

Ethnicity, socioeconomic status, income inequality, and colorectal cancer outcomes: Evidence from the 4C2 Collaboration

Running title: Colorectal cancer in the four corner states

Precis: This study is an example of how NCI-designated cancer centers can work together to address the concerns in their catchment areas. In the southern Rocky Mountain region, colorectal cancer outcomes is influenced by income inequality and low socioeconomic status.

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ABSTRACT

Purpose. National Cancer Institute (NCI)-Designated Cancer Centers are required to assess and address the needs of their catchments. In rural regions, catchment areas are vast, populations small, and infrastructure for data capture limited, making analyses of cancer patterns challenging.

Methods. The four NCI-Designated Comprehensive Cancer Centers in the southern Rocky Mountain region formed the Four Corners Collaboration (4C2) to address these challenges. Colorectal cancer (CRC) was identified as a disease site where disparities exist. The 4C2 leaders examined how geographic and sociodemographic characteristics were correlated to stage at diagnosis and survival in the region and compared those relationships to a sample from the Surveillance, Epidemiology, and End Results (SEER) Program.

Results. In 4C2, Hispanics were more likely to live in socioeconomically disadvantaged areas relative to their counterparts in the SEER program. These residency patterns were positively correlated with later stage diagnosis and higher mortality. Living in an area with high income inequality was positively associated with mortality for Non-Hispanic whites in 4C2. In SEER, Hispanics had a slightly higher likelihood of distant stage disease and disadvantaged socioeconomic status was associated with poor survival.

Conclusion. CRC interventions in 4C2 will target socioeconomically disadvantaged areas, especially those with higher income inequality, to improve outcomes among Hispanics and Non-Hispanic whites. The collaboration demonstrates how bringing NCI-Designated Cancer Centers together to identify and address common population catchment issues provides opportunity for pooled analyses of small, but important populations, and thus capitalize on synergies among researchers to reduce cancer disparities.

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INTRODUCTION

National Cancer Institute (NCI)-Designated Cancer Centers are tasked with understanding and improving cancer outcomes in their catchment areas[1], defined by where patients live and where the center conducts research and outreach to reduce the cancer burden, risks, and inequities. Centers focus their efforts on cancers that have a high incidence or mortality, and on cancers that display group level disparities in risk or outcomes. Groups are defined by race/ethnicity, geography (urban, rural, frontier), environmental or occupational exposures (e.g., mining, oil and gas extraction), socioeconomic conditions (e.g., uninsured, poverty), and cancer-related risk factors (e.g., smoking, low vaccine rates)[1].

In response to the NCI's mandate to address cancer burden within their catchment area, four NCI-Designated Comprehensive Cancer Centers in the southern Rocky Mountain region formed the Four Corners Collaborative (4C2) to address cancer problems common to the region. The collaboration comprises the University of Arizona Cancer Center, the University of Colorado Cancer Center, the University of New Mexico Comprehensive Cancer Center, and the Huntsman Cancer Institute at the University of Utah. These centers define their catchment area as their respective states and share attributes such as environmental exposures (e.g., sun exposure, mining), rural and frontier regions, and a high percentage of Hispanics relative to the United States (U.S.) population[2]. Leaders from each center's Cancer Prevention and Control and Community Outreach and Engagement programs meet regularly to discuss ways in which to reduce the cancer burden in their catchment areas using synergistic approaches.

The 4C2 leaders identified invasive colorectal cancer (CRC) as an important problem, disproportionately affecting Hispanics, rural, and low-income communities[3]. This paper describes the patterns of CRC diagnosis and survival within the region compared to a national

sample. Our goal is to better understand how the 4C2 region differs from patterns observed nationally. Our study is an example of how NCI-Designated Cancer Centers can collaboratively address common problems, and demonstrates the importance of understanding regional patterns in diagnosis and outcomes.

CATCHMENT ASSESSMENT

Fig. 1 includes maps of the region, with a star indicating the location of the NCI-Designated Comprehensive Cancer Centers. These maps demonstrate the overlap between rural and frontier residency, low socioeconomic status and income inequality as defined by the Gini Index[4], and Hispanic ethnicity. Much of Utah, Colorado, and New Mexico is sparsely populated, and with many residents experiencing poverty. While New Mexico has the fourth-highest percentage of residents experiencing poverty in the nation based on median household income[5], Utah and Colorado are among the wealthiest states, but their wealth is concentrated in a few urban counties or rural counties with a robust outdoor recreation industry. Arizona, Colorado, and New Mexico also have many counties with high levels of income inequality when comparing the wealthiest to the poorest households[6]. Each of the 4C2 states have Health Professional Shortage Areas (HPSA) with approximately 41% and 60% of Arizona and Utah, respectively, designated as an HPSA[7]. Hispanics are the largest ethnic minority in 4C2, ranging from 14% in Utah to 49% in New Mexico compared to 18% of the U.S. population[2].

CRC is the second most common cancer for men and women[8] and the third leading cause of cancer death among Hispanics[9]. Given the constellation of ecological characteristics in 4C2 (geographic regions comprising rural and frontier areas, range of socioeconomic status and income inequality), we organize our analysis around individual race/ethnicity (Non-Hispanic white (NHW) and Hispanic) while controlling for county-level variables (socioeconomic status,

income inequality, and rurality). We hypothesized that differences in stage and mortality for NHWs and Hispanics in 4C2 compared to national patterns may be related to the characteristics of where the population resides. We compared our findings to those observed in a sample extracted from the NCI Surveillance, Epidemiology, and End Results (SEER) Program, excluding Utah and New Mexico which are part of the 4C2. This comparison demonstrates the importance of understanding local and regional catchment areas that can differ from patterns observed in national datasets.

