Early-Onset Colorectal Cancer Survival Differences and Potential Geographic Determinants Among Men and Women in Utah

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Abstract

By 2030, early-onset colorectal cancer (EOCRC) is expected to become the leading cancer-related cause of death for people age 20 to 49. To improve understanding of this phenomenon, we analyzed the geographic determinants of EOCRC in Utah by examining county-level incidence and mortality. We linked data from the Utah Population Database to the Utah Cancer Registry to identify residents (age 18–49) diagnosed with EOCRC between 2000 and 2020, and we used spatial empirical Bayes smoothing to determine county-level hotspots. We identified 1,867 EOCRC diagnoses (52.7% in male patients, 69.2% in non-Hispanic White patients). Ten counties (34%) were classified as hotspots, with high EOCRC incidence or mortality. Hotspot status was unrelated to incidence rates, but non-Hispanic ethnic-minority men (incidence rate ratio, 1.49; 95% CI, 1.15–1.91), Hispanic White men and women (incidence rate ratio, 2.24; 95% CI, 2.00–2.51), and Hispanic ethnic-minority men and women (incidence rate ratio, 4.59; 95% CI, 3.50–5.91) were more likely to be diagnosed with EOCRC. After adjustment for income and obesity,

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adults living in hotspots had a 31% higher hazard for death (HR, 1.31; 95% CI, 1.02–1.69). Survival was poorest for adults with a late-stage diagnosis living in hotspots (chi square (1) = 4.0; p = .045). Adults who were married or who had a life partner had a lower hazard for death than single adults (HR, 0.73; 95% CI, 0.58–0.92). The risk for EOCRC is elevated in 34% of Utah counties, warranting future research and interventions aimed at increasing screening and survival in the population age 18 to 49.

Early-onset colorectal cancer (EOCRC)—that is, colorectal cancer (CRC) diagnosed in individuals younger than age 50—is the second most common cancer and third leading cause of cancer mortality in people younger than age 50 in the United States[1]; by 2030, it is projected to become the leading cause of cancer-related death for those age 20 to 49.[2,3] Potentially masking the exponential surge in EOCRC incidence over the past 2 decades, CRC incidence in the over-55 age group has declined within the past decade because of an increase in screening rates.[4] Moreover, although overall CRC incidence in the United States increased by 1.27% each year between 2001 and 2007, and 3.0% annually between 2012 and 2017, the greatest average annual percentage change in incidence occurred among those age 20 to 24.[5] Because EOCRC is more likely than later-onset CRC to lead to poor outcomes, the U.S. Preventive Services Task Force now recommends the initiation of CRC screening at age 45 instead of age 50.[6]

Experts remain puzzled as to the cause of the alarming rise in EOCRC, but some potential factors include the Western-style diet, obesity, physical inactivity, socioeconomic status, and antibiotic use, especially during the early prenatal to adolescent period.[7,8] A family history of CRC and a genetic predisposition for the disease are known risk factors.[9] A Utah-focused study by Ochs-Balcom et al[10] found that, for patients of any age, having a first-, second-, or third-degree relative with EOCRC conferred a 2.64-fold, 1.96-fold, and 1.3-fold higher risk for developing CRC, respectively. When considering disease-specific risk factors for EOCRC, however, it is important to also examine the intersection of early-life exposures and geographic factors that may contribute to increased EOCRC incidence.[11–13]

Disparities in EOCRC incidence in the United States are exacerbated when geography is considered.[14] For example, disparities are apparent among residents of rural versus urban areas in both CRC risk factors and many social determinants of health (e.g., smoking, obesity, and health care access and utilization). Low rates of CRC screening have been associated with low socioeconomic status, low household income, lack of health insurance, and smoking, among other factors, likely contributing to the increasing disparity in EOCRC incidence in these populations.[14–16] Siegel et al[17] identified distinct geographic areas in the United States where CRC mortality is highest among those age 50 and older; these regions, as well as additional areas identified in other studies,[5,18] have been identified as EOCRC hotspots—that is, counties with high EOCRC mortality rates.[19] Specifically, African American men younger than age 50 with a diagnosis of advanced-stage CRC have a significantly higher EOCRC mortality burden and worse survival in hotspots, compared with White men in nonhotspot counties.[19] A complementary study, focused on EOCRC in women, found that a higher proportion of the population is African American in EOCRC hotspot counties than in nonhotspot counties.[18] These two novel studies provide insight

into the contributions of socioeconomic status and community-level factors to the EOCRC epidemic, yet a more granular investigation of factors not captured in these studies is warranted.

Factors contributing to EOCRC disparities include biology/genetics, diet/environment, preventive lifestyle behaviors, rural residence, environmental contamination, and access to high-quality health services, as well as social and political factors.[13,14,20–22] To better understand the etiology of EOCRC, this study sought to identify and characterize EOCRC hotspot counties in Utah by examining the variance in EOCRC incidence and survival that could be explained by personal- and county-level factors. We hypothesized that patients with EOCRC residing in hotspot counties in Utah would have significantly worse EOCRC survival compared with patients in coldspot counties. We also hypothesized that rurality and county-level factors would contribute to explaining EOCRC incidence and survival.

MATERIALS AND METHODS

Study Design and Data Sources

We used an ecologic design to examine EOCRC incidence and mortality for the period 2000 to 2020 in women and men age 18 to 49 residing in all 29 Utah counties. Cases and deaths specific for EOCRC were obtained from the Utah Cancer Registry and linked with data from the Utah Population Database. Death-certificate data were collected as available, as well as demographic information, residential histories, clinical characteristics, and survival information. County-level factors were obtained from the U.S. Census Bureau's 2019 American Community Survey, based on the preceding 5-year period (2015–2019),[23] and from the 2019 County Health Rankings.[24] This study was approved by the University of Utah Institutional Review Board and by the Resource for Genetic and Epidemiologic Research, the regulatory body overseeing usage of Utah Population Database data.

Study Population

We used the Utah Cancer Registry and SEER site codes (C18.0, C18.2–C18.9, C19.9, C20.9, C26.0) to identify men and women age 18 to 49 who received a primary diagnosis of CRC between the years 2000 and 2020 while living in Utah. A total of 1,867 patients with EOCRC were identified, of whom 52.7% were male, 69.2% non-Hispanic (NH) White, 21.7% Hispanic White, 3.6% NH multiracial, 3.2% Hispanic ethnic-minority (non-White), 1.0% NH Asian American, 0.5% NH Black, 0.5% NH Native Hawaiian/other Pacific Islander, and 0.2% NH American Indian-Alaska Native; 0.1% had unknown race and ethnicity. Eleven patients had residences in more than one county and thus could not be situated within a single county. The remaining 1,856 patients with EOCRC were included in the geospatial analyses.

