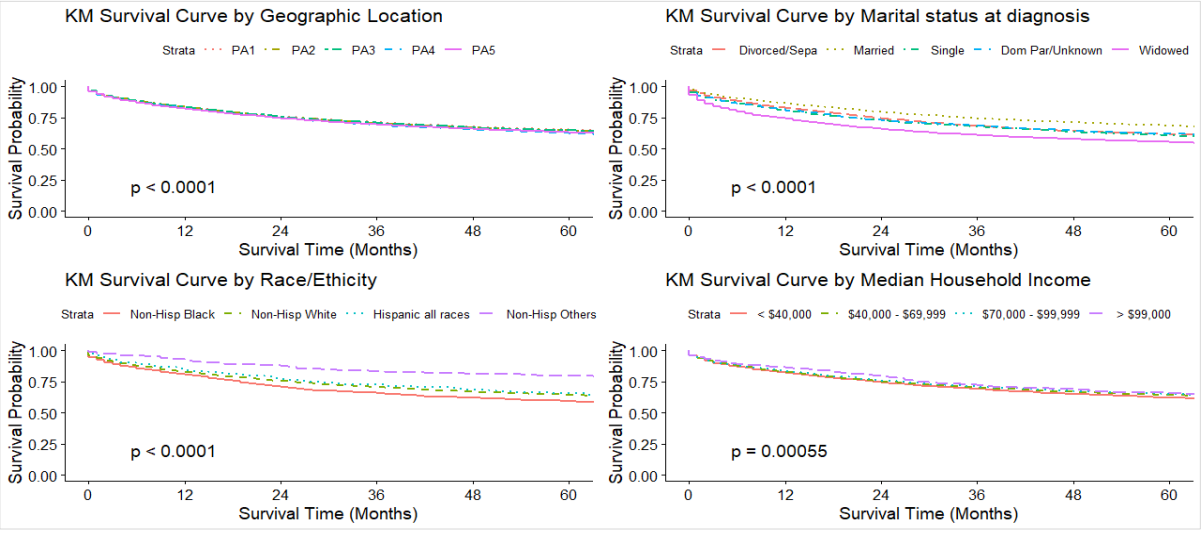


Fig. 1. Kaplan–Meier Five-Year Survival Curves by Demographic Characteristics

There was strong evidence of a statistically significant difference between the groups when comparing unadjusted five-year survival rates by tumor characteristics (diagnosis) (Fig. 2). In terms of cancer grade at diagnosis, Grades III and IV had the lowest survival rates, while Grade I had the highest

(P-value < 0.0001). Regarding cancer stage at diagnosis, distant stage had the lowest survival rate, while localized stage had the highest (P-value < 0.0001.