METHODS

Data

Population-based cancer incidence and survival data were obtained from three sources: the Arizona Cancer Registry[10], the Colorado Central Cancer Registry[11], and the SEER Program[12]. Data from New Mexico and Utah were extracted from the SEER-18 data and aggregated with the Arizona and Colorado registries to create the 4C2 sample. The remaining SEER registries include Atlanta, greater California, Connecticut, Detroit, greater Georgia, rural Georgia, Hawaii, Iowa, Kentucky, Los Angeles, Louisiana, New Jersey, San Francisco-Oakland, San Jose-Monterey, Seattle-Puget Sound, and the Alaska Native Tumor Registry[13]. This collection of registries (except Alaskan Native Tumor Registry) comprise the comparison population ('SEER-15' henceforth). The SEER Program compiles county-level attributes measuring rurality and socioeconomic status (SES)[14].

Study sample

The sample comprised patients diagnosed with invasive CRC between 2006 and 2010 with vital status through 2016 in 4C2 (N=29,031) and SEER-15 (N=183,862) using primary site

codes from the *International Classification of Diseases for Oncology, 3rd Edition* for colon (C18.0-C18.9 and C26.0, N=20,684 4C2; N=130,889 SEER-15) and rectum (C19.9 and C20.9, N=8,347 4C2; N=52,973 SEER-15). We restrict the sample to Hispanic White and NHW (excluded N=2,023 4C2; N=39,010 SEER-15). We also excluded patients with unknown county of residence (N=53 4C2; N=19 SEER-15), those for whom invasive CRC was not their first primary malignancy (N=5,258 4C2; N=36,863 SEER-15), and those identified by death certificate or autopsy (N=609 4C2; 1,526 SEER-15). The study sample comprised 21,389 patients from 4C2 and 113,177 patients from SEER-15.

Outcomes

The primary outcomes were distant or unknown stage at diagnosis and all-cause survival. We estimated cancer-specific survival as a secondary outcome. Stage at diagnosis was defined using the SEER summary stage (local, regional, distant, unknown). Tumors are categorized by registries as ‘unknown’ when there is insufficient information to assign a stage. These cases are often believed to be distant stage tumors where a further clinical work-up is deemed unnecessary or alternatively, the data are missing[15]. In our sample, nearly 73% of patients diagnosed with unknown stage tumors had no evidence of cancer-directed treatment in the registry.

All-cause mortality was calculated as months from date of diagnosis to date of last known follow-up, date of death, or end of the study period (December 31, 2016). We also estimated cancer-specific mortality, where follow-up time was censored at date of death for patients who died of a cause other than CRC (**Appendix Table 1**). Patients with unknown cause of death were excluded from cancer-specific survival analyses (N=631 4C2; 645 SEER-15).

Variables

Demographic variables were age at diagnosis (<50 years, 50+ years), sex (male, female), and race/ethnicity (Hispanic, NHW). Age groups reflect the ages below and above the recommended screening age of 50 years[16]. Rurality was defined using the 2013 Rural Urban Continuum Codes and 2010 Census population density estimates to classify county of residence at diagnosis as frontier (RUCC codes 4-9 with <7 persons per square mile), rural (RUCC codes 4-9 with 7+ persons per square mile), or urban (RUCC codes 1-3).

The SEER socioeconomic status measure, the Yost Index, reflects an index score derived from county-level information from the 2006 through 2010 American Community Survey 5-year estimates on educational attainment, proportion working class, median household income, median rent and house values, proportion of residents living 150% below the poverty level, and proportion unemployed[4]. The Yost Index has face validity[17, 18] and prior studies report that the Yost Index has an independent association with breast cancer survival after adjustment for individual and institutional characteristics, suggesting that area level characteristics have an important role in predicting mortality[19]. Counties were categorized as ‘disadvantaged’ if the county socioeconomic index value was below the U.S. median and as ‘advantaged’ if at or above the U.S. median.

The Gini Index (0 to 1) measures income inequality in a county where a value closer to one indicates a greater income inequality[20]. We obtained county-level Gini Index scores from the 2006 through 2010 American Community Survey 5-year estimates[4], then categorized a county ‘high income inequality’ if the county Gini Index was above the median Gini Index nationally (median = 0.429) and ‘low income inequality’ if the county Gini Index was at or below the median national Gini Index.

Because the dataset does not contain patient-level information on cancer screening and risk factors, we used data from the 2006 through 2010 Behavioral Risk Factor Surveillance System (BRFSS) surveys to generate prevalence estimates for whether 4C2 residents met colorectal cancer screening guidelines, if they were current smokers, obese, or physically inactive and compared them to national estimates, excluding the 4C2[21]. We also generated estimates for Hispanic Whites and NHWs. These findings provide context for our study and are reported in the Appendix.

Statistical Analyses

Chi-square tests were used to evaluate statistically significant differences for bivariate analyses within and between 4C2 and SEER-15. Adjusted logistic regression models were used to estimate the likelihood of a distant stage and unknown stage at diagnosis. Standard errors of models that include area-level explanatory variables were adjusted for clustering to account for correlations between observations within a county using the generalized estimation equation method. For ease of interpretation, we report marginal effects along with 95% confidence intervals and p-values. Marginal effects are interpreted as average differences in the probability of distant or unknown stage at diagnosis between a category (for example, Hispanic ethnicity) and its reference (NHW). Adjusted Cox proportional hazards models were used to estimate the hazard ratios for mortality. The proportional hazards assumption was evaluated using scaled Schoenfeld residuals correlated with time. All statistical tests were two-sided, with a *P* value of less than 0.05 considered statistically significant except in Table 1 where the sample sizes are large, and we focus on differences with a *P* value of less than 0.01. Analyses were conducted using SAS 9.4 software (SAS Institute, Cary, N.C.).