Incidence and Mortality Rates

County-level incidence and mortality were determined by calculating crude rates, or the total number of EOCRC cases and deaths per county, between 2000 and 2020, divided by the total population at risk (i.e., the total population age 18–49 in each Utah county between 2000 and 2020, according to National Center for Health Statistics data)[25] and multiplied by

100,000. For mortality, we identified patients with EOCRC who had a CRC-specific primary cause of death according to the International Classification of Diseases, Tenth Revision (codes C18.0, C18.2–C18.9, C19.9, C20.9, C26.0). Age-adjusted rates were calculated for Utah overall, and within hotspot and coldspot counties, using the 2000 U.S. standard population. Age-adjusted rates could not be reliably estimated for specific counties because certain age categories had a small number of cases and deaths.

County-Level Factors

From the American Community Survey, we extracted for each county the percentages of the following: individuals who completed college, households with an income of less than $25,000, population by race and ethnicity, unemployed individuals, and individuals without health insurance (i.e., uninsured). From the County Health Rankings, we extracted for each county the percentage of individuals with access to exercise opportunities, obesity, and a current smoking status or physical inactivity; the number of primary care physicians per 100,000 persons; the number of violent crimes per 100,000 persons; and the food environment index (values range from 0 = worst to 10 = best). We also calculated the percentage of ZIP codes in each county designated as nonurban (rural) and urban using the 2010 Rural-Urban Commuting Areas ZIP code-based classifications. We aggregated the secondary Rural-Urban Commuting Areas codes into nonurban and urban.[26]

Geospatial Analysis: Hotspots for Incidence or Mortality

We conducted separate hotspot analyses for EOCRC incidence and mortality. We initially aimed to employ three geospatial methods to determine hotspots across Utah's 29 counties.[27] However, upon inspecting the data, we found that over 40% of EOCRC diagnoses and CRC-specific deaths were clustered in a single county, which limited our ability to test local and global indicators of spatial association. For this reason, we focused our analysis of hotspots using the spatial empirical Bayes smoothing method in GeoDa version 1.18.0,[28] while using ArcGIS Pro for mapping (Esri, Redlands, CA). The spatial empirical Bayes smoothing method calculates smoothed rates using the overall population size in each county as weights; thus, the rates of counties with smaller populations are adjusted more than those of counties with larger populations. We categorized the smoothed rates into quartiles and identified counties in the fourth quartile as hotspot counties for EOCRC incidence, mortality, or both. Counties with zero EOCRC cases or deaths were constrained from being classified as a hotspot for incidence or mortality.

Data Analysis

We tested bivariate differences between hotspot and coldspot counties for personal- and county-level factors using the chi square test for categorical factors and the independent t test for continuous factors. For continuous factors with evidence of non-normal distribution, we used the nonparametric Wilcoxon rank sum test; we also used this test for all county-level factors. A p value of less than .05 was used to infer significance. Survival curves were plotted using the Kaplan-Meier survival estimator. We calculated survival times by subtracting the date of death, or last follow-up visit, from the diagnosis date, transforming the result into months. A threshold of 240 months was applied to estimate the restricted mean survival.

We also tested multivariable models. We used Poisson regression to estimate incidence rate ratios and 95% CIs. We used the county-specific total population between 2000 and 2020, stratified by age groups and race and ethnicity, as the offset or exposure variable in the Poisson model and included county-level factors that reached significance in our bivariate analyses. We estimated four Poisson models and used a final model separately for men and women. Given the smaller number of events across racial and ethnic groups, we did not stratify results by race or ethnicity. We used Cox proportional hazards to estimate hazard ratios and their 95% CIs. We estimated four hazards models and used a final model separately for men and women. For our Cox proportional hazards models, we calculated a generalized R^2 following Allison's adaptation[29] of the Cox and Snell method (Rogers et al[19]). Data analyses were conducted in R Studio, version 1.3.1093 (R version 4.0.5).

RESULTS

Hotspot Characteristics

Between 2000 and 2020, the crude EOCRC incidence rate was 7.03 and the crude EOCRC-specific mortality rate was 1.93 per 100,000; the age-adjusted incidence and mortality rates across all counties were 8.38 and 2.31 per 100,000, respectively. Ten of Utah's 29 counties (34.48%) were classified as hotspots for EOCRC incidence, mortality, or both (Fig. 1). A list of all counties, their hotspot classifications, and their associated EOCRC rates is shown in Table 1. Average crude rates and empirical smoothed rates by hotspot classification are shown in Table 2. The age-adjusted incidence rates for hotspot and coldspot counties were 8.48 and 8.36 per 100,000, respectively; the age-adjusted mortality rates for hotspot and coldspot counties were 2.60 and 2.25 per 100,000, respectively.

We found no significant differences in the frequencies of incidence and mortality between hotspot and coldspot counties (Table 3). Mean survival was 7 months lower in hotspot-compared with coldspot counties (167 vs. 174 months), but this difference did not meet the significance threshold (p < .05; Table 3). Of the personal-level factors, more divorced, separated, or widowed adults (hotspot, 15.45% vs. coldspot, 11.66%) and fewer single or never-married adults (hotspot, 12.12% vs. coldspot, 17.43%) lived in hotspot counties. Of the county-level factors (Table 4), hotspot counties had a significantly lower percentage of adults with obesity than did coldspot counties (24.20% vs. 27.84%).

Multivariable Analyses

Hotspot classification was not significantly associated with EOCRC incidence (Table 5). However, age at diagnosis and race and ethnicity were associated with EOCRC incidence, regardless of hotspot classification. Adults age 40 to 49 had a 93% and 67% higher incidence, respectively, than adults age 18 to 29 (incidence rate ratio, 0.07; 95% CI, 0.06–0.08) and adults age 30 to 39 (incidence rate ratio, 0.33; 95% CI, 0.30–0.37). Non-Hispanic ethnic-minority adults (incidence rate ratio, 1.26; 95% CI, 1.03–1.53) and Hispanic White adults (incidence rate ratio, 2.24; 95% CI, 2.00–2.51) had a higher incidence than NH White adults, whereas Hispanic ethnic-minority adults had a more than threefold higher incidence than NH White adults (incidence rate ratio, 4.59; 95% CI, 3.50–5.91).

When we stratified the results by sex, the findings for men were similar to the overall model (Table 6). Among women, although we found no evidence of a difference in incidence between NH White and NH ethnic-minority women, we found a significant association between EOCRC incidence and the percentage of households with income below $25,000. Women living in counties where a greater percentage of households had incomes under $25,000 had a 3% higher incidence of EOCRC (incidence rate ratio, 1.03; 95% CI, 1.004–1.06).