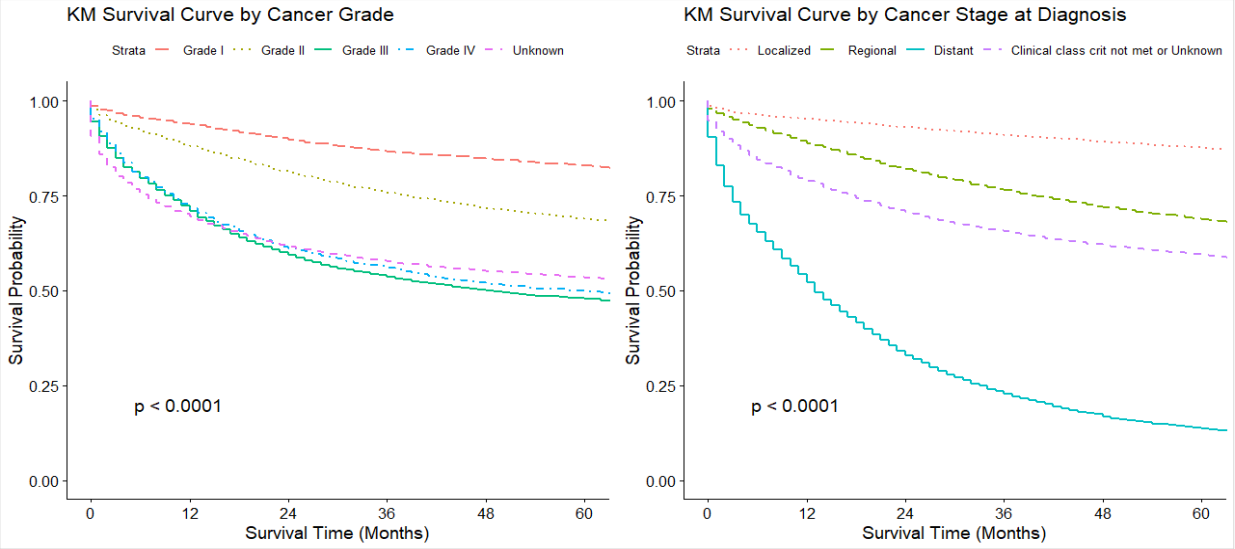


Fig. 2. Kaplan–Meier Five-Year Survival by Diagnosis Type

Finally, when comparing unadjusted five-year survival rates due to CRC by treatment regimen using Kaplan-Meier curves, there was strong evidence of a statistically significant difference between the groups (Fig. 3). The unadjusted treatment effects for patients who received chemotherapy or radiation were inconsistent, whereas those who underwent surgery had the highest survival rates compared to those who did not receive the treatments (all P-values < 0.0001). In terms of surgery-radiation sequence, individuals who received radiation after surgery had the lowest survival rate, while those who received radiation before and after surgery had the highest (P-value < 0.0001).

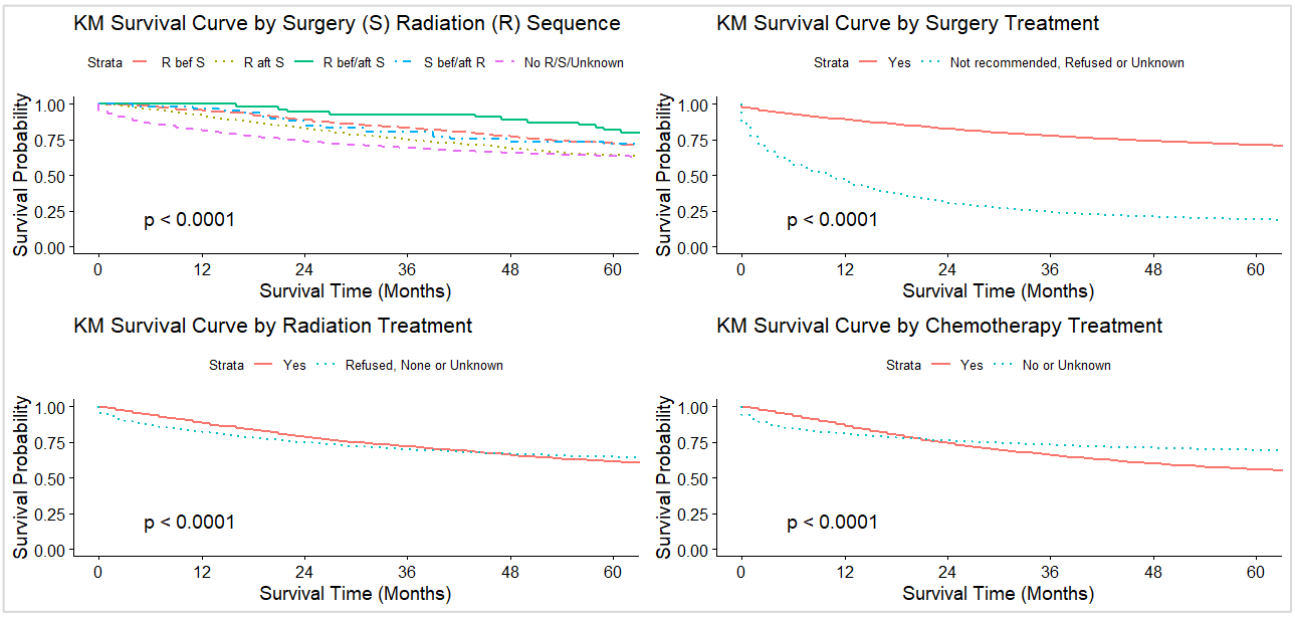

Fig. 3. Kaplan–Meier Five-Year Survival Curves by Treatment Regimen.