RESULTS

Descriptive Characteristics

Table 1 reports descriptive characteristics of patients in 4C2 (columns 1-3) and SEER-15 (columns 4-6); each sample is stratified by race/ethnicity. There is a higher percentage of Hispanics in 4C2 relative to the SEER-15 regions (18% versus 12%). Age and sex distributions are similar between 4C2 and SEER-15. In 4C2, a lower proportion of Hispanics live in urban counties (80%) compared to NHWs (87%). This difference becomes striking when compared to the SEER-15 sample where nearly 99% of Hispanics live in urban areas. In contrast, NHWs in SEER-15 are more likely to live in rural areas. A higher percentage of Hispanics live in frontier counties, which are common to 4C2, than NHWs (8% versus 4%).

The overall percentage of patients who live in socioeconomically advantaged counties is similar between 4C2 and SEER-15. However, residence in a socioeconomically advantaged county varies by race/ethnicity in all samples. Fewer Hispanics live in socioeconomically advantaged counties than NHWs in 4C2 (71% compared to 85%) whereas approximately 95% of Hispanics live in socioeconomically advantaged counties in SEER-15, which is a higher percentage than observed in NHWs (83%). A slightly higher percentage of NHWs live in socioeconomically advantaged counties in 4C2 relative to NHWs in SEER-15 (85% versus 83%).

A greater percentage of Hispanics live in counties of higher income inequality than NHWs in 4C2 (77% versus 67%), but less so than Hispanics in SEER-15 (88%). A greater percentage of Hispanics in 4C2 live in socioeconomically disadvantaged and high income inequality counties (21%) than NHWs (11%), whereas a greater percentage of NHWs live in socioeconomically advantaged and low income inequality counties (29%) than Hispanics (16%), suggesting a greater degree of ethnic segregation into high and low socioeconomic counties as

well as a larger gap between poor and rich within socioeconomically advantaged counties for NHWs. In contrast, Hispanics in SEER-15 tend to live in socioeconomically advantaged counties with higher income inequality relative to NHWs and a greater percentage of NHWs live in socioeconomically disadvantaged counties with high income inequality relative to Hispanics (15% versus 5%). Most (80%) Hispanics in SEER-15 come from the California registry where all counties are overwhelmingly urban and socioeconomically advantaged.

A slightly higher percentage of Hispanics with distant or unknown stage disease are in 4C2 compared to SEER-15. NHWs in 4C2 also have a higher percentage of unknown stage disease compared to NHWs in SEER-15. Fewer NHWs are diagnosed with distant stage disease than Hispanics, but the difference is small (1 to 3 percentage points). All-cause survival is slightly lower in 4C2 with 53% surviving 5 years compared to 56% 5-year survival in SEER-15. Hispanics and NHWs have similar survival in 4C2 whereas Hispanics in SEER-15 are more likely to survive 5 years than their NHW counterparts. Mortality patterns are similar when considering 5-year cancer-specific survival, although fewer Hispanics survive 5 years compared to NHWs in 4C2 (63% compared to 65%).

Stage at diagnosis

Table 2 reports the likelihood of a distant stage CRC at diagnosis, adjusting for sociodemographic and geographic characteristic. Hispanics in 4C2 are 2 percentage points more likely to be diagnosed with distant stage disease than NHWs (column 1, $p < 0.05$). Patients aged 50 years and older are less likely to be diagnosed with distant stage disease than younger patients, regardless of sample (ranging from about 5 to 7 percentage points, $p < 0.001$). Hispanics in SEER-15 are slightly more (1 percentage point, $p < 0.05$) likely to be diagnosed with distant

stage CRC whereas NHWs in frontier areas are 7.1 percentage points less likely to be diagnosed with distant stage CRC ($p<0.01$).

Table 3 reports the likelihood of an unknown stage CRC at diagnosis. In 4C2, Hispanics and rural residents are less likely to be diagnosed with unknown stage (1 and 2 percentage points, $p<0.05$, respectively). Older age is associated with an increased risk of unknown stage disease for NHWs (3 percentage points, $p<0.001$). High income inequality, regardless of whether in a socioeconomically advantaged or disadvantaged county, was associated with a 4 to 5 percentage point increase in the likelihood of unknown stage disease for Hispanics ($p<0.05$). Residence in a disadvantaged socioeconomic county or a socioeconomically advantaged county with high income inequality was associated with a 4 to 5 percentage point increase in unknown stage disease for NHWs ($p<0.001$). We do not observe a difference in the likelihood of unknown stage disease by ethnicity, socioeconomic status, or income inequality in SEER-15. Frontier residence is associated with a 6 percentage point increased risk of unknown stage disease ($p<0.001$).

Mortality

Table 4 reports hazard ratios and 95% confidence intervals for all-cause mortality, controlling for covariates. Hispanics are less likely to die in five years relative to NHWs in SEER-15 (HR=0.91; 95% C.I. 0.89 to 0.94), but do not have a survival advantage in 4C2. In stratified samples, residing in counties with higher income inequality, regardless of socioeconomic advantage of the county, is a risk factor for all-cause mortality for NHWs in 4C2 (socioeconomically advantaged HR=1.12; 95% CI=1.06 to 1.18 and socioeconomically disadvantaged HR=1.28; 95% CI=1.15 to 1.41). Coefficients were much smaller in the SEER-15 sample. These relationships remain in estimations for cancer-specific mortality (**Appendix**

Table A1). Additionally, NHWs residing in frontier counties of 4C2 are more likely to die from cancer than those in urban counties (HR=1.23; 95% CI 1.08 to 1.41).