Hotspot classification was significantly associated with EOCRC-specific mortality when accounting for stage at diagnosis (Table 7). Adults living in hotspot counties had a 31% higher hazard for EOCRC-specific death compared with those in coldspot counties (HR, 1.31; 95% CI, 1.02–1.69). Likewise, compared with localized tumors, the hazard for CRC-specific death was higher for regional (HR, 4.42; 95% CI, 3.10–6.30), distant/metastatic (HR, 40.41; 95% CI, 28.79–56.73), and unknown tumor stages (HR, 6.28; 95% CI, 3.54–11.16). When we examined differences in survival probabilities in individuals with late-stage diagnoses (i.e., distant/metastatic disease), adults living in hotspot counties had a lower probability of survival than did their counterparts in coldspot counties (chi square (1) = 4.0; p = .045; Fig. 2). We found no significant differences in late-stage survival between hotspot- and coldspot counties when stratified by sex (Fig. 2).

Marital status was also associated with EOCRC survival; adults who were married or who had a life partner had a 27% lower hazard for EOCRC-specific death compared with single or never-married adults (HR, 0.73; 95% CI, 0.58–0.92). Stratification of the models by sex revealed several differences from the overall model (Table 8). First, hotspot classification was not associated with EOCRC survival when examined separately for women and men. Second, marital status was not associated with EOCRC survival for women. Third, we saw a significant association between race and ethnicity and EOCRC survival among men. Non-Hispanic Native Hawaiian/other Pacific Islander men had a 265% higher hazard for CRC-specific death compared with NH White men (HR, 3.65; 95% CI, 1.16–11.52).

DISCUSSION

In this ecological study, we aimed to identify and characterize EOCRC hotspot counties in Utah by examining the variance in EOCRC incidence and survival that could be explained by personal- and county-level factors. Of the 1,856 patients included in our study, all age 18 to 49 and diagnosed with EOCRC between 2000 and 2020, those living in hotspot counties had notably worse survival, with a 31% higher hazard of CRC-specific mortality than their counterparts in coldspot counties. Outcome determinants were specific to patients diagnosed with CRC, which varied across counties; up to 34% of counties had higher incidence or mortality relative to other counties in Utah. Age and race and ethnicity were found to be predictive of CRC incidence rather than hotspot classification. When accounting for stage at diagnosis, individuals living in hotspots had worse EOCRC survival than those residing in coldspot counties.

Although fewer single or never-married adults resided in hotspot counties than divorced, separated, or widowed adults, they had similar survival rates; this could suggest that

formerly partnered individuals differ in risk in more nuanced ways than the never-married. The distribution of frequencies across marital status is consistent with a nationwide analysis of EOCRC hotspots across the United States.[19] Marital status is a known predictor of cancer-related prevention behavior and survival outcomes,[30] including CRC prevention and survival,[31,32] which may stem from spousal/social support.[33] In our study, hotspot counties had fewer adults with obesity than coldspot counties. These findings contrast with those of a prior nationwide analysis that found a higher percentage of adults with obesity in hotspot counties.[19] However, the percentage of adults with obesity at the county level was unassociated with EOCRC incidence and survival. Therefore, this county-level factor does not explain EOCRC outcomes in Utah.

Our findings demonstrate the impacts of known EOCRC determinants, as well as of unique findings, on the intersectionality of sex and socioeconomic status. Results of our Poisson regression analyses indicate that younger age groups (18–29 and 30–39) are less likely to be diagnosed with EOCRC compared with the older age group (40–49); these findings are consistent with those of prior U.S.-based studies reporting EOCRC incidence by age at diagnosis. For example, using SEER 18 data, Ansa et al[34] reported an EOCRC incidence rate of 2.3 per 100,000 (95% CI, 2.3–2.4) among individuals younger than age 40 and 22.5 per 100,000 (95% CI, 22.1–22.8) among those age 40 to 49. With respect to race and ethnicity, NH White adults in our study were less likely than ethnic-minority adults to be diagnosed with EOCRC. The Non-Hispanic Black population has long been known to have the highest burden of CRC and now also has a higher incidence of EOCRC.[35,36] As recommended by Muller et al,[14] population-level data analysis is warranted to determine whether the recent U.S. Preventive Services Task Force recommendation that the CRC screening age be lowered to 45 is affecting EOCRC incidence in populations that often face cancer disparities.

A finding that, to our knowledge, has not been previously identified is that women living in areas in which a greater proportion of households have incomes below $25,000 are more likely to be diagnosed with EOCRC. Prior research by Aloysius et al[37] has focused on the impacts of socioeconomic determinants of health (e.g., high school completion, poverty, household income, employment status, insurance status) on EOCRC survival. In increasing knowledge of the risk factors that may contribute to EOCRC disparities, our findings highlight the importance of addressing socioeconomic barriers across the continuum of EOCRC, from diagnosis to treatment.

When we stratified by stage at diagnosis (or when stage at diagnosis was similar between hotspot- and coldspot counties), we observed worse survival for patients with EOCRC living in hotspot counties, supporting our hypothesis that EOCRC survival, accounting for stage, would differ between hotspot- and coldspot counties. These survival differences are likely attributable to variations in socioeconomic and social factors. The confluence of insurance status, household income, and marital status significantly affects CRC diagnostic stage, treatment, and survival.[38–40] Numerous studies have confirmed that individuals with health insurance and those who are married are more likely to be diagnosed with CRC at an earlier stage, receive definitive treatment, and have longer survival,[38,39,41–43] whereas lower household income is associated with higher cancer-specific mortality.[40] Therefore,

interventions aimed at reducing CRC risk, or increasing rates of CRC screening, should focus on strengthening community resources to help overcome the structural barriers often associated with household income and insurance status.[44]

Among all determinants of EOCRC survival, stage at diagnosis explained the largest proportion of variance, regardless of hotspot classification. However, those living in hotspots were more likely to die sooner after receiving a late-stage EOCRC diagnosis than their counterparts living in coldspots. Future studies will be needed to identify causal contributors to this relationship. For example, those residing in hotspot counties who are diagnosed with late-stage EOCRC may fare worse because of differences in access to or quality of CRC treatment or treatment adherence. We agree with Wang et al[42] that these possibilities highlight a potential role of both individual-level sociodemographic variables and psychosocial characteristics, as well as county-level factors. This may be explained, in part, by factors such as travel time, distance, financial strain, and screening resistance, which merit further investigation.

Our multivariable analyses revealed that participants in our sample who were married or who had a life partner had a greater likelihood of EOCRC survival compared with adults who never married or were single, regardless if they lived in a hotspot- or coldspot county. These results are consistent with other literature highlighting the prognostic significance of marital status for cancer survival.[32,45] Even after controlling for disease stage, age, race, and surgery, the survival benefits associated with marital status are seen across multiple cancers—including breast, colorectal, esophageal, prostate, and other cancers with greater impact among men than women.[41,42] For CRC specifically, marriage is found to increase the odds of undergoing CRC screening and has a protective effect on survival[31,43,46]; research is limited, however, on the influence of marital status on survival for patients with EOCRC. Increased CRC survival among those who are married, have a life partner, or have other forms of high social support is likely attributable to psychosocial factors, including the availability of emotional support, assistance in monitoring health status, and aid in coping with treatment and shaping preventive health behaviors.[46–48] Moreover, individuals with established support systems often experience reduced cortisol levels associated with chronic psychological stress, thereby reducing various inflammatory markers that may provide the opportunity for precancerous cells to grow and flourish.[32,49,50] Although social support has a positive impact on health and health-promoting behaviors, more interventional research is warranted to focus on increasing the survival benefit associated with EOCRC for single or never-married individuals, and for patients with poor social relationships.