## Factors Associated with CRC Mortality: Cox Proportional Hazards Regression Analysis

As shown in Table 3, a 5-year increase in age was associated with a 13% higher risk of mortality from CRC, HR = 1.13 (95% CI: 1.12, 1.13). Male patients had a 12% higher risk of CRC mortality compared to females, HR = 1.12 (95% CI: 1.08, 1.15). Patients from counties not adjacent to metropolitan areas had a 13% higher risk, HR = 1.13 (95% CI: 1.09, 1.18), while those from adjacent counties had an 8% higher risk compared to patients from metropolitan areas with populations over a million, HR = 1.08 (95% CI: 1.03, 1.13). NHB patients had an 18% higher risk of CRC mortality, HR = 1.18 (95% CI: 1.11, 1.26), while NHO patients had a 23% lower risk, HR = 0.77 (95% CI: 0.60, 0.99), compared to NHW patients. Compared to married patients, those who were divorced or separated had a 21% higher risk, HR = 1.21 (95% CI: 1.15, 1.27); single patients had a 31% higher risk, HR = 1.31 (95% CI: 1.24, 1.38); patients with a domestic partner or unknown marital status had a 14% higher risk, HR = 1.14 (95% CI: 1.07, 1.21); and widowed patients had a 25% higher risk, HR = 1.25 (95% CI: 1.20, 1.31).

Patients with Grade II, III, IV, and unknown cancer grades had 57%, HR = 1.57 (95% CI: 1.44, 1.71), 144%, HR = 2.44 (95% CI: 2.23, 2.68), 149%, HR = 2.49 (95% CI: 2.24, 2.77), and 64%, HR = 1.64 (95% CI: 1.49, 1.80) higher risks of mortality, respectively, compared to those with Grade I cancer. Compared to patients diagnosed with local cancer stage, regional, distant, and clinical criteria not met or unknown cancer stages were associated with 165%, HR = 2.65 (95% CI: 2.51, 2.80), 853%, HR = 9.53 (95% CI: 8.99, 10.10), and 179%, HR = 2.79 (95% CI: 2.62, 2.96) higher risks, respectively.

The risk of CRC mortality was 233% higher, HR = 3.33 (95% CI: 3.18, 3.48), for patients where surgery was not recommended, refused, or unknown, compared to those who underwent surgery. Patients who received radiation only after surgery had a 74% higher risk of mortality, HR = 1.74 (95% CI: 1.02, 2.95), compared to those who received radiation both before and after surgery. While the five-year unadjusted Kaplan-Meier plots showed inconsistent outcomes for patients who received chemotherapy and radiation, the adjusted Cox regression model indicated improved outcomes for both treatments.

Table 3. Multiple Cox Regression Model of CRC Death adjusted for Demographic Characteristics, Diagnosis and Treatment.

| Characteristics | Hazard Ratio (95% CI) [1] | P-Value [2] | P-Value [3] |
|---|---|---|---|
| Age (Unit = 5 years) | 1.13 (1.12, 1.13) | | <.0001 |
| Sex (Ref = Female) | 1.12 (1.08, 1.15) | | <.0001 |
| Geographic Location (Ref = Over a million population) | | | <.0001 |
| 250,000 to one million population | 1.02 (0.97, 1.08) | 0.3513 | |
| Metropolitan with < 250 thousand population | 0.98 (0.92, 1.04) | 0.4681 | |