Data from BRFSS surveys provide context for these findings. **Appendix Table A2** reports that rural residents in 4C2 were less likely to be screened for colorectal cancer relative urban residents in 4C2 and compared to residents outside 4C2. Hispanics in 4C2 who lived in urban areas were more likely to smoke than Hispanics outside 4C2 but were also less likely to be obese and physically inactive. Fewer NHWs living in rural areas within 4C2 met colorectal cancer screening guidelines but were less likely to smoke and be obese and more likely to be physically active than their counterparts outside 4C2. These findings suggest that the absence of screening for residents in 4C2 and smoking prevalence for Hispanics in urban areas may partially explain some of the differences we observe.

DISCUSSION

We compared sample characteristics, disease stage at diagnosis, and mortality in 4C2 and SEER-15 for patients with invasive CRC, stratified by Hispanics and NHWs. By comparing national and regional samples, we can determine whether national patterns are mirrored at the regional level where NCI-Designated Cancer Centers are intended to have the greatest impact on their catchment areas. In our study, Hispanics in 4C2 are more likely to live in socioeconomically disadvantaged counties than Hispanics in SEER-15, but with less income inequality. Similarly, compared to NHWs in 4C2, Hispanics are more likely to live in socioeconomically disadvantaged and greater income inequality counties. These socioeconomic patterns influenced cancer stage at diagnosis and survival differently by race/ethnicity.

An expansive literature supports that income inequality leads to adverse health outcomes, including late stage CRC[22, 23]. Given our findings, 4C2 leaders could target their interventions, particularly those related to screening and access to care, to socioeconomically disadvantaged counties with high levels of income inequality where many Hispanics reside. Fig. 1 (panel b) identifies areas of high priority for targeting prevention and control resources. However, the findings also highlight a deeper societal imperative to reduce income inequities where cancer centers must play a broader role to reduce disparities. Cancer centers can embrace this challenge through participating in statewide efforts in developing of state cancer plans and coordinating with other grassroots organizations to reduce the causes of disparities such as equal opportunity to education, employment, housing, insurance coverage, and healthy environments. Most NCI-designated centers have or are creating Community Outreach and Engagement organizational structures that can facilitate these efforts.

We also find a lower likelihood of distant stage at diagnosis for patients aged 50 years and older. We hypothesize this relationship is due to guidelines that recommend routine screening for colorectal cancer starting at age 50[16]. Few individuals younger than age 50 receive screening and thus likely symptomatic and later stage at diagnosis. In contrast, there is also a higher likelihood of unknown stage for patients age 50 and older. One possible explanation is that older patients may be less likely to undergo full diagnostic procedures required to assign a stage.

Our study has limitations. First, we have limited information on patients' screening behavior and no information on distance to an NCI-Designated Cancer Center. Both conditions impact whether a cancer is detected, staged, and treated expediently and with newer therapies that may have a survival benefit[24]. However, prevalence estimates generated from the

individual-level BRFSS data provide context for some of our area-based and group-level findings, suggesting that lower screening rates and higher smoking prevalence may partially explain the differences we observe. Second, we do not have individual measures of the social determinants of health, which are likely correlated with income inequality and are poorly correlated with area level measures such as the Yost Index[25, 26]. Last, we do not have data on where patients were treated. Treating institutions may have heavy caseloads, resulting in diagnostic delays and poor follow-up to abnormal CRC screening. A call to action for the 4C2 leaders is to enhance data collection on population health needs, specifically targeting those areas identified as having disparate outcomes. These data can be further enhanced by robust linkages within and across the 4C2 and their cancer registries.

Our study highlights the importance of understanding the needs of a catchment area, which may deviate from national trends regarding race/ethnicity, residency, and socioeconomic status. Deviation from national trends, as we found, may be more prominent when examining under-represented groups such as Hispanics and rural residents. Approaches to reducing disparities need to be tailored to the conditions and patterns within a region, and based on our findings, the societal conditions contributing to income inequality.

The 4C2 collaboration allows for catchment area analyses and transference of ideas and approaches to addressing disparities that would not otherwise occur. The collaboration also allows for enhanced data collection on small, but important population health needs. As a unified group of NCI-designated centers, the 4C2 can advocate for registries to report individual data on comorbidities, risk factors, and screening behavior that can be accomplished with linked data. Both Colorado and Utah have All Payer Claims Data that can fill these gaps.

Given our findings, future interventions for CRC prevention, early detection, and treatment will focus on socioeconomically disadvantaged and high income inequality counties. Leveraging the resources with community outreach and engagement, leaders in 4C2 will focus on risk factors associated with living in these counties that can contribute to higher mortality for both Hispanics and NHWs. The greater challenge of reducing societal inequality will require extensive collaboration with leaders beyond the cancer centers and beyond cancer, but a necessary challenge for centers to embrace. There are many actions cancer centers can take to address the how these disparities impact cancer outcomes. We list just a few. First, centers can address financial burden for the patients they serve by screening for financial burden throughout cancer treatment and connect patients to services that will help address their needs including food and housing insecurity. Second, cancer centers can support community organizations that serve low-income patients diagnosed with cancer. These organizations often provide unrestricted grants for basic needs outside of treatment. Centers must do more than refer patients to these organizations but must also provide financial support to the organizations. Many health care systems can donate to charitable organizations and/or co-sponsor fund raising events that support patients. These two steps are especially critical in Health Professional Shortage Areas where patients have few resources. Third, cancer centers can support local and national policies that provide access to coverage and that remove co-pays for screening services. Fourth, cancer centers can engage in research that delivers preventive services (screening, smoking cessation) in the community. These steps will reduce financial barriers for patients and stabilize local safety net organizations.