Limitations

Our study is not without limitations. First, very rural and small counties may not have been identified as hotspots because of a limited number of events/cases. However, a key strength of the Bayesian approach is that, for counties with very limited data, we can borrow strength from the observed data and derive reasonable posterior estimates for EOCRC incidence and mortality. In turn, we estimated smoothed mortality rates for counties with a small number of deaths (i.e., < 10), a limitation of our prior geospatial analyses.[19,51] Second, the limited number of events among underrepresented racial and ethnic groups included in our study

may have underestimated the true incidence and burden of disease within these populations. However, our study includes results for specific racial and ethnic groups to provide a foundation for future efforts to examine racial and ethnic differences in EOCRC survival among Utahans. Third, the use of each patient's residence at baseline did not permit us to account for time-varying changes in residence and associated-county characteristics. Yet by including county-level factors, we were able to advance understanding of how multiple levels within an ecological system contribute to both EOCRC risk and survival. Finally, we did not focus on individual cancer-prevention determinants (e.g., screening reluctance, family history of CRC, distance to care) or temporal changes relevant to CRC during our study timeframe (e.g., patient navigation, advancements in screening options and treatment).

CONCLUSION

Using spatial analytical methodology, we identified 10 Utah counties (34%) as hotspots with high EOCRC incidence, EOCRC mortality, or both. The incidence of EOCRC was elevated among NH ethnic-minority men, Hispanic White men and women, and Hispanic ethnic-minority men and women compared with their NH White counterparts. Among Utahan adults younger than age 50, residing in a hotspot county increased the risk of EOCRC mortality independent of late-stage diagnosis, whereas marital status was a key social determinant of survival. These findings provide insight for future research, policy changes, and interventions aimed at improving CRC survival and increasing CRC screening uptake in individuals younger than age 50.

ACKNOWLEDGMENT

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PRACTICAL APPLICATIONS

- Future researchers may use our spatial analytical method to identify state-specific geographic determinants of colorectal cancer incidence and mortality.

- The higher incidence of early-onset colorectal cancer (EOCRC) among non-Hispanic ethnic-minority men, as well as among Hispanic White and Hispanic ethnic-minority men and women, suggests that racial- and ethnicity-specific colorectal cancer screening strategies should be considered for patients younger than the previously recommended initiation age of 50.

- Although healthy behaviors are prominent among the White population in western states, EOCRC incidence is rising most rapidly in the West. Our Utah-focused study provides insight into personal- and county-level factors that may be contributing to disturbing trends in EOCRC incidence and mortality across the United States.

- Adults in Utah with a late-stage EOCRC diagnosis who live in the 10 counties we identified as EOCRC hotspots are at increased risk of dying, emphasizing the need for researchers and health care providers to better understand how to serve these communities.