| | | | |
|---|---|---|---|
| Adjacent to a metropolitan | 1.08 (1.03, 1.13) | 0.0007 | |
| Not adjacent to a metropolitan | 1.13 (1.09, 1.18) | <.0001 | |
| Race/Ethnicity (Ref = Non-Hispanic White) | | | <.0001 |
| Non-Hispanic Black | 1.18 (1.11, 1.26) | <.0001 | |
| Hispanic (All Races) | 0.93 (0.77, 1.13) | 0.4835 | |
| Non-Hispanic Others | 0.77 (0.60, 0.99) | 0.0408 | |
| Marital status at diagnosis (Ref = Married (including common law)) | | | <.0001 |
| Divorced or Separated | 1.21 (1.15, 1.27) | <.0001 | |
| Single (never married) | 1.31 (1.24, 1.38) | <.0001 | |
| Domestic Partner or Unknown | 1.14 (1.07, 1.21) | <.0001 | |
| Widowed | 1.25 (1.20, 1.31) | <.0001 | |
| Year of Diagnosis (Ref = 2000 - 2005) | | | <.0001 |
| 2006- 2010 | 0.96 (0.91, 1.01) | 0.1048 | |
| 2011- 2016 | 0.87 (0.82, 0.91) | <.0001 | |
| Cancer Grade (Ref = Grade I) | | | <.0001 |
| Grade II | 1.57 (1.44, 1.71) | <.0001 | |
| Grade III | 2.44 (2.23, 2.68) | <.0001 | |
| Grade IV | 2.49 (2.24, 2.77) | <.0001 | |
| Unknown | 1.64 (1.49, 1.80) | <.0001 | |
| Cancer Stage at Diagnosis (Ref = Localized) | | | <.0001 |
| Reginal | 2.65 (2.51, 2.80) | <.0001 | |
| Distant | 9.53 (8.99, 10.10) | <.0001 | |
| Clinical classification criteria not met or Unknown | 2.79 (2.62, 2.96) | <.0001 | |
| Chemotherapy (Ref = Yes) | | | <.0001 |
| No or Unknown | 1.08 (1.04, 1.13) | <.0001 | |
| Radiation (Ref = Yes) | | | <.0001 |
| Refused, None or Unknown | 1.33 (1.22, 1.44) | <.0001 | |
| Surgery (Ref = Yes) | | | <.0001 |
| Not recommended, Refused or Unknown | 3.33 (3.18, 3.48) | <.0001 | |
| Surgery Radiation Sequence (Ref = Radiation before and after surgery) | | | <.0001 |
| Radiation prior to surgery | 1.68 (0.99, 2.85) | 0.0541 | |

| | | | |
|---|---|---|---|
| Radiation after surgery | 1.74 (1.02, 2.95) | 0.0406 | |
| Surgery both before and after radiation | 1.14 (0.57, 2.26) | 0.7095 | |
| No radiation and/or no surgery or Unknown | 1.09 (0.64, 1.86) | 0.7389 | |

[1] Estimates from Maximum Likelihood Method.

[2] P-Values from Wald's Chi-Square Test for each Category.

[3] P-Values from Wald's Chi-Square Test for the Co-Variables.

## Discussion

This study highlights significant disparities in colorectal cancer (CRC) survival rates in Kentucky, with poorer outcomes observed among NHB patients, rural residents, those with late-stage diagnoses, and those lacking surgical options. These findings underscore the need for targeted interventions to improve CRC survival in Kentucky by addressing these critical factors.

Our analysis of survival rates revealed significant geographic disparities, with patients in non-metropolitan areas experiencing worse outcomes. This aligns with Yao et al. (2017), which highlights the impact of rurality on healthcare access and cancer outcomes. Similarly, O'Shaughnessy et al. (2025) identified barriers such as low education levels, low socioeconomic status, and inadequate healthcare access due to rurality as contributors to poor CRC survival rates.

A study from Georgia by Tsai et al. (2024) found that rural patients had a 10% higher risk of CRC related death compared to those in non-rural areas. Comparisons across U.S. studies further support this trend, Henley et al. (2017) and Blake et al. (2017) reported that CRC mortality is consistently higher in rural areas, with rural patients facing a 16–22% increased risk of CRC death. These studies attribute poorer CRC outcomes in rural areas to barriers such as limited access to cancer screening, fewer treatment options, and transportation challenges. These geographic disparities highlight the urgent need for targeted public health initiatives that improve screening and treatment accessibility in underserved areas, where residents often face challenges related to transportation, health literacy, and economic instability.

Racial disparities in CRC outcomes are evident in our findings, particularly the lower survival rates among NHB patients compared to NHW patients. This aligns with research by Holowatyj et al. (2016), which found that NHB individuals experience higher CRC mortality than NHW individuals (HR = 1.35, CI: 1.26–1.45). A similar trend was reported by Cabral et al. (2023).

Additionally, Ramkumar et al. (2022) observed that racial and ethnic minorities, including Hispanic and NHB individuals, have higher CRC mortality rates, often due to residing in socioeconomically disadvantaged areas and experiencing disparities in cancer outcomes. These persistent inequities in access to timely diagnostic and treatment services may contribute to these disparities. For example, treatment delays and forgoing treatment are more common among NHB patients and those living in socioeconomically disadvantaged or rural areas (Nogueira et al., 2023; Carethers et al., 2020; Herb et al., 2022; Obrochta et al., 2021).

A recent study from Georgia also demonstrated the critical role of area-level socioeconomic status in CRC outcomes. Tsai et al. (2024) found that NHB patients living in low-education areas had a 20% higher risk of CRC-related death. This evidence underscores the need for targeted interventions to

improve survival rates among NHB populations and low-resource communities.