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Table 1 Descriptive statistics, invasive colorectal cancer diagnosed between 2006 and 2010, 4C2 and SEER-15, N (%)

Characteristics	4C2			SEER-15			P
	Overall (N=21,389)	Hispanic Whites (N=3,745)	Non-Hispanic Whites (N=17,644)	Overall (N=113,177)	Hispanic Whites (N=13,287)	Non-Hispanic Whites (N=99,890)	
Race/ethnicity							*
Hispanic white	3,745 (17.5)	N/A	N/A	13,287 (11.7)	N/A	N/A	
Non-Hispanic white	17,644 (82.5)	N/A	N/A	99,890 (88.3)	N/A	N/A	
Age, years							†, §, ¶
<50	2,414 (11.3)	610 (16.3)	1,804 (10.2)	12,603 (11.1)	2,512 (18.9)	10,091 (10.1)	
50+	18,975 (88.7)	3,135 (83.7)	15,840 (89.8)	100,574 (88.9)	10,775 (81.1)	89,799 (89.9)	
Sex							§, ¶
Male	11,226 (52.5)	2,048 (54.7)	9,178 (52.0)	58,515 (51.7)	7,197 (54.2)	51,318 (51.4)	
Female	10,163 (47.5)	1,697 (45.3)	8,466 (48.0)	54,662 (48.3)	6,090 (45.8)	48,572 (48.6)	
Rurality							*, †, ‡, §, ¶
Urban	18,356 (85.8)	3,005 (80.2)	15,351 (87.0)	97,891 (86.5)	13,085 (98.5)	84,806 (84.9)	
Rural	2,068 (9.7)	437 (11.7)	1,631 (9.2)	15,286 (13.5)	193 (1.5)	14,984 (15.0)	
Frontier	965 (4.5)	303 (8.1)	662 (3.8)	^	^	^	
Socioeconomic Status							*, †, ‡, §, ¶
Advantaged	17,742 (82.9)	2,675 (71.4)	15,067 (85.4)	95,349 (84.2)	12,642 (95.1)	82,707 (82.8)	
Disadvantaged	3,647 (17.1)	1,070 (28.6)	2,577 (14.6)	17,828 (15.8)	645 (4.9)	17,183 (17.2)	
Gini Index							*, †, ‡, §, ¶
Low inequality	6,694 (31.3)	876 (23.4)	5,818 (33.0)	28,884 (25.5)	1,601 (12.0)	27,283 (27.3)	
High inequality	14,695 (68.7)	2,869 (76.6)	11,826 (67.0)	84,293 (74.5)	11,686 (88.0)	72,607 (72.7)	
SES*Gini Index							*, †, ‡, §, ¶
Advantaged SES, Low Inequality	5,706 (26.7)	601 (16.0)	5,105 (28.9)	26,390 (23.3)	1,572 (11.8)	24,818 (24.8)	
Advantaged SES, High Inequality	12,036 (56.3)	2,074 (55.4)	9,962 (56.5)	68,959 (60.9)	11,070 (83.3)	57,889 (58.0)	
Disadvantaged SES, Low Inequality	988 (4.6)	275 (7.3)	713 (4.0)	2,494 (2.2)	29 (0.2)	2,465 (2.5)	
Disadvantaged SES, High Inequality	2,659 (12.4)	795 (21.2)	1,864 (10.6)	15,334 (13.5)	616 (4.6)	14,718 (14.7)	
Stage							*, †, ‡, §, ¶
Localized	8,525 (39.9)	1,403 (37.5)	7,122 (40.4)	44,991 (39.8)	5,013 (37.7)	39,978 (40.0)	
Regional	7,134 (33.4)	1,286 (34.3)	5,848 (33.1)	40,619 (35.9)	4,877 (36.7)	35,742 (35.8)	
Distant	4,222 (19.7)	817 (21.8)	3,405 (19.3)	22,499 (19.9)	2,756 (20.7)	19,743 (19.8)	
Unknown	1,508 (7.1)	239 (6.4)	1,269 (7.2)	5,068 (4.5)	641 (4.8)	4,427 (4.4)	

5-year survival

All-cause	52.9	52.6	53.0	55.6	59.1	55.1	*, †, ‡, ¶
Cancer-specific	65.1	63.4	65.4	68.4	68.8	68.4	*, †, ‡

Notes: 4C2 states are Arizona, Colorado, New Mexico and Utah. SEER-15 includes SEER-18 registries exclusive of New Mexico, Utah, and the Alaskan Native Tumor Registry. Percentages shown in parentheses and for observed all-cause and cancer-specific survival. ^Data are combined with rural due to small sample size of Hispanics in frontier counties of SEER-15. P-values computed using Chi-square test for proportions and log rank test for survival with comparisons denoted as: *Overall difference between 4C2 and SEER-15; †Difference between 4C2 and SEER-15 among Hispanic whites; ‡Difference between 4C2 and SEER-15 among Non-Hispanic whites; §Difference between Hispanic and Non-Hispanic Whites within 4C2; ¶Difference between Hispanic and Non-Hispanic Whites within SEER-15. Only differences significant at p<0.01 are shown.