- Marital status appears to be a key social determinant of EOCRC survival, suggesting an important role for social support. Further work is needed to better understand the role of support by family members and/or non-household members.
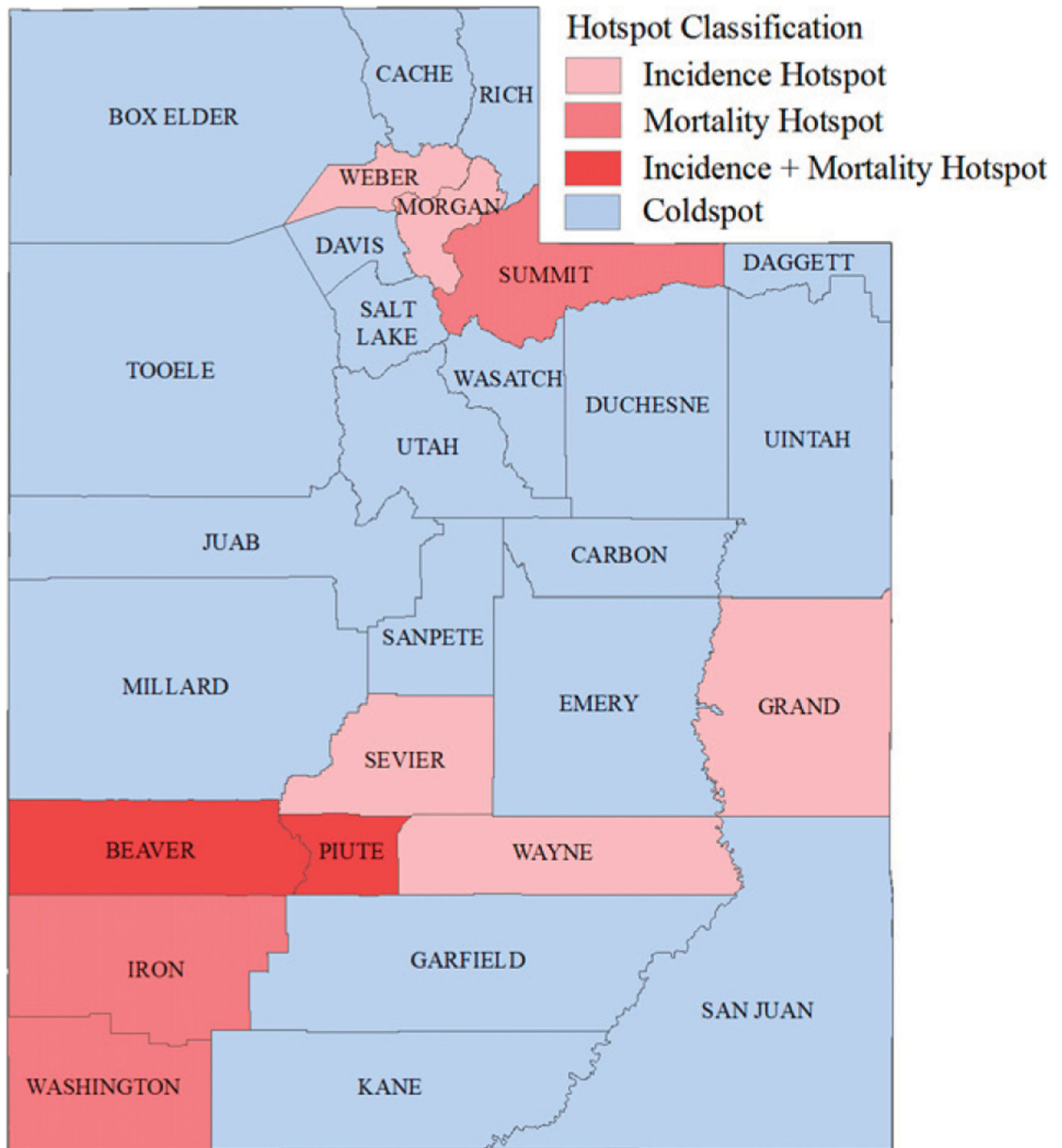
FIGURE 1.
Early-Onset Colorectal Cancer Hotspots for Incidence, Mortality, or Both: Incidence and Mortality Determined Using Spatial Empirical Bayes Smoothed Rates Quartiles for Utah Residents (Male and Female) Age 18 to 49
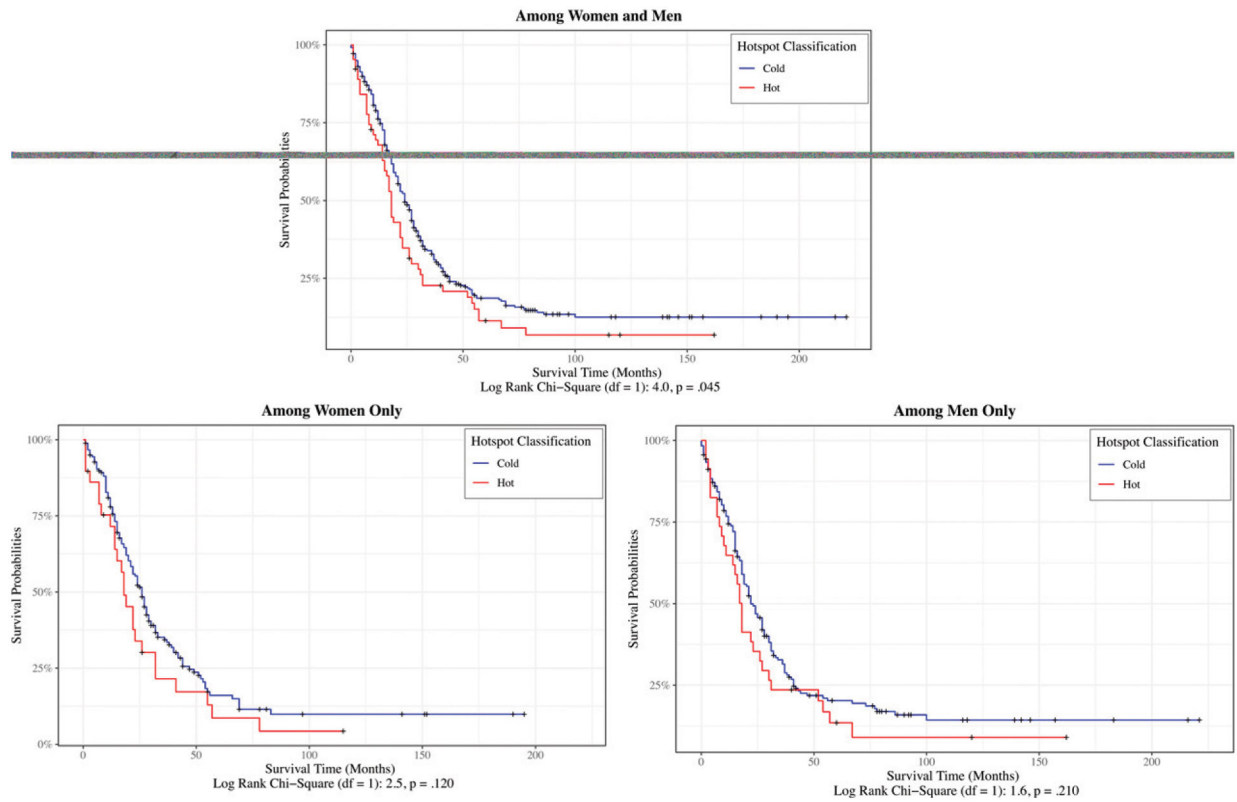
FIGURE 2.

Kaplan-Meier-Specific Survival Curves for Early-Onset Colorectal Cancer (Patients Age 18–49) With Late-Stage Diagnosis (Distant/Metastatic Disease) Among Women and Men, Women Only, and Men Only, by Hotspot-County Classification in Utah (2000–2020) Ticks represent censored data.

TABLE 1.

EOCRC Incidence and Mortality in Coldspot and Hotspot Counties and Associated Rates in Utah (2000–2020) Among Adults Age 18 to 49

County, Utah	Hotspot Classification[a]	EOCRC Incidence Rates per 100,000		EOCRC Mortality Rates per 100,000	
		Crude	Spatial Empirical Bayes Smoothed[b]	Crude	Spatial Empirical Bayes Smoothed[b]
Beaver	Hot	5.99	7.62	3.99	2.16
Box Elder	Cold	7.94	7.34	2.65	1.91
Cache	Cold	6.19	6.98	1.46	2.01
Carbon	Cold	6.85	6.31	1.14	1.49
Daggett	Cold	0.00	6.66	0.00	1.67
Davis	Cold	7.40	7.40	1.74	2.08
Duchesne	Cold	9.33	6.63	3.33	1.53
Emery	Cold	1.21	3.77	0.00	1.53
Garfield	Cold	5.49	6.26	0.00	2.09[c]
Grand	Hot	14.10	9.59	2.56	1.45
Iron	Hot	7.13	6.52	2.07	2.42
Juab	Cold	7.28	6.19	2.43	1.49
Kane	Cold	2.04	6.37	0.00	2.38[c]
Millard	Cold	8.52	6.67	1.06	1.87
Morgan	Hot	2.59	7.41	1.30	2.07
Piute	Hot	10.88	8.28	10.88	2.52
Rich	Cold	18.33	7.38	6.11	1.93
Salt Lake	Cold	7.34	7.27	2.14	2.05
San Juan	Cold	4.17	4.57	2.50	1.30
Sanpete	Cold	3.54	5.89	1.18	1.46
Sevier	Hot	9.23	7.45	2.46	1.94
Summit	Hot	7.11	7.38	1.18	2.14
Tooele	Cold	6.84	7.11	1.71	1.92
Uintah	Cold	4.91	5.38	1.40	1.67
Utah	Cold	6.19	6.41	1.47	1.67

County, Utah	Hotspot Classification[a]	EOCRC Incidence Rates per 100,000		EOCRC Mortality Rates per 100,000	
		Crude	Spatial Empirical Bayes Smoothed[b]	Crude	Spatial Empirical Bayes Smoothed[b]
Wasatch	Cold	10.66	7.33	2.78	1.99
Washington	Hot	6.54	6.56	2.67	2.42
Wayne	Hot	10.28	7.78	0.00	1.97
Weber	Hot	7.89	7.49	2.28	1.91

Abbreviation: EOCRC, early-onset colorectal cancer.