The study also emphasizes the importance of timely diagnosis and treatment in improving CRC outcomes. Delays in receiving care have been linked to advanced disease stages, which correlate with poorer prognoses. Chow et al. (2021) highlighted that certain demographic groups, including those with Medicaid insurance, face greater delays in specialist care following a CRC diagnosis. Our findings reinforce the need for healthcare systems to implement more efficient pathways for diagnosis and treatment, particularly for high-risk populations, to mitigate the adverse effects of delayed care.

In examining treatment modalities, we found that NHB patients had lower rates of chemotherapy and surgery compared to other racial groups, which may partially explain their poorer survival outcomes. Similar patterns have been documented in studies by Afshar et al. (2021), which identified disparities in treatment access and adherence among racial minorities. Such disparities not only reflect systemic inequalities within the healthcare system but also highlight the necessity for tailored treatment approaches that consider the unique barriers faced by different demographics.

Our findings on late-stage diagnosis and increased mortality risk align with existing literature. Walters et al. (2013) indicated that stage at diagnosis is a strong predictor of cancer mortality, potentially explaining differences in survival rates. Haggar et al. (2009) reported that patients diagnosed with distant-stage CRC had a 20-fold increased risk of CRC-related death. Similarly, Tsai et al. (2024) demonstrated that late-stage diagnosis was associated with a 16.5–22.5 times higher CRC mortality risk in five regions of Georgia, all characterized by lower socioeconomic status. Barriers contributing to this outcome may include the absence of early diagnosis or screening programs, limited access to adequate care, and a shortage of trained healthcare professionals, which may also explain disparities observed in Kentucky (Greiner et al., 2004; White et al., 2020).

## Study strengths and limitations

To the best of our knowledge, this is the first comprehensive study that examined various contributing factors demographic characteristics, tumor characteristics, and treatment modalities in relation to CRC mortality in Kentucky. This is particularly important because Kentucky has larger underserved areas with a shortage of health professionals (Griffith et al., 2020), which may lead to worse cancer outcomes. Thus, findings from our study are vital to inform culturally tailored interventions aimed at improving CRC survival through addressing the key factors. For example, education programs tailored to the NHB population may be needed for improving awareness of CRC risk. Other approaches, such as patient navigation programs, may also be beneficial for rural residents and those who are diagnosed with advanced stage of CRC.

Despite the significant contributions of this research, certain limitations should be acknowledged. The retrospective nature of the study relies on existing data, which may be subject to biases such as incomplete records or inaccuracies in coding. Additionally, while we focused on race/ethnicity and geographic location, other influential factors—such as comorbidities, lifestyle choices, and genetic predispositions—were not comprehensively analyzed. More importantly, several barriers associated with rural residency (e.g., lack of transportation and limited healthcare facilities) are strongly linked to poorer CRC survival; however, we were unable to evaluate these factors due to the absence of relevant data in the SEER

program. Future studies should aim to incorporate a broader range of factors to provide a more comprehensive understanding of CRC outcome disparities in Kentucky.

In conclusion, this study contributes to the limited body of evidence on the multifaceted factors driving CRC disparities in Kentucky. By examining the interplay of race, geography (rural residency), socioeconomic status, late diagnosis, and limited surgical options, we can better inform public health strategies aimed at improving cancer outcomes. These findings highlight the urgent need for targeted interventions, expanded access to care, and policy changes to reduce CRC-related health disparities. Furthermore, ongoing research is crucial to uncover the root causes of these disparities and develop tailored interventions that address the unique needs of diverse populations, ultimately fostering more equitable CRC outcomes.

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Conflicts of interest

The authors declare no conflict of interest.

## Authors' contributions

Jemal Gishe contributed to study conceptualization, methodology, formal analysis, original draft writing, and review and editing of the manuscript. Francis Pleban contributed to the development of the introduction, conducted the literature review, and participated in original draft writing and review and editing of the manuscript. Mohamed Kanu contributed to the development of the discussion section, original draft writing, and review and editing of the manuscript. Elizabeth Brown contributed to the review and editing of the manuscript. Meng-Han Tsai contributed to the methodology, original draft writing, and review and editing of the manuscript. All authors reviewed and approved the final version of the manuscript..

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