Table 2 Likelihood of distant stage diagnosis among invasive colorectal cancer patients with known stage, 4C2 and SEER-15, 2006-2010, marginal effects (95% confidence intervals)

Independent Variables	4C2			SEER-15		
	Overall (N=19,881)	Hispanic Whites (N=3,506)	Non-Hispanic Whites (N=16,375)	Overall (N=108,109)	Hispanic Whites (N=12,646)	Non-Hispanic Whites (N=95,463)
Race/ethnicity						
Hispanic white	0.020* (0.005 to 0.036)	N/A	N/A	0.007* (0.0004 to 0.014)	N/A	N/A
Non-Hispanic white	Reference			Reference		
Age, years						
<50	Reference	Reference	Reference	Reference	Reference	Reference
50+	-0.062*** (-0.087 to -0.037)	-0.047* (-0.084 to -0.010)	-0.066*** (-0.094 to -0.038)	-0.055*** (-0.063 to -0.047)	-0.074*** (-0.089 to -0.060)	-0.051*** (-0.059 to -0.042)
Sex						
Male	-0.003 (-0.016 to 0.010)	0.007 (-0.016 to 0.029)	-0.004 (-0.019 to 0.010)	-0.001 (-0.006 to 0.003)	-0.002 (-0.014 to 0.010)	-0.001 (-0.006 to 0.004)
Female	Reference	Reference	Reference	Reference	Reference	Reference
Rurality						
Urban	Reference	Reference	Reference	Reference	Reference	Reference
Rural	0.006 (-0.016 to 0.027)	-0.029 (-0.079 to 0.020)	0.013 (-0.013 to 0.039)	0.009 (-0.0001 to 0.018)	0.013 (-0.053 to 0.078)	0.009 (-0.0005 to 0.019)
Frontier	0.019 (-0.012 to 0.049)	-0.026 (-0.085 to 0.033)	0.032 (-0.005 to 0.069)	-0.054 (-0.118 to 0.009)	--	-0.071** (-0.125 to -0.017)
SES*Gini Index						
Advantaged SES, Low income inequality	Reference	Reference	Reference	Reference	Reference	Reference
Advantaged SES, High income inequality	0.006 (-0.009 to 0.020)	0.007 (-0.022 to 0.036)	0.006 (-0.011 to 0.023)	0.0005 (-0.006 to 0.007)	-0.011 (-0.030 to 0.009)	0.001 (-0.005 to 0.008)
Disadvantaged SES, Low income inequality	0.016 (-0.016 to 0.047)	0.047 (-0.009 to 0.102)	0.009 (-0.035 to 0.052)	0.012 (-0.004 to 0.027)	-0.125 (-0.288 to 0.038)	0.014 (-0.002 to 0.029)
Disadvantaged SES, High income inequality	0.001 (-0.022 to 0.024)	0.040 (-0.004 to 0.084)	-0.009 (-0.033 to 0.014)	0.001 (-0.010 to 0.011)	0.005 (-0.030 to 0.040)	0.0004 (-0.011 to 0.012)

Notes: 4C2 states are Arizona, Colorado, New Mexico and Utah. SEER-15 includes SEER-18 registries exclusive of New Mexico, Utah, and the Alaskan Native Tumor Registry. Estimate is suppressed for Hispanics living in frontier counties in SEER-15 due to small sample size. SES=socioeconomic status. N/A=not applicable. The levels of statistical significance are noted as follows: * $p < 0.05$, ** $p < 0.01$, *** $p < 0.001$.

Table 3 Likelihood of unknown stage diagnosis among invasive colorectal cancer patients, 4C2 and SEER-15, 2006-2010, marginal effects (95% confidence intervals)

Independent Variables	4C2			SEER-15		
	Overall (N=21,389)	Hispanic Whites (N=3,745)	Non-Hispanic Whites (N=17,644)	Overall (N=113,177)	Hispanic Whites (N=13,287)	Non-Hispanic Whites (N=99,890)
Race/ethnicity						
Hispanic white	-0.011* (-0.022 to -0.001)	N/A	N/A	0.005 (-0.001 to 0.010)	N/A	N/A
Non-Hispanic white	Reference			Reference		
Age, years						
<50	Reference	Reference	Reference	Reference	Reference	Reference
50+	0.028*** (0.016 to 0.039)	0.017 (-0.015 to 0.049)	0.030*** (0.019 to 0.041)	0.016*** (0.012 to 0.021)	0.017** (0.006 to 0.028)	0.016*** (0.012 to 0.020)
Sex						
Male	0.006 (-0.002 to 0.014)	0.010 (-0.012 to 0.033)	0.004 (-0.004 to 0.012)	-0.010*** (-0.012 to -0.007)	-0.004 (-0.010 to 0.003)	-0.010*** (-0.013 to -0.008)
Female	Reference	Reference	Reference	Reference	Reference	Reference
Rurality						
Urban	Reference	Reference	Reference	Reference	Reference	Reference
Rural	-0.020* (-0.035 to -0.005)	-0.015 (-0.060 to 0.030)	-0.022** (-0.036 to -0.008)	0.002 (-0.003 to 0.008)	0.007 (-0.019 to 0.034)	0.002 (-0.004 to 0.008)
Frontier	-0.007 (-0.027 to 0.014)	-0.048 (-0.102 to 0.006)	0.010 (-0.014 to 0.035)	0.061*** (0.031 to 0.091)	--	0.059*** (0.029 to 0.088)
SES*Gini Index						
Advantaged SES, Low income inequality	Reference	Reference	Reference	Reference	Reference	Reference
Advantaged SES, High income inequality	0.039*** (0.030 to 0.048)	0.035* (0.003 to 0.067)	0.040*** (0.031 to 0.048)	0.003 (-0.004 to 0.011)	0.006 (-0.007 to 0.018)	0.003 (-0.005 to 0.011)
Disadvantaged SES, Low income inequality	0.027** (0.007 to 0.048)	0.029 (-0.030 to 0.088)	0.030** (0.009 to 0.052)	-0.005 (-0.014 to 0.004)	-0.022 (-0.059 to 0.014)	-0.005 (-0.014 to 0.004)
Disadvantaged SES, High income inequality	0.052*** (0.037 to 0.067)	0.046* (0.002 to 0.090)	0.054*** (0.038 to 0.070)	-0.007 (-0.014 to 0.001)	-0.011 (-0.028 to 0.006)	-0.006 (-0.013 to 0.001)

Notes: 4C2 states are Arizona, Colorado, New Mexico and Utah. SEER includes SEER-18 registries exclusive of New Mexico, Utah, and the Alaskan Native Tumor Registry. Estimate is suppressed for Hispanics living in frontier counties in SEER-18 due to small sample size. SES=socioeconomic status. N/A=not applicable. The levels of statistical significance are noted as follows: * $p < 0.05$, ** $p < 0.01$, *** $p < 0.001$.