[a]Hotspot classification was determined by counties with spatial Empirical Bayes smoothed rates that fell in the top quartile for either incidence or mortality.

[b]Empirical Bayes smoothed rates were weighted by county population of women and men age 18 to 49, between 2000 and 2020.

[c]County had zero events and was constrained to coldspot regardless of the spatial Empirical Bayes smoothed rate.

TABLE 2.

EOCRC Incidence and Mortality in Utah (2000–2020) by Hotspot Classification Among Adults Age 18 to 49

	EOCRC Incidence Rates per 100,000			EOCRC Mortality Rates per 100,000		
	Crude	Spatial Empirical Bayes Smoothed		Crude	Spatial Empirical Bayes Smoothed	
Hotspot Classification[a]	Mean (SE)	Mean (SE)		Mean (SE)	Mean (SE)	
Coldspot (19 Counties)	6.54 (0.91)	6.42 (0.22)		1.74 (0.33)	1.79 (0.06)	
Hotspot (10 Counties)	8.17 (0.99)	7.61 (0.28)		2.94 (0.94)	2.10 (0.10)	

Abbreviation: EOCRC, early-onset colorectal cancer.

[a]Hotspot classification was determined by counties with spatial Empirical Bayes smoothed rates that fell in the top quartile for either incidence or mortality. Empirical Bayes smoothed rates were weighted by county population of women and men age 18 to 49, between 2000 and 2020.

TABLE 3.

Summary of Personal-Level Factors by Hotspot Classification for EOCRC in Utah (2000–2020) Among Adults Age 18 to 49

Patient Characteristic	Number (%)[b] or Mean (SE)	EOCRC Hotspot Counties[a]		p[c]
		Hotspot Number (%)[b] or Mean (SE)	Coldspot Number (%)[b] or Mean (SE)	
Total Cases	1,856 (100)	330 (17.78)	1,526 (82.22)	.890
Total Deaths	511 (100)	101 (19.77)	410 (80.23)	.945
Mean Survival (Months)[d]	172.27 (2.51)	166.51 (5.98)	173.59 (2.76)	.240
Age in Years, Mean	41.11 (0.16)	41.51 (0.38)	41.02 (0.17)	.130
Age at Diagnosis (%)				.118
18–29 Years	136 (7.33)	25 (7.58)	111 (7.27)	
30–39 Years	489 (26.35)	72 (21.82)	417 (27.33)	
40–49 Years	1,231 (66.33)	233 (70.61)	998 (65.40)	
Race and Ethnicity (%)				.101
NH American Indian-Alaska Native	*	*	*	
NH Asian	19 (1.02)	*	19 (1.25)	
NH Black	*	*	*	
NH Islander	*	*	*	
NH Multiple	64 (3.45)	11 (3.33)	53 (3.48)	
NH White	1,286 (69.33)	247 (74.85)	1,039 (68.13)	
Hispanic White	404 (21.78)	57 (17.27)	347 (22.75)	
Hispanic Ethnic Minority	59 (3.18)	13 (3.94)	46 (3.02)	
Sex (%)				.680
Female	878 (47.31)	160 (48.48)	718 (47.05)	
Male	978 (52.69)	170 (51.52)	808 (52.95)	
BMI (%)				.912
Underweight	32 (1.92)	*	25 (1.83)	
Normal	608 (36.41)	113 (37.29)	495 (36.21)	
Overweight	541 (32.40)	97 (32.01)	444 (32.48)	
Obese	489 (29.28)	86 (28.38)	403 (29.48)	

| Patient Characteristic | **EOCRC Hotspot Counties**[a] | | | |
	Number (%)[b] or Mean (SE)	Hotspot Number (%)[b] or Mean (SE)	Coldspot Number (%)[b] or Mean (SE)	p[c]
Marital Status (%)				.048
Single or Never Married	306 (16.49)	40 (12.12)	266 (17.43)	
Married or Life Partnered	1,279 (68.91)	231 (70.00)	1,048 (68.68)	
Divorced, Separated, or Widowed	229 (12.34)	51 (15.45)	178 (11.66)	
Unknown	42 (2.26)	*	34 (2.23)	
Tumor Side (%)[e]				.360
Right	415 (22.36)	67 (20.30)	348 (22.80)	
Left	1,441 (77.64)	263 (79.70)	1,178 (77.20)	
Stage (%)				.325
Local	679 (36.58)	121 (36.67)	558 (36.57)	
Regional	603 (32.50)	114 (34.55)	489 (32.04)	
Distant/Metastatic	424 (22.84)	64 (19.39)	360 (23.59)	
Unknown	150 (8.08)	31 (9.39)	119 (7.80)	
Year of Diagnosis (%)				.422
2000–2004	352 (18.97)	68 (20.61)	284 (18.61)	
2005–2009	408 (21.98)	77 (23.33)	331 (21.69)	
2010–2014	526 (29.09)	96 (29.09)	430 (28.18)	
2015–2019	570 (30.71)	89 (26.97)	481 (31.52)	

Abbreviations: EOCRC, early-onset colorectal cancer; NH, non-Hispanic; BMI, body mass index.

[a] Hotspot classification was determined by counties with spatial Empirical Bayes smoothed rates that fell in the top quartile for either incidence or mortality.

[b] In accordance with Utah Department of Health Data Suppression Guidelines, an asterisk (*) denotes counts of < 11 (see https://uofuhealth.utah.edu/utah-cancer-registry/research/).

[c] The p value was derived from the chi square test, independent *t* test, Wilcoxon rank sum test, or log-rank test, as appropriate.

[d] Calculated using the Kaplan-Meier method.

[e] Right was defined using International Classification of Diseases for Oncology, Third Edition (ICD-0–3) codes 180, 181, 182, 183, and 184, and left was defined using codes 185, 186, 187, 188, 189, 199, 209, and 260. In accordance with Utah Department of Health Data Suppression Guidelines, an asterisk (*) denotes counts of < 11 (see https://uofuhealth.utah.edu/utah-cancer-registry/research/).

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TABLE 4.

Summary of County-Level Factors by Hotspot Classification for EOCRC in Utah (2000–2020) Among Adults Age 18 to 49

County Characteristic	EOCRC Hotspot Counties [a]			
	Hotspot Mean (SE)	Coldspot Mean (SE)	P [b]	Spearman Correlation (ρ) [c]
Race and Ethnicity				
% NH American Indian-Alaska Native	1.07 (0.35)	3.78 (2.44)	.513	−0.13
% NH Asian	0.68 (0.20)	0.89 (0.22)	.818	−0.05
% NH Black	0.50 (0.10)	0.43 (0.11)	.313	0.20
% NH Islander	0.35 (0.16)	0.32 (0.08)	.765	−0.06
% NH Multiple	1.39 (0.24)	1.46 (0.20)	.731	−0.07
% NH White	87.14 (1.99)	83.62 (2.53)	.429	0.16
% NH Other	0.06 (0.03)	0.08 (0.02)	.543	−0.12
% Hispanic/Latinx	8.81 (1.52)	9.42 (0.89)	.668	−0.09
% Household Income < $25,000	18.10 (2.11)	15.75 (1.36)	.247	0.23
% Completed College	25.78 (3.13)	21.71 (1.82)	.211	0.24
% Unemployed	3.75 (0.44)	4.13 (0.51)	.875	−0.03
% Uninsured	12.23 (1.39)	10.56 (1.01)	.377	0.17
% Access to Exercise Opportunities	71.70 (8.29)	67.26 (4.73)	.383	0.17
Food Environment Index [d]	7.16 (0.46)	7.12 (0.27)	.783	0.06
% Obesity	24.20 (1.50)	27.84 (0.67)	.024	−0.43
% Smoking	9.50 (0.43)	9.89 (0.44)	.623	−0.10
% Physical Inactivity	17.70 (1.18)	18.47 (0.65)	.562	−0.11
PCP per 100,000 Persons	63.90 (12.74)	44.56 (4.21)	.314	0.20
Violent crimes per 100,000 Persons	163.25 (32.04)	166.17 (27.35)	.978	0.01
% Nonurban (Rural)	66.92 (14.90)	63.73 (10.31)	1.0	0.00

Abbreviations: EOCRC, early-onset colorectal cancer; NH, non-Hispanic; PCP, primary care physician.

[a]Hotspot classification was determined by counties with spatial Empirical Bayes smoothed rates that fell in the top quartile for either incidence or mortality.

[b]The p value was derived from the Wilcoxon rank sum test.

[c] Spearman correlation with being classified as a hotspot for EOCRC incidence or mortality.

[d] Indicator of access to healthy foods, from 0 = worst to 10 = best.

TABLE 5.

Multivariate Poisson Regression Models for EOCRC Incidence in Utah (2000–2020) Among Adults Age 18 to 49

Predictors	EOCRC Incidence			
	Model 1 IRR [95% CI]	Model 2 IRR [95% CI]	Model 3 IRR [95% CI]	Model 4 IRR [95% CI]
Hotspot Classification [a]				
Coldspot	Ref	Ref	Ref	Ref
Hotspot	1.08 [0.96–1.21]	1.03 [0.91–1.15]	1.06 [0.94–1.19]	1.01 [0.89–1.15]
Age at Diagnosis				
18–29 Years		**0.07 [0.06–0.08]**	**0.07 [0.06–0.08]**	**0.07 [0.06–0.08]**
30–39 Years		**0.34 [0.30–0.37]**	**0.33 [0.30–0.37]**	**0.33 [0.30–0.37]**
40–49 Years		Ref	Ref	Ref
Race and Ethnicity (%) [b]				
NH White			Ref	Ref
NH Ethnic Minority			**1.26 [1.03–1.53]**	**1.26 [1.03–1.53]**
Hispanic White			**2.24 [2.00–2.50]**	**2.24 [2.00–2.51]**
Hispanic Ethnic Minority			**4.58 [3.49–5.89]**	**4.59 [3.50–5.91]**
% Household Income < $25,000				1.02 [1.00–1.03]
% Obesity				1.00 [0.98–1.02]

Abbreviations: EOCRC, early-onset colorectal cancer; IRR, incidence rate ratio; NH, non-Hispanic.

Bold indicates significance at p < .05.

[a] Hotspot classification was determined by counties with spatial Empirical Bayes smoothed rates that fell in the top quartile for either incidence or mortality.

[b] Racial and ethnic categories were based on the available population breakdown on U.S. Centers for Disease Control and Prevention WONDER online database bridged-race population estimates, which did not include a multiracial category, and which grouped Asian Americans and Pacific Islanders.

TABLE 6.

Multivariate Poisson Regression Models for EOCRC Incidence in Utah (2000–2020) Stratified by Sex Among Adults Age 18 to 49

| | EOCRC Incidence | | | |
| | Women | | Men | |
Predictors	Number of Cases	IRR [95% CI]	Number of Cases	IRR [95% CI]
Hotspot Classification [a]				
Coldspot	718 (81.78)	Ref	808 (82.62)	Ref
Hotspot	160 (18.22)	0.97 [0.80–1.18]	170 (17.38)	1.08 [0.90–1.31]
Age at Diagnosis				
18–29 Years	62 (7.06)	**0.07 [0.05–0.08]**	74 (7.57)	**0.08 [0.06–0.09]**
30–39 Years	221 (25.17)	**0.32 [0.28–0.38]**	268 (27.40)	**0.35 [0.30–0.41]**
40–49 Years	595 (67.77)	Ref	636 (65.03)	Ref
Race andEthnicity (%) [b]				
NH White	612 (69.78)	Ref	674 (68.92)	Ref
NH Ethnic Minority	41 (4.68)	1.09 [0.78–1.48]	65 (6.65)	**1.49 [1.15–1.91]**
Hispanic White	195 (22.23)	**2.43 [2.06–2.85]**	209 (21.37)	**2.19 [1.87–2.55]**
Hispanic Ethnic Minority	29 (3.31)	**5.67 [3.82–8.07]**	30 (3.07)	**4.17 [2.83–5.90]**
% Household Income < $25,000	NA	**1.03 [1.004–1.06]**	NA	1.02 [0.99–1.04]
% Obesity	NA	1.01 [0.98–1.04]	NA	0.99 [0.96–1.01]

Abbreviations: EOCRC, early-onset colorectal cancer; IRR, incidence rate ratio; NH, non-Hispanic; NA, not available.

Bold indicates significance at p < .05.

[a] Hotspot classification was determined by counties with spatial Empirical Bayes smoothed rates that fell in the top quartile for either incidence or mortality.

[b] Racial and ethnic categories were based on the available population breakdown on U.S. Centers for Disease Control and Prevention WONDER online database bridged-race population estimates, which did not include a multiracial category, and which grouped Asian Americans and Pacific Islanders.

TABLE 7.

Multivariate Cox Proportional Hazards Regression Models for EOCRC-Specific Deaths in Utah (2000–2020) Among Adults Age 18 to 49

Predictors	Number of Deaths[a]	EOCRC Survival			
		Model 1 HR [95% CI]	Model 2 HR [95% CI]	Model 3 HR [95% CI]	Model 4 HR [95% CI]
Hotspot Classification [b]					
Coldspot	410 (80.23)	Ref	Ref	Ref	Ref
Hotspot	101 (19.77)	1.14 [0.92–1.41]	**1.38 [1.11–1.73]**	**1.39 [1.11–1.74]**	**1.31 [1.02–1.69]**
Age at Diagnosis					
18–29 Years	37 (7.24)		1.40 [1.00–1.98]	1.28 [0.90–1.81]	1.28 [0.90–1.81]
30–39 Years	131 (25.64)		1.14 [0.93–1.40]	1.12 [0.91–1.37]	1.12 [0.91–1.38]
40–49 Years	343 (67.12)		Ref	Ref	Ref
Race and Ethnicity					
NH American Indian-Alaska Native	*		0.26 [0.04–1.89]	0.26 [0.04–1.88]	0.20 [0.03–1.53]
NH Asian	*		1.18 [0.44–3.16]	1.23 [0.46–3.30]	1.23 [0.46–3.31]
NH Black	*		0.38 [0.12–1.20]	0.40 [0.13–1.28]	0.40 [0.13–1.26]
NH Islander	*		2.06 [0.66–6.45]	2.13 [0.68–6.67]	2.13 [0.68–6.66]
NH Multiple	15 (2.94)		0.85 [0.51–1.42]	0.82 [0.49–1.38]	0.82 [0.49–1.38]
NH White	370 (72.41)		Ref	Ref	Ref
Hispanic White	100 (19.57)		0.90 [0.72–1.13]	0.90 [0.72–1.12]	0.91 [0.72–1.13]
Hispanic Ethnic Minority	15 (2.94)		1.11 [0.66–1.86]	1.07 [0.64–1.80]	1.09 [0.65–1.84]
Stage					
Local	40 (7.83)		Ref	Ref	Ref
Regional	132 (25.83)		**4.44 [3.11–6.32]**	**4.42 [3.10–6.30]**	**4.42 [3.10–6.30]**
Distant/Metastatic	322 (63.01)		**40.88 [29.14–57.34]**	**40.31 [28.72–56.58]**	**40.41 [28.79–56.73]**
Unknown	17 (3.33)		**6.36 [3.58–11.29]**	**6.28 [3.54–11.16]**	**6.32 [3.56–11.23]**
Marital Status					
Single or Never Married	97 (18.98)			Ref	Ref
Married or Life Partner	335 (65.56)			**0.73 [0.58–0.92]**	**0.73 [0.58–0.92]**
Divorced, Separated, or Widowed	77 (15.07)			0.82 [0.60–1.12]	0.81 [0.59–1.11]

| Predictors | Number of Deaths [a] | EOCRC Survival | | | |
		Model 1 HR [95% CI]	Model 2 HR [95% CI]	Model 3 HR [95% CI]	Model 4 HR [95% CI]
Unknown	*			**0.18 [0.04–0.72]**	**0.18 [0.04–0.72]**
% Household Income < $25,000	NA				1.02 [0.98–1.05]
% Obesity	NA				1.00 [0.97–1.03]
Generalized R^2		0.07%	37.32%	37.81%	37.84%

Abbreviations: EOCRC, early-onset colorectal cancer; NH, non-Hispanic; NA, not available.

Bold indicates statistical significance (p < .05).

[a] In accordance with Utah Department of Health Data Suppression Guidelines, an asterisk (*) denotes counts of < 11 (see https://uofuhealth.utah.edu/utah-cancer-registry/research/).

[b] Hotspot classification was determined by counties with spatial Empirical Bayes smoothed rates that fell in the top quartile for either incidence or mortality.

TABLE 8.

Multivariate Cox Proportional Hazards Regression Models for EOCRC-Specific Deaths in Utah (2000–2020) Among Women and Men Age 18 to 49

	EOCRC Survival			
	Women		Men	
Predictors	Number of Deaths [a]	HR [95% CI]	Number of Deaths [a]	HR [95% CI]
Hotspot Classification [b]				
Coldspot	188 (80.34)	Ref	222 (80.14)	Ref
Hotspot	46 (19.66)	1.39 [0.96–2.01]	55 (19.86)	1.29 [0.88–1.88]
Age at Diagnosis				
18–29 Years	15 (6.41)	1.19 [0.69–2.05]	22 (7.94)	1.26 [0.79–2.02]
30–39 Years	55 (23.50)	1.18 [0.86–1.62]	76 (27.44)	1.08 [0.82–1.43]
40–49 Years	164 (70.09)	Ref	179 (64.62)	Ref
Race and Ethnicity				
NH American Indian-Alaska Native	*	0.72 [0.08–6.13]	*	—
NH Asian	*	0.86 [0.21–3.47]	*	2.02 [0.50–8.22]
NH Black	*	0.53 [0.06–4.33]	*	0.31 [0.07–1.26]
NH Islander	*	—	*	**3.65 [1.16–11.52]**
NH Multiple	*	1.27 [0.59–2.73]	*	0.59 [0.29–1.22]
NH White	172 (73.50)	Ref	198 (71.48)	Ref
Hispanic White	44 (18.80)	0.95 [0.68–1.33]	56 (20.22)	0.87 [0.64–1.18]
Hispanic Ethnic Minority	*	0.93 [0.43–2.02]	*	1.34 [0.66–2.75]
Stage				
Local	13 (5.56)	Ref	27 (9.75)	Ref
Regional	58 (24.79)	6.60 [3.61–12.07]	74 (26.71)	**3.30 [2.12–5.14]**
Distant/Metastatic	155 (66.24)	**68.41 [37.99–123.18]**	167 (60.29)	**29.63 [19.48–45.09]**
Unknown	*	**9.85 [4.04–24.04]**	*	**4.70 [2.18–10.13]**
Marital Status				
Single or Never Married	38 (16.24)	Ref	59	Ref
Married or Life Partner	154 (65.81)	0.92 [0.64, 1.32]	181	**0.65 [0.47, 0.88]**

EOCRC Survival

Predictors	Women		Men	
	Number of Deaths[a]	HR [95% CI]	Number of Deaths[a]	HR [95% CI]
Divorced, Separated, or Widowed	40 (17.09)	0.78 [0.49, 1.23]	37	**1.01 [0.64, 1.59]**
Unknown	*	0.41 [0.09, 1.88]	*	-
% Household Income < $25,000	NA	1.04 [1.00, 1.09]	NA	0.99 [0.94, 1.04]
% Obesity	NA	0.99 [0.94, 1.04]	NA	1.00 [0.96, 1.05]
Generalized R^2	40.83%		36.44%	

Abbreviations: EOCRC, early-onset colorectal cancer; NH, non-Hispanic; NA, not available.

Bold indicates significance at p < .05.

[a] In accordance with Utah Department of Health Data Suppression Guidelines, an asterisk (*) denotes counts of < 11 (see https://uofuhealth.utah.edu/utah-cancer-registry/research/).

[b] Hotspot classification was determined by counties with spatial Empirical Bayes smoothed rates that fell in the top quartile for either incidence or mortality.