Table 4 All-cause mortality for patients diagnosed with invasive colorectal cancer between 2006 and 2010 (vital status through 2016), 4C2 and SEER-15, hazard ratios (95% confidence intervals)

Independent Variables	4C2			SEER-15		
	Overall (N=21,389)	Hispanic Whites (N=3,745)	Non-Hispanic Whites (N=17,644)	Overall (N=113,177)	Hispanic Whites (N=13,287)	Non-Hispanic Whites (N=99,890)
Race/ethnicity						
Hispanic white	0.95 (0.91 to 1.00)	N/A	N/A	0.91*** (0.89 to 0.94)	N/A	N/A
Non-Hispanic white	Reference			Reference		
Age, years						
<50	Reference	Reference	Reference	Reference	Reference	Reference
50+	1.63*** (1.52 to 1.74)	1.44*** (1.26 to 1.65)	1.69*** (1.56 to 1.83)	1.78*** (1.72 to 1.83)	1.42*** (1.32 to 1.52)	1.86*** (1.80 to 1.93)
Sex						
Male	0.95* (0.90 to 1.00)	0.98 (0.86 to 1.12)	0.94* (0.89 to 0.99)	0.92*** (0.90 to 0.95)	1.09*** (1.04 to 1.14)	0.91*** (0.89 to 0.93)
Female	Reference	Reference	Reference	Reference	Reference	Reference
Rurality						
Urban	Reference	Reference	Reference	Reference	Reference	Reference
Rural	1.01 (0.94 to 1.08)	1.12 (0.96 to 1.31)	0.99 (0.91 to 1.07)	1.03* (1.00 to 1.06)	1.14 (0.93 to 1.40)	1.03* (1.00 to 1.06)
Frontier	1.04 (0.95 to 1.14)	1.02 (0.85 to 1.23)	1.05 (0.95 to 1.18)	1.01 (0.79 to 1.30)	--	0.99 (0.76 to 1.28)
SES*Gini Index						
Advantaged SES, Low income inequality	Reference	Reference	Reference	Reference	Reference	Reference
Advantaged SES, High income inequality	1.12*** (1.07 to 1.18)	1.11 (0.98 to 1.27)	1.12*** (1.06 to 1.18)	1.01 (0.99 to 1.03)	0.96 (0.89 to 1.04)	1.01 (0.99 to 1.03)
Disadvantaged SES, Low income inequality	1.12* (1.00 to 1.24)	1.26* (1.02 to 1.55)	1.07 (0.95 to 1.21)	1.07* (1.01 to 1.13)	0.91 (0.52 to 1.60)	1.07* (1.01 to 1.13)
Disadvantaged SES, High income inequality	1.24*** (1.13 to 1.36)	1.17 (0.99 to 1.37)	1.28*** (1.15 to 1.41)	1.07*** (1.04 to 1.10)	1.10 (0.97 to 1.26)	1.07*** (1.04 to 1.10)

Notes: 4C2 states are Arizona, Colorado, New Mexico and Utah. SEER-15 includes SEER-18 registries exclusive of New Mexico, Utah, and the Alaskan Native Tumor Registry. Estimate is suppressed for Hispanics living in frontier counties in SEER due to small sample size. SES=socioeconomic status. N/A=not applicable. The levels of statistical significance are noted as follows: *p < 0.05, **p < 0.01, ***p < 0.001.

Appendix Table A1 Cancer-specific mortality for patients diagnosed with invasive colorectal cancer between 2006 and 2010 (vital status through 2016), 4C2 and SEER-15, hazard ratios (95% confidence intervals)

Independent Variables	4C2			SEER-15		
	Overall (N=20,758)	Hispanic Whites (N=3,647)	Non-Hispanic Whites (N=17,111)	Overall (N=112,532)	Hispanic Whites (N=13,069)	Non-Hispanic Whites (N=99,463)
Race/ethnicity						
Hispanic white	1.02 (0.95 to 1.08)	N/A	N/A	0.92*** (0.88 to 0.97)	N/A	N/A
Non-Hispanic white	Reference			Reference		
Age, years						
<50	Reference	Reference	Reference	Reference	Reference	Reference
50+	1.48*** (1.32 to 1.65)	1.45** (1.14 to 1.84)	1.48*** (1.30 to 1.68)	1.58*** (1.51 to 1.66)	1.29*** (1.14 to 1.44)	1.66*** (1.57 to 1.75)
Sex						
Male	0.88*** (0.82 to 0.94)	0.88 (0.74 to 1.03)	0.88*** (0.82 to 0.94)	0.86*** (0.83 to 0.88)	1.09** (1.02 to 1.15)	0.84*** (0.81 to 0.86)
Female	Reference	Reference	Reference	Reference	Reference	Reference
Rurality						
Urban	Reference	Reference	Reference	Reference	Reference	Reference
Rural	1.09 (0.99 to 1.19)	1.06 (0.87 to 1.29)	1.10 (0.99 to 1.21)	1.05* (1.01 to 1.08)	1.13 (0.88 to 1.46)	1.05* (1.01 to 1.09)
Frontier	1.16* (1.03 to 1.30)	0.97 (0.77 to 1.23)	1.23** (1.08 to 1.41)	1.07 (0.78 to 1.48)	--	1.06 (0.76 to 1.48)
SES*Gini Index						
Advantaged SES, Low income inequality	Reference	Reference	Reference	Reference	Reference	Reference
Advantaged SES, High income inequality	1.07* (1.01 to 1.14)	1.03 (0.88 to 1.20)	1.09* (1.02 to 1.16)	1.01 (0.98 to 1.04)	0.99 (0.90 to 1.08)	1.01 (0.99 to 1.04)
Disadvantaged SES, Low income inequality	1.02 (0.89 to 1.17)	1.19 (0.92 to 1.55)	0.98 (0.84 to 1.15)	1.06 (0.99 to 1.14)	1.05 (0.55 to 2.01)	1.06 (0.99 to 1.14)
Disadvantaged SES, High income inequality	1.13* (1.01 to 1.27)	1.12 (0.91 to 1.36)	1.18* (1.04 to 1.34)	1.05* (1.01 to 1.09)	1.12 (0.95 to 1.31)	1.04* (1.00 to 1.08)

Notes: 4C2 states are Arizona, Colorado, New Mexico and Utah. SEER-15 includes SEER-18 registries exclusive of New Mexico, Utah, and the Alaskan Native Tumor Registry. Estimate is suppressed for Hispanics living in frontier counties in SEER-15 due to small sample size. SES=socioeconomic status. N/A=not applicable. The levels of statistical significance are noted as follows: *p < 0.05, **p < 0.01, ***p < 0.001.

Appendix Table A2 Prevalence of colorectal cancer screening and risk behaviors, ages 18 years and older, 2006-2010

	4C2				Other US				<i>P</i>
	Overall	Rural	Urban	<i>P</i>	Overall	Rural	Urban	<i>P</i>	
Overall									
Met CRC screening guidelines (ages 50-75) ¹	61.2% (59.9-62.4)	53.1% (51.8-54.4)	62.6% (61.2-64.0)	<0.001	62.9% (62.6-63.2)	58.3% (57.8-58.8)	64.0% (63.7-64.4)	<0.001	0.008
Current smoker ²	16.3% (15.9-16.7)	19.0% (18.4-19.6)	15.8% (15.3-16.3)	<0.001	18.7% (18.6-18.8)	22.7% (22.4-22.9)	17.8% (17.6-17.9)	<0.001	<0.001
Obese ³	23.0% (22.5-23.4)	24.4% (23.8-25.1)	22.7% (22.1-23.3)	<0.001	26.9% (26.7-27.0)	30.4% (30.2-30.7)	26.1% (25.9-26.2)	<0.001	<0.001
Physically Inactive ⁴	20.1% (19.6-20.5)	23.9% (23.3-24.5)	19.4% (18.9-19.9)	<0.001	24.6% (24.5-24.7)	28.1% (27.9-28.3)	23.8% (23.7-24.0)	<0.001	<0.001
Hispanic Whites									
Met CRC screening guidelines (ages 50-75)	51.5% (46.9-56.1)	47.0% (43.0-51.1)	52.9% (47.1-58.7)	0.115	49.2% (47.2-51.2)	47.8% (42.8-52.9)	49.3% (47.2-51.4)	0.609	0.363
Current smoker	18.1% (16.7-19.5)	20.3% (18.6-22.1)	17.6% (15.8-19.3)	0.026	14.8% (14.1-15.4)	20.8% (18.9-22.8)	14.4% (13.7-15.0)	<0.001	<0.001
Obese	26.7% (25.1-28.3)	28.3% (26.4-30.3)	26.3% (24.3-28.2)	0.150	29.7% (28.9-30.4)	33.2% (30.9-35.6)	29.5% (28.6-30.3)	0.002	0.002
Physically Inactive	27.0% (25.5-28.5)	31.0% (29.1-33.0)	26.0% (24.2-27.8)	<0.001	31.1% (30.3-31.8)	34.6% (32.3-36.9)	30.9% (30.1-31.7)	0.002	<0.001
Non-Hispanic Whites									
Met CRC screening guidelines (ages 50-75)	64.2% (62.9-65.6)	56.6% (55.1-58.1)	65.4% (63.9-67.0)	<0.001	65.1% (64.8-65.4)	59.7% (59.1-60.2)	66.8% (66.4-67.1)	<0.001	0.186
Current smoker	15.3% (14.8-15.8)	17.9% (17.2-18.6)	14.9% (14.4-15.4)	<0.001	19.0% (18.9-19.1)	22.3% (22.0-22.5)	18.1% (17.9-18.2)	<0.001	<0.001
Obese	21.1% (20.5-21.6)	21.4% (20.7-22.1)	21.0% (20.4-21.6)	0.483	25.5% (25.4-25.6)	29.2% (28.9-29.5)	24.5% (24.3-24.6)	<0.001	<0.001
Physically Inactive	17.3% (16.9-17.8)	20.7% (20.1-21.4)	16.8% (16.3-17.3)	<0.001	22.2% (22.1-22.4)	26.8% (26.6-27.1)	20.9% (20.8-21.1)	<0.001	<0.001

¹Had FOBT within past year, or sigmoidoscopy within past 5 years and FOBT within past 3 years, or colonoscopy within past 10 years. Data represents 2008 and 2010 only.

²Has smoked 100 or more cigarettes in lifetime and now smokes some or every day.

³Body mass index is 30 or greater.

⁴Engaged in no leisure-time physical activity during the past month.

95% confidence intervals shown in parentheses.

Fig. 1 Intersection of ethnicity, socioeconomic status, income inequality, and rurality, 4C2, 2006-